THE ROLE OF ADVANCED MAGNETIC RESONANCE IMAGING SEQUENCES: ARTERIAL SPIN LABELING AND SUSCEPTIBILITY WEIGHTED ANGIOGRAPHY IN NON INVASIVE ASSESSMENT OF INTRACRANIAL DURAL ARTERIO VENOUS FISTULAE

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CERTIFICATE

This is to certify that the work incorporated in this thesis titled ***"The role of advanced Magnetic Resonance Imaging sequences: Arterial Spin Labelling and Susceptibility Weighted Angiography in non-invasive assessment of intracranial Dural Arterio Venous Fistulae"*** *for the degree for DM "(NEUROIMAGING AND INTERVENTIONAL NEURORADIOLOGY)" has been carried out by Dr. Manoj Gopinath under our supervision and guidance. The work done in connection with this thesis has been carried out by the candidate himself and is genuine.*

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DECLARATION

I hereby declare that this thesis titled ***"The role of advanced Magnetic Resonance Imaging sequences: Arterial Spin Labelling and Susceptibility Weighted Angiography in non-invasive assessment of intracranial dural arterio venous fistulae"*** *has been prepared by me under the supervision and guidance of Dr Bejoy Thomas (Professor), Dr.Santhosh K (Associate Professor) and Dr.Kapilamoorthy TR (Professor & HOD), Department of Imaging Sciences and Interventional Radiology, Sree Chitra Institute for Medical Sciences and Technology, Trivandrum.*

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CONTENTS

INTRODUCTION

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Intracranial Dural Arterio Venous Fistulae (DAVF) are abnormal communications between dural arteries and dural venous sinuses, meningeal veins or cortical venous channels. (1) They constitute 10-15% of intracranial vascular malformations. (2)

The exact etiopathogenesis of DAVFs is not yet fully understood but a direct association with cortical venous sinus thrombosis has been well documented. (3) Various classifications have evolved over the years for assessing DAVFs with all of them being based on the pattern of venous drainage as this aspect has been found to be the most important in deciding the course of illness, clinical presentation, modality of treatment and complications.(4)

The clinical presentation of DAVFs is intimately linked with the venous drainage pattern of the shunt. Symptoms are often classified as benign or aggressive and the treatment for the latter group should be expedient. Benign presentation include symptoms like headache, tinnitus, proptosis, reduction in visual acuity etc while aggressive presentation includes haemorrhgic and non haemorrhgic focal neurological deficits.(5)

The presentation of DAVF is usually with nonspecific symptoms which makes the clinical diagnosis of this entity difficult. This makes neuroimaging the mainstay of diagnosis of this entity. Even though multiple imaging modalities including CT, CTA, MRI, MRA have all been used and shown to be useful in diagnosis, the gold standard remains DSA. (6) In recent past newer MRI sequences like SWI and ASL have been explored in evaluation of shunting intracranial lesions including DAVF and have shown some promise but no prospective studies are available to validate the value of these modalities.

Endovascular treatment has been at the forefront of DAVF management for the past few years and with an ever improving array of devices, agents and hardware technology, it is expected to be the treatment of choice in DAVF in the future.

DAVFs receive numerous arterial feeders from predominantly ECA but often from ICA as well as vertebral arteries and drain into dural venous sinuses, meningeal veins and oftentimes with cortical venous reflux into pial veins. Recruitment of new arterial twigs is part of progression of the disease process and is often seen on follow up of patients post embolization. Presently DSA is the primary diagnostic as well as follow up modality in all cases of DAVF. This entails repeated exposure of the patient to iodinated contrast, radiation as well as complications associated with the angiographic procedure. Hence, developing a non-invasive imaging modality which would be useful not only for diagnosis, but also for post treatment monitoring of DAVF would be a very useful advancement. This could obviate the hazards of contrast injection, radiation exposure and angiography. In this regard ASL has shown promise in evaluation of intracranial shunts with early results showing feasibility of evolving this into a clinically relevant tool. (7) This study is an attempt to understand the usefulness of ASL in noninvasive evaluation of DAVF and to analyse its potential when compared to conventional DSA in diagnosis and follow up of intracranial DAVF.

AIMS & OBJECTIVES

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To assess the role of advanced MRI sequences including Arterial Spin Labeling and Susceptibility Weighted Angiography in evaluation of Intracranial Dural Arterio Venous Fistulae and to assess whether these sequences, singly or in combination can play a significant role in noninvasive diagnosis of the disease and provide relevant details of its angioanatomy.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

INTRODUCTION

DAVF are an uncommon neurovascular lesion occurring in about 0.16 per 100,000 adults per year, it has been estimated that dural lesions represent just 10% to 15% of all intracranial AV shunts. They present clinically with headaches, visual deterioration, tinnitus, non-hemorrhagic neurologic deficits and intracranial hemorrhage. The symptomatology depends on location of the fistula and presence or absence of cortical venous reflux. DSA is the modality of choice for diagnosis and planning interventional management and also for follow up of these lesions. DAVF are primarily treated with endovascular approach. (8)

HISTORICAL PERSPECTIVE

The knowledge regarding intracranial DAVFs has come a long way since the first description in literature by Rizzoli in 1873 and the first angiographic demonstration by Sachs in 1931. (9) Over the years many authors have contributed to the existing body of knowledge and improved our understanding of this fascinating disease entity. Newton in 1969 studied the vascular supply of intracranial vascular malformations and described vascular supply to be pial, mixed pial dural and only dural and highlighted the role of dural arteries in supplying these vascular lesions using angiography. He also noted that dural lesions may also receive arterial supply from ICA, ECA or Vertebral arteries and that presence of ECA supply on one side should be evaluated by contralateral ECA assessment. (1) In last few decades a lot of work has gone into understanding DAVF as evidenced by a plethora of articles in literature. Our present description and understanding of the disease is based on landmark articles published regarding the natural history, clinical course and management of the disease. (5) (10) (4) (2) (11) (12)

PATHOPHYSIOLOGY

The exact etiopathogenesis of intracranial DAVF has been a matter of debate for decades and even now even though many postulations have been made, no single description is considered valid. An association with cerebral venous sinus thrombosis appears to be an accepted factor by most authors. (13) Hypercoagulable states including trauma, tumor, dehydration and genetically associated hypercoagulable states are all implicated in the disease process. The two main schools of thought are that of acquired process and that of congenital origin. The former implicates venous hypertension owing to prior venous sinus thrombosis leading to local ischemic environment. This triggers angiogenic growth factors like VEGF and BFGF. These in turn promote neovascularization leading to the formation of small fistulae between the dural arterial branches and the dural sinus. This concept was well illustrated by Lawson et al in their study on rat models with surgically induced venous hypertension, where they found evidence of neo angiogenesis in the dura after a period of time. (14) The latter theory suggests presence of dormant embryologic fistulae in the dural sinus wall in all individuals which then open up due to increasing venous pressure as a sequelae of venous sinus thrombosis. (15) Miyachi et al explained the role of emissary veins in formation of DAVF in their hypothesis. (16) Nagm et al proposed hemodynamic abnormality in the congenital dural shunts as a cause for DAVF and supported their hypothesis with histopathological correlation in one of their cases. (17) A similar explanation was offered by Brainin et al for their cases of posterior fossa DAVF where they felt that a pressure activated mechanism was the cause for evolution of these lesions. (18). Once formed the propagation of the disease entity appears to be along a final common pathway with worsening venous hypertension leading to increased neoangiogenesis and recruitment of adjacent small arterial feeders further increasing the shunt and arterialization of venous channels with the vicious cycle taking over.

CLASSIFICATION

With better and better understanding of the disease process attempts were made to classify DAVF into subtypes which might eventually help in management and follow up of patients. The essence of all the evolved classification systems was the venous drainage which from very early on was known to be the basis of clinical presentation and also directly linked to the severity of the disease. (19)

The first formal classification was proposed by Djindjian and Merland in 1978 where they used superselective ECA angiography to classify DAVF based on venous drainage and correlated them with severity of illness. (15)

Table: 1 **Djindian and Merland classification of DAVF (1978)**

TYPE	DESCRIPTION
I	Drainage into sinus
II	Drainage into sinus with reflux into cortical veins
III	Drainage into cortical veins directly
IV	Presence of venous dilatation

Djindjian's classification was modified almost simultaneously in 1995 by two groups Borden et al and Cognard et al with emphasis on the role of classification in prognostication and management. Borden and Shucart named it as Dural Arteriovenous fistulous malformation, to convey the fact that more than one fistula may be present and that it is acquired rather than congenital. They unified the intracranial as well as spinal DAVF under one classification. (20)

Table: 2 **Borden and Shucart classification of DAVF (1995)**

TYPE	DESCRIPTION
I	Drainage in to venous sinus or meningeal vein. Benign presentation and course
II	Drainage into dural sinus or meningeal veins with flow into cortical veins Often present with neurological deficit or bleed
III	Drainage directly into cortical veins Often present with neurological deficit or bleed

Cognard et al in 1995 reviewed the clinical presentation and angiographic characteristics of 258 patients of DAVF and correlated the two and then suggested a 5 tier classification of DAVF with direct correlation with management and prognostication information. (21)

Table: 3 **Cognard classification of DAVF (1995)**

TYPE	DESCRIPTION
I	Antegrade flow into dural venous sinus
II a	Retrograde flow into dural sinus
II b	Antegrade flow into dural sinus with cortical venous reflux
II a +b	Retrograde flow into dural sinus with cortical venous reflux.
III	Direct cortical venous reflux without sinus drainage
IV	Direct cortical venous reflux with focal ectasia
V	Drainage into spinal perimedullary veins

The classifications proposed by Borden and Cognard remain the most popular and have been most commonly used in studies available in literature. The Borden system is characterized by its simplicity and unification of cranial as well as spinal shunts and Cognard system for its correlation of clinical and radiological parameters with management decisions.

In 2014 Baltsavias et al reviewed the details of both the Borden as well as Cognard classification system and noted that both had significant shortcomings in classifying DAVFs. They themselves suggested a new classification system which they called the 'DES' system (an acronym for Directness, Exclusivity and Strain) with regard to the venous drainage of the shunt which was the main factor in presentation, course and management of the disease. (22)

The very fact that there are numerous classification systems with various descriptions of the same disease entity goes to prove that DAVFs are complex vascular lesions and no single classification system can do justice to the myriad nuances of angioanatomy, clinical presentation and management strategies.

CLINICAL PRESENTATION

The clinical presentation of intracranial DAVFs covers a wide spectrum of symptoms with completely asymptomatic patient at one end with fatal hemorrhage or quadriplegia at the other end. The symptomatology and presentation is directly dependent on the location of the fistula, the venous drainage pattern and the presence or absence of cortical venous reflux.

The clinical symptoms are often classified as benign and aggressive. Benign symptoms include: Headache, tinnitus, ocular and visual symptoms. Aggressive symptoms include: Haemorrhage, Nonhaemorrhagic focal neurological deficits, dementia, seizures. There is a significant correlation of aggressive symptoms with presence of cortical venous reflux. (23) (24)

Pulsatile tinnitus was the commonest symptoms in DAVFs located in transverse and sigmoid sinus regions. This is due to increased volume of venous flow in venous channels adjacent to middle ear. Cavernous sinus DAVFs most commonly presented with ocular symptoms with chemosis, proptosis, diminished acuity, diplopia and headache. This is attributed to reversal of flow within the SOV due to raised pressure within the cavernous sinus owing to arterialised inflow from the shunt. Tentorial fistulae and anterior cranial fossa fistulae presented most often with haemorrhage due to high incidence of CVR. Myelopathy is a presentation of patients with spinal perimedullary venous drainage typically extending upto the conus medullaris. Those patient in whom venous

drainage was limited to cervical cord and showed venous egress through radicular veins, show no features of myelopathy. (23)(25)(26)

NATURAL HISTORY

The information gained from the natural history of any disease entity is invaluable in planning a management protocol which would optimize the risk benefit ratio and offer the best prognosis for the patient. The same is applicable for intracranial DAVFs. Haemorrhage remains the most dreaded complications with adverse impact on patient outcome and vascular malformations including DAVF are known causes. (27) (28) (29)

Brown et al in 1994 conducted amongst the earliest natural history studies in DAVF with a group of 54 patients and assessed angiographic predictors of haemorrhage and clinical outcome in the untreated group. They noted a 1.8% rate of risk of bleed per year and noted fistula in petrosal and straight sinus, CVR and venous ectasia to be high risk for bleed. (30)

The first real effort to study DAVFs and assess their natural history in a prospective study was made by the Canadian team of Davies et al in 1997 and their results were published as a two part series dealing with benign and aggressive lesions respectively. (31) (32) In the benign cohort of 55 patients most fistulae were located in transverse and cavernous sinuses (52 cases) and 27% had prior history of trauma. The patients with lesion in transverse sinus presented with headache and tinnitus whereas the cavernous sinus lesions presented with typical ocular features. 58% of the cases were followed up on conservative management. All patients in the conservative management group and most in the treated group showed either stable disease or improvement over time. None worsened. Thus they opined that Borden Grade I lesions, without CVR, should be conservatively managed and followed up and treated only for palliation of disabling symptoms or features of

neurological deficit if any. On the other hand in the cohort of 46 patients with aggressive symptoms and Borden II and III fistulae the natural history was poor. 30% were on conservative treatment. 10% NHFND and 19% each of haemorrhagic presentation and death was noted. They concluded that untreated Borden II and III lesions as well as residual CVR after treatment both had an unfavourable outcome and must be treated.

Soderman et al studied a cohort of 89 patients with Borden II and III DAVF. They noted that Borden II lesions were commonest in transverse sigmoid sinus region whereas Borden type III fistulae were commonest in the tentorium. 32 patients presented with haemorrhage. The annual incidence of haemorrhage was appx 6% and was noted to be significantly higher in patients with prior history of bleed. The results of this study revealed a lower incidence of haemorrhage compared to the literature available at that time.(33)

Gross et al studied a patient cohort of 56 patients and 34% were Borden type I, 17% were Borden type II and 49% were Borden type III fistulae. They too illustrated that Type I fistulae do not pose a significant threat of bleed and merit only follow up. They also noted that there is a 13% spontaneous occlusion rate of fistula which reinforces the validity of conservative management. Those cases with CVR ie Borden Type II and III showed a 30% rate of bleed and 30% rate of NHFND. The cohort as a whole had 6% annual haemorrhage rate and 3% overall mortality. Only 3% cases showed spontaneous occlusion. Cases with venous ectasia had a much higher bleed rate of 21%. The authors suggested that this warranted urgent and complete treatment at the earliest.(4) (34)

In a series of 118 DAVFs with CVR, Van Dijk in 2002, demonstrated an annual mortality rate of 10%, and a total neurological event rate of 15% with 8.1% haemorrhagic and 6.9% non

haemorrhagic events. This enforced the aggressive management strategy for all DAVFs with CVR irrespective of site and presentation. (35)

Recurrence of DAVF following complete obliteration after embolization has been reported in upto 14% cases. This has been ascribed to incomplete percolation of embolic agent to the venous side. Thus even after angiographic cure, patients must be kept on follow up to detect recurrence and plan another sitting of curative embolization. (36)(37)

EVALUATION AND DIAGNOSIS

Intracranial DAVF are abnormal connections between dural arteries and meningeal veins, dural sinuses or cortical veins without any intervening capillary nidus. They are usually located in the vicinity of a dural sinus. Since the presence of CVR has been proven to be a feature of increased risk for haemorrhage and also because progression from benign to aggressive type has been documented, early diagnosis and treatment is mandatory for a good outcome. Given the diverse spectra of clinical presentation and very nonspecific nature of symptoms, the diagnosis is often delayed. (38) CT and MRI including CT angiography and MR angiography, are the commonly used modalities which have been used to evaluate DAVF, but without doubt DSA remains the gold standard for diagnosis as well as follow up of DAVF.

DIGITAL SUBTRACTION ANGIOGRAPHY

DSA is universally accepted as the gold standard modality in evaluation of intracranial DAVF. It has unmatched temporal resolution, spatial resolution and contrast resolution and is presently the investigation of choice for confirmatory diagnosis and also for post treatment follow up of DAVF patients. DSA information is also central and essential for planning any Neurointerventional procedure.

A complete DSA study should include a 6 vessel angiography including bilateral ICAs, ECAs and Vertebral arteries. Selective injections of ECA branches and 3D rotational angiogram from the main involved feeding artery is essential in accurate diagnosis and treatment planning. The aim of DSA is to identify the fistulous site, demonstrate all the arterial feeders both dural as well as pial if any, illustrate the venous drainage pattern, presence of retrograde venous drainage, presence of cortical venous reflux and venous ectasia since each has a direct bearing on both the prognosis and management of the patient. The venous drainage of the normal cerebral parenchyma and circulation time is also studied in DSA. These angiographic details will facilitate classification of the DAVF based on the Cognard or Borden classification model. (39) Tortuous engorged veins in venous phase can also be demonstrated and this sign is attributed to venous congestion of normal parenchyma and presence of this sign is thought to have a role in predicting aggressive presentation and poor prognosis even in the absence of CVR (40)

Even though DSA remains the gold standard and the only validated modality to provide all the relevant details required for therapeutic decision making, it is not without its own demerits in the form of procedural complications and adverse contrast reactions not mentioning radiation hazard of repeated studies. (41) Kaufman et al in their large series have reported a neurological complication rate of approximately 2% and mortality rate of 0.06% with diagnostic angiographic procedures. (42)

COMPUTED TOMOGRAPHY

Given the nonspecific clinical presentation and vague symptomatology the first imaging modality to be employed is usually NCCT. However the sensitivity and specificity of NCCT is diagnosing DAVF is low. In many situations, the scan will be normal. The various indirect findings include,

cerebral edema, hyperdense vascular structures signifying dilated venous channels, bony resorption and prominent osseous foramina.(39) (43)

COMPUTED TOMOGRAPHY ANGIOGRAPHY

CTA has the potential to illustrate the vascular details of DAVF along with the parenchymal details of the brain parenchyma. Meckel et al demonstrated the role of helical MDCT angiography in arterial phase in identifying not only the fistulous point but also in demonstrating the retrograde flow and CVR based on differential density within these structures. They suggested that this arterialization of cerebral veins must be looked for in the appropriate clinical scenario. (44)

Beijer et al in a small case series demonstrated the value of 4D CTA in evaluation DAVF and showed correct identification of fistulous site and pattern of venous drainage but acknowledged the lower spatial and temporal resolution compared to DSA. (45) In a similar series Lee et al demonstrated the role of hybrid CTA in avoiding the bone related artefacts and improving the diagnostic quality of images in evaluation of DAVF. (46)

With CT and CTA the exposure to iodinated contrast and repeated radiation exposure remain a cause for concern and none of the studies have conclusively demonstrated sensitivity or specificity comparable to DSA. Thus their role in management of DAVF has remained limited.

MAGNETIC RESONANCE IMAGING

MRI has often been used as a non invasive imaging tool in diagnosis and follow up of DAVF patients. In a patient with non specific headache and non localizing neurological symptoms, MRI is often the first imaging modality to suggest possibility of cerebral venous sinus thrombosis or DAVF. In their evaluation of pulsatile tinnitus with MRI, Dietz et al noted that DAVF was the commonest pathology in their series and suggested that the important features to look for included

prominent extracranial vasculature, trans osseous vessels, patency of dural sinuses and stenosis of transverse sinuses. They suggested MRI as the first imaging modality in evaluation but accepted that DSA still remained the most dependable investigation. (47) In 2005, Kitajima et al noted the importance of identifying cortical venous drainage in DAVF and analyzed the role of contrast enhanced MRI in identification of venous reflux. They noted that Contrast Enhanced MRI (CEMRI) was better than non contrast scans in identification of CVR and also that 3D MPRAGE sequences were superior to T1 sequences owing to the higher spatial resolution and ability to follow the vessels in the subarachnoid space. (48) Kwon et also documented the vital role of cortical venous reflux and its association with aggressive symptoms and need for urgent treatment. They correlated the presence of prominent leptomeningeal and medullary vascular structures on MRI as predictors of poor prognosis. They proposed MRI as a complimentary tool for evaluation of DAVF. (49) Bink et al studied the role of 3T MRI in assessment of DAVF. They looked at the presence and site of fistula, venous drainage and feeders and whether management planning could be based on MRI alone. Even though the sensitivity was > 84%, it was felt that DSA would still be required for planning treatment. (50) In 2016 Lin et al compared the role of CT and MRI in evaluation of symptomatic DAVF. They found that both CT as well as MRI performed well with high sensitivity and accuracy. MRI was noted to be marginally better than CT. They also noted that use of contrast enhancement and MRA did not increase the diagnostic accuracy of the investigation. (43)

MAGNETIC RESONANCE ANGIOGRAPHY

Meckel et al in 2007 evaluated the role of time resolved 3D contrast enhanced MRA in evaluation of DAVF in a series of 14 patients. They attempted to locate the fistula site, grade the fistula type and also confirm post treatment obliteration of shunt with MRA. They correctly assessed the side

and location of fistula and also confirmed post treatment occlusion in all cases but were correct only in 80% cases when it came to grading of the fistula type. They suggested this technique as a suitable follow up method but not as a replacement for DSA. (51)

In 2009 Farb et al published their experience of time resolved contrast enhanced MRA at 3T in evaluation of site and grade of DAVF. They utilized TRICKS (Time resolved imaging in contrast kinetics) model and compared it to DSA as gold standard. In their series of 40 patients with 20 fistulae, they achieved a 93% accuracy in correctly identifying the presence and grade of fistula. They concluded that time resolved MRA is a suitable modality for screening and surveillance of patients in specific clinical situations. (52)

Azuma et al compared 3D non contrast TOF MRA at 3T with DSA in evaluation of DAVF in 26 patients. They got encouraging results of interobserver and intermodality agreement for fistula site, arterial feeder and venous drainage. Inspite of good results with MRA the authors accepted that treatment planning would still merit DSA evaluation.(53)

SUSCEPTIBILITY WEIGHTED IMAGING

The utility of SWI in the evaluation of various cerebral vascular diseases and stroke has been demonstrated by several authors. (54) (55) Saini et al in 2009 were the first to report the utility of SWI in identification of cranial DAVF when they noted the prominence of venous channels on SWI in a patient with DAVF. They could correctly identify the site of fistula and also could show partial reversibility of this venous prominence after embolization of the shunt. They attributed these findings to the prolonged circulation time leading to greater oxygen extraction and increased desaturation within the venous channels. (56)

Noguchi et al realized the value of SWI in imaging cerebral veins and in a small series of 10 patients they analyzed the role of SWI and DSC perfusion in identifying retrograde cortical venous drainage in patients with cerebral DAVF. They noticed that DSC sequence was sensitive for cortical veins and SWI for deeper medullary veins and when used in combination performed well in identifying retrograde venous drainage. (57)

Gasparetto et al demonstrated the presence of retrograde leptomeningeal venous drainage in a patient with transverse sinus DAVF who had presented with progressive dementia. Since venous drainage has direct bearing on the prognosis and also since conventional MR sequences were not sensitive enough to identify this aspect of the condition, they suggested routine use of SWI in evaluation of all suspected DAVF cases. (58)

In a very small series of 6 patients, Guillon et al studied the various facets of SWI in DAVF cases. They evaluated the fistulous point, presence or absence of cortical venous reflux and presence or absence of pseudophlebetic pattern using SWI. They arrived at a conclusion that SWI is definitely useful in identifying the fistulous point which was seen as a focal hyperintensity within the receiving vein and also in identifying venous congestion which was seen as increased number, caliber and prominence of venous structures. (59)

Nakagawa et al published a larger series of 17 patients with DAVF in 2013. They compared SWI with DSA in pre and post treatment evaluation of DAVF. They noted that pre treatment SWI images revealed hyperintensity within the cortical vein which was suggestive of presence of shunting with cortical venous drainage. This abnormal signal was noted to disappear in post treatment scans. They concluded that SWI could provide a good noninvasive option in evaluation and follow up of DAVF. (60)

In 2016 Hodel et al studied the combined accuracy of SWI and ASL in evaluation of intracranial shunting lesions. Out of their series of 63 cases, 10 were DAVF. This study showed an excellent correlation with DSA. They demonstrated that this combined use of ASL and SWI was a good non contrast option compared with CEMRA in evaluation of DAVF. (61)

Jain et al in their series of 26 patients assessed the role of SWI in pretreatment evaluation of patients with intracranial DAVF. They specifically evaluated localization of fistula, cortical venous reflux and venous ectasia. Their study showed a significant difference between SWI and conventional MRI sequences with high accuracy rates for SWI. They suggested inclusion of SWI in routine pretreatment imaging of DAVF. (62)

DIFFUSION WEIGHTED IMAGING

In a retrospective study of 56 DAVF patients, Sato et al in 2011, evaluated the effects of cortical venous reflux on the brain parenchyma with DWI. Their hypothesis was that presence of cortical venous reflux leads to adverse hemodynamic changes and brain parenchymal dysfunction which is revealed by low ADC values in the affected regions. They noted lower ADC values in involved areas in more severe disease and also in pretreatment conditions compared to less severe disease and post treatment conditions respectively. Even though this study was a retrospective study the idea was novel and provided an opportunity to have an objective criteria for assessment of severity of disease as well as post treatment follow up of patients. (64)

ARTERIAL SPIN LABELLING

In ASL perfusion study, a radiofrequency pulse is used to label protons in blood at a fixed proximal plane. These labelled protons then flow into the imaging plane where they generate signal. Over time, signal decay takes place and equilibrium of spins is reached and under normal circumstances

no signal is seen beyond the capillary level. In cases with intracranial shunts, this arterial signal goes via the shunt into the venous side and can be identified with ease. (6) (65)

Diebler et al in their remarkable series of papers on the role of ASL in clinical practice described the various causes of focal, regional and global hyperperfusion. They noted that vascular malformations are a cause of local hyperperfusion states and demonstrated that ASL can be used for depiction of this phenomenon with very good success rates. (66)

In 2008, Wolf et al published a similar study in their small series of 7 patients with intracranial vascular malformations. They evaluated the role of continuous ASL in imaging of these vascular malformations. They noted that in all the cases there was increased signal intensity seen in the nidus as well as in the draining veins and adjacent parenchyma with reduced perfusion in deeper regions like the thalamus due to the steal effect. They concluded that CASL was in a position to provide a simple and quantifiable evaluation tool in vascular malformations. (7)

Robson et al demonstrated a unique technique of time resolved vessel selective MRA using ASL sequence. They used varying labeling delays and vessel selective ASL pulses. They achieved a temporal resolution of 200msec. They concluded that this ASL based technique could give information similar to DSA without using any exogenous contrast agent. (67)

Sakamoto et al were the first to report the value of ASL in a case of cavernous sinus DAVF. They demonstrated ASL signal in bilateral SOVs which was confirmed to have disappeared in post embolization imaging. They suggested that ASL could be useful in follow up of such cases. (68)

Noguchi et al were the first to present their results in a series of 16 patients with DAVF where they had used ASL to evaluate the venous drainage from the shunt site and then grade the DAVF accordingly. They observed 100% accuracy in identifying venous sinus signal in Borden 1 and

Borden II cases and also cortical venous signal in Borden III cases. Their results were inferior with only 25% accuracy when it came to identifying cortical venous reflux in Borden II cases. They concluded that ASL could play some role in evaluation of DAVF and that it required further study. (69)

Iryo et al in 2013 evaluated the role of 4D ASL MRA at 3T in assessment of intracranial DAVF. Theirs was a small series of 9 patients and their findings were compared to DSA. They evaluated the fistula site, arterial feeders and venous drainage and observed good to excellent agreement between modalities. (70) (71)

Amukotuwa et al in an elaborate review of artefacts seen with clinically relevant imaging with 3D pseudocontinous ASL discussed in depth the presence of venous ASL signal in shunting lesion of the brain. The authors hoped that after validation by further studies absence of ASL signal may in the future be taken as confirmation of absence of shunting lesion and similarly presence of ASL signal in venous side would necessitate further intensive evaluation to identify an underlying shunt. They also demonstrated a case of DAVF where cortical venous reflux was very well depicted in a Cognard 2b lesion. (72)

Sunwoo et al in 2015 evaluated the degree of AV shunting in a series of 40 patients with intracranial vascular malformations. They noted the presence of venous signal in all shunting lesions and also noted that the intensity of venous signal was correlating well with the extent of shunting which in turn had very good correlation with the shunt volume on DSA evaluation. (73)

Amukotuwa et al carried out a retrospective study in 34 patients with intracranial DAVF and evaluated 3D pseudocontinous ASL sequences for delineation of venous drainage and Borden grade of fistula. They noted that even though this new modality could not replace DSA in

evaluation of DAVF, it could identify high grade DAVF with high accuracy and warranted inclusion in the routine protocol of MRI screening of DAVF patients.(74)

Hodel et al studied a group of 63 patients with intracranial shunting lesion of which 10 were DAVF. They evaluated the accuracy of ASL and SWI combined against the conventional MRI imaging. They observed that combined ASL and SWI had much higher agreement with DSA than conventional MRI. This combination of sequences could provide an attractive non contrast method for work up of DAVF cases. (61)

Yamamoto et al in 2016 retrospectively studied a small group of 13 patients with DAVF and evaluated the role of ASL in them. They compared conventional MRI and ASL technique at 3T in detection of DAVF and also compared pre and post treatment ASL images for interval changes. The authors concluded that even though the spatial and temporal resolution was limited and the grade of DAVF could not be accurately predicted, this sequence was very useful for identifying the presence of shunt and in post procedure follow up of patients.(75)

POSITRON EMISSION TOMOGRAPHY

Iwama et al used PET to study the metabolic changes in patients with DAVF. Even though the importance of venous drainage in DAVF was established, little was known about the haemodynamic and metabolic changes of these patients. The authors evaluated a small group of 10 patients both pre and post treatment and estimated the rCBF, rCBV and rOEF in all the cases. They observed that rCBF was low and rOEF was high in those areas receiving cortical venous reflux from the fistula prior to intervention and normalized after the treatment procedure was done. (77)

TREATMENT

Intracranial DAVF with benign presentation are usually managed with conservative measures and treatment is reserved for the patients with intractable symptoms. DAVF with clinical or angiographic aggressive presentation warrants a more expeditious management plan. (78) (79)

In 2003 Satomi et al evaluated the results of conservative management of benign DAVF in 119 patients. 73 patients were just observed, 43 underwent palliative embolization and 1 underwent surgery for severe symptoms. They noted that over 98% cases the disease was maintained at tolerable state and only 2% progressed to aggressive features. Thus this approach coupled with good clinical and imaging follow up is a suitable option for benign presentation of DAVF. (80)

Rammos et al in 2014 reviewed in depth, endovascular management of DAVF. They noted that with time endovascular approach had become the modality of choice for treatment. They also remarked that transarterial route had become the commonest approach with availability of liquid embolic agents. Transvenous route was useful for fistulae at cavernous sinus and also for those with isolated sinus segments in drainage. (84)

In 2016, Gross et al presented amongst the largest series of cases and dealt in depth with management issues including occlusion rates, recurrence rates and clinical course following endovascular management of DAVF. They also commented on the slow shift of management practice from surgery to endovascular treatment with coil embolization and NBCA use to the newer liquid embolic EVOH agents. They noted that after the induction of liquid embolic agents, the occlusion rates had significantly improved. In their series of 251 patients, they noted an initial occlusion rate of 70%, recurrence rate of 3% and permanent complication rate of 3%. (85)

Serulle et al suggested conservative management for Cognard 1 and 2a lesions with spontaneous thrombosis seen in slow flow cases and with use of carotid compression techniques. They stressed on placing such patients on imaging follow up to detect worsening of lesion grade over time. (38)

COMPLICATIONS

Like all endovascular procedures, embolization of intracranial DAVF also bear some risk of procedural complications.

Lv et al reported an overall complication rate of 12%. They confronted bradycardia suggestive of trigemino cardiac reflex in 2 patients with tentorial DAVFs. Cranial neuropathy was noted during embolization of cavernous sinus DAVFs. Parenchymal infarcts due to arterial or venous occlusions were rare. Stuck catheter and Onyx migration were procedure related and could be avoided by improvement of technique. (87)

Baltsavias et al in their series of 170 patients reported an occlusion rate of above 60%. They did not have any mortality but reported appx 2% permanent as well as temporary neurological deficits. They also reported temporary self limiting diplopia in 3 patients following embolization. (24)

MATERIALS & METHODS

MATERIALS AND METHODS

Institutional Ethics Committee (IEC) approval was obtained vide letter No. SCT/IEC/808/AUGUST-2015 dated 26 Oct 2015. (Appx D) This was a prospective study conducted in Department of IS&IR, SCTIMST, between 27 October 2015 and 30 June 2017. Consecutive patients who were suspected to have intracranial DAVF were evaluated for inclusion into the study.

Informed written consent was obtained from each and every patient/guardian after explanation of all aspects of the study as per consent form and details were noted as per proforma. (Appx A and Appx B)

All patients underwent both MRI and DSA evaluation within two weeks of each other and those cases who were diagnosed to have had DAVF were included in the study. No pregnant woman, person incapable of giving consent, prisoner, staff, student or healthy volunteer was inducted into this study.

Inclusion Criteria:

1. All patients referred to SCTIMST and diagnosed to have intracranial DAVF between 2015 and 2017.
2. All patients among the above group who underwent MRI and DSA study between 2 weeks of each other.
3. All patients of DAVF who were treated prior to 2015 but remained on follow up with residual/recurrent fistulae and underwent MRI and DSA as part of follow up imaging or repeat treatment planning.

Exclusion Criteria:

1. Any patient withholding consent for inclusion in the study.
2. Patients with any other treated or untreated intracranial vascular malformations.
3. Patients in whom MRI or DSA was contraindicated and not done.
4. Patients who underwent MRA and DSA with more than 2 weeks interval between the two.
5. Patients with non-diagnostic quality images due to technical factors.

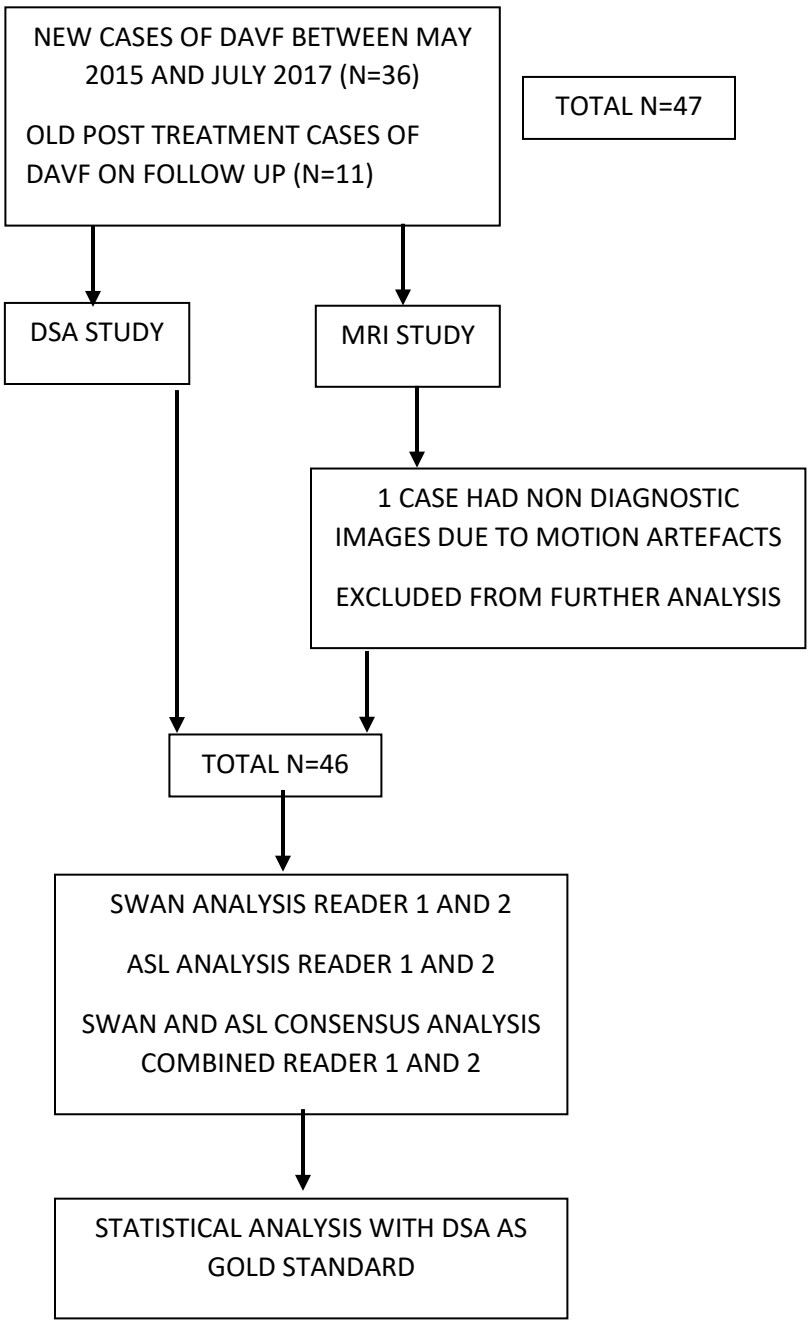
STUDY DESIGN

1. IEC approval was obtained vide letter No. SCT/IEC/808/AUGUST-2015 dated 26 Oct 2015
2. Written informed consent of all eligible patients was obtained.
3. Patients' history and other clinical details were documented as per Performa.
4. Patients underwent MRI including ASL and SWAN and also DSA within 2 weeks of each other, as per existing hospital protocol for pre procedure evaluation of DAVF.
5. These patients were also followed up after 6-9 months, as per existing institution protocol, when they were evaluated again by MRI including ASL, SWAN as well as DSA within two weeks of each other.
6. MRI data of patients ie ASL, SWAN and a combination of ASL along with SWAN were separately analyzed by two independent neuroradiologists (BT and MG) with 20 and 2 years of experience respectively; who were blinded to the details of the cases. The DSA data was analyzed by a single interventional neuroradiologist, (SK) with 15 years of experience, who was also blinded to the clinical and imaging details of the cases.
7. MRI was analyzed for ASL and SWAN sequences of each patient, first independently and then in combination for location, number, venous drainage, venous reflux, pseudophlebetic

pattern, and Cognard and Borden classification of DAVF.

8. Angiograms (DSA) were analyzed for location and number, venous drainage and reflux, arterial supply, pseudophlebetic pattern and Cognard and Borden classification of DAVF.
9. Statistical analysis of the data was performed and sensitivity, specificity and accuracy of the modalities were calculated as also the positive and negative predictive values, and kappa coefficient of inter observer and intermodality variability was also calculated.

FLOWCHART OF STUDY DESIGN



STUDY PROTOCOLS

MAGNETIC RESONANCE IMAGING

MRI was performed on a 3 Tesla system (Discovery 750W, GE, Milwaukee, USA). The sequences included sagittal 3D FLAIR, SWAN, DWI, ADC, and 3D ASL.

SWAN

Parameters:

SWI like 3D Gradient Echo sequence, TR/TE- 42.7/25.6msec, Flip Angle- 15degrees, FOV- 220x 220mm, Matrix- 288 x 384, ST- 2.4mm, NEX- 1, BW- 31.25 kHz, AT- 4min 5sec. Magnitude and Minimum Intensity images were viewed.

3D ASL

Parameters:

Stack-of-spirals 3D-fast-spin echo pseudocontinous ASL sequence was used. TR/TE/PLD 4852/10.7/2025ms, FOV 240x240mm, NEX 3, spiral readout of eight arms x 512 samples, 30 x 4.0 mm axial sections with whole brain coverage, and time duration of 4 min 22 s. Fusion with 3D FLAIR sequences was performed using the proprietary READYview software (GE Healthcare, Milwaukee, USA).

DIGITAL SUBTRACTION ANGIOGRAPHY

All DSA studies were done on biplane flat panel unit (Innova 3131, GE, Milwaukee, USA). All diagnostic angiograms were conducted under local anesthesia after premedication administration. The right common femoral artery was punctured, and a 6f or 5F short femoral sheath was secured. Heparin was used as anticoagulant in the dose 50U/Kg body weight. The angiograms were done using 5F vertebral glide or Judkins right coronary catheter with 0.035 Terumo guidewire. Iohexol or Iodixanol was used as contrast agents for the studies. Angiograms of bilateral CCAs, ICAs, ECAs and vertebral arteries were obtained. After identification of shunt, selective angiograms of ECA branches commonly IMA, occipital arteries and ascending pharyngeal arteries were also obtained. After conclusion of the diagnostic study the femoral short sheath was removed and haemostasis achieved by manual compression.

DEFINITIONS

Presence of fistula

SWAN - Hyperintensity within a venous structure either dural venous sinus or cortical vein; on magnitude images; where the signal was noted to be brighter than the normal expected bright signal within the normal veins distant from the involved site.

ASL- Bright signal within a venous structure, either dural venous sinus or cortical vein. Exclusion of ASL related artefacts was mandatory.

Fistulous point

SWAN - Site where hyperintensity was noted within a venous structure either dural venous sinus or cortical vein, with signal intensity similar to arterial signal, at circle of Willis

ASL- Site where ASL signal was first noted within a venous structure either dural venous sinus or cortical vein, with signal intensity similar to arterial signal, at circle of Willis.

Cortical venous reflux

SWAN - Hyperintensity seen within a cortical vein adjacent to the identified fistulous point where the signal intensity was noted to be more than that within normal veins distant from the involved site.

ASL- Bright signal within a cortical vein adjacent to the previously identified fistulous point.

Pseudophlebetic pattern

SWAN - Pseudophlebetic pattern was defined as presence of multiple, dilated, tortuous, prominent venous channels either cortical, medullary or both; compared to normal brain parenchyma.

ASL- Pseudophlebetic pattern was not commented upon.

Grading of fistula

Both Borden and Cognard grading was used to evaluate the fistulae.

On SWAN images abnormal hyperintensity within the dural sinus adjacent to fistulous point without any abnormal signal in adjacent cortical veins was taken as Borden Grade I, abnormal hyperintensity seen within both the dural sinus as well as adjacent cortical vein was taken as Borden grade II and abnormal signal only within the adjacent cortical vein without any abnormal signal within the dural sinus was taken as Borden Grade III fistula.

On SWAN images abnormal hyperintensity only downstream within the dural sinus adjacent to the FP was taken as Cognard Grade 1. Abnormal signal only upstream from the FP, within the dural sinus, was taken as Cognard Grade 2a. Abnormal signal only downstream from FP with

signal within adjacent cortical veins was taken as Cognard Grade 2b. Abnormal signal both upstream as well as downstream from FP with signal within adjacent cortical vein was taken as Cognard Grade 2a+b. Abnormal signal only within cortical veins adjacent to FP without upstream or downstream signal within dural sinus was taken as Cognard Grade 3. These features of Cognard Grade 3 when associated with a visible ectatic venous sac was graded Cognard Grade 4. The visualization of abnormal signal within perimedullary veins around the spinal cord led to Cognard Grading 5.

Benign grading was considered with Borden Grade 1 and Cognard Grade 1 and 2a

Aggressive grading was considered with Borden Grade II and III and with Cognard 2b, 2a+b, 3, 4 and 5

STATISTICS

The patient demographic data, clinical features were tabulated in Microsoft Excel format. Two neuroradiologists interpreted the SWAN and ASL findings separately and independently, after 4 week interval to avoid memory bias. Later a consensus reading of ASL and SWAN combined was done by the two readers. The DSA findings were compiled by an interventional neuroradiologist and this was taken as gold standard. The above analysis was also tabulated using Microsoft Excel format.

Data analysis was done using IBM SPSS statistics 23.0 software.

Interobserver agreement and Kappa values were obtained for the two readers who evaluated MRI (ASL and SWAN)

Intermodality agreement and Kappa values were obtained for ASL and SWAN separately and also ASL and SWAN combined as compared to DSA as gold standard.

Kappa values ≤ 0 was taken as indicating no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as good, and 0.81–1.00 as excellent agreement.

Sensitivity, specificity, positive predictive value and negative predictive value for the ASL, SWAN and ASL and SWAN combined were also obtained.

RESULTS

RESULTS

DEMOGRAPHIC DETAILS

A total of 46 consecutive patients with intracranial DAVF, who presented to the institute between 27 October 2015 and 30 June 2017 were included in this prospective study.

The age of patients in the study ranged from 12 to 69 years, with mean age of 44 years.

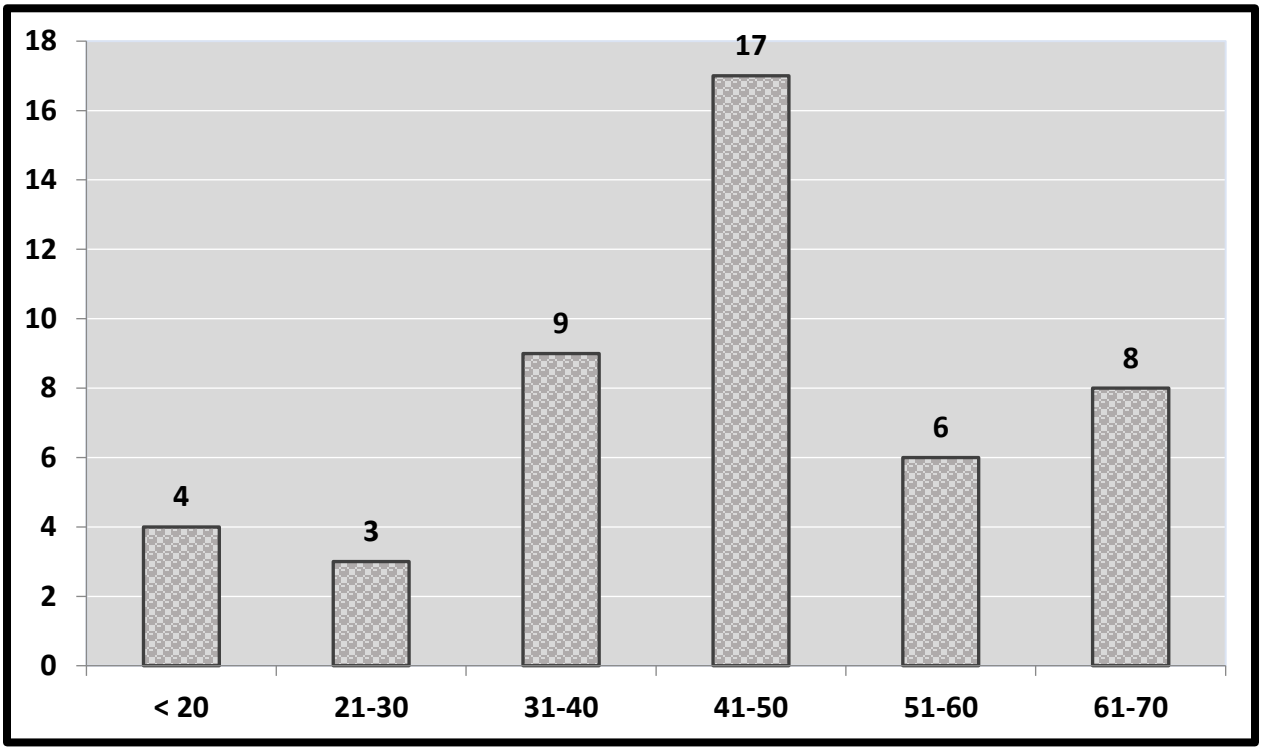


Figure No 1: AGE IN YEARS

The 46 patients included in the study were a consecutive series with no bias towards, age or sex. There were 30 males and 16 females in the study group. The male to female sex ratio within the cohort was 1.9:1.

All patients with prior treatment for DAVF as well as new patients presenting for the first time were included in the cohort. There were 11 patients with residual/recurrent fistulae and 35 patients had presented for the first time to the institute.

CLINICAL PRESENTATION

The commonest presentation of our patients was with chronic headache. 37 patients (79%) presented with this as their primary complaint. The other symptoms that the patients presented with included visual complaints, tinnitus, seizures, dementia, motor weakness, paresthesia.

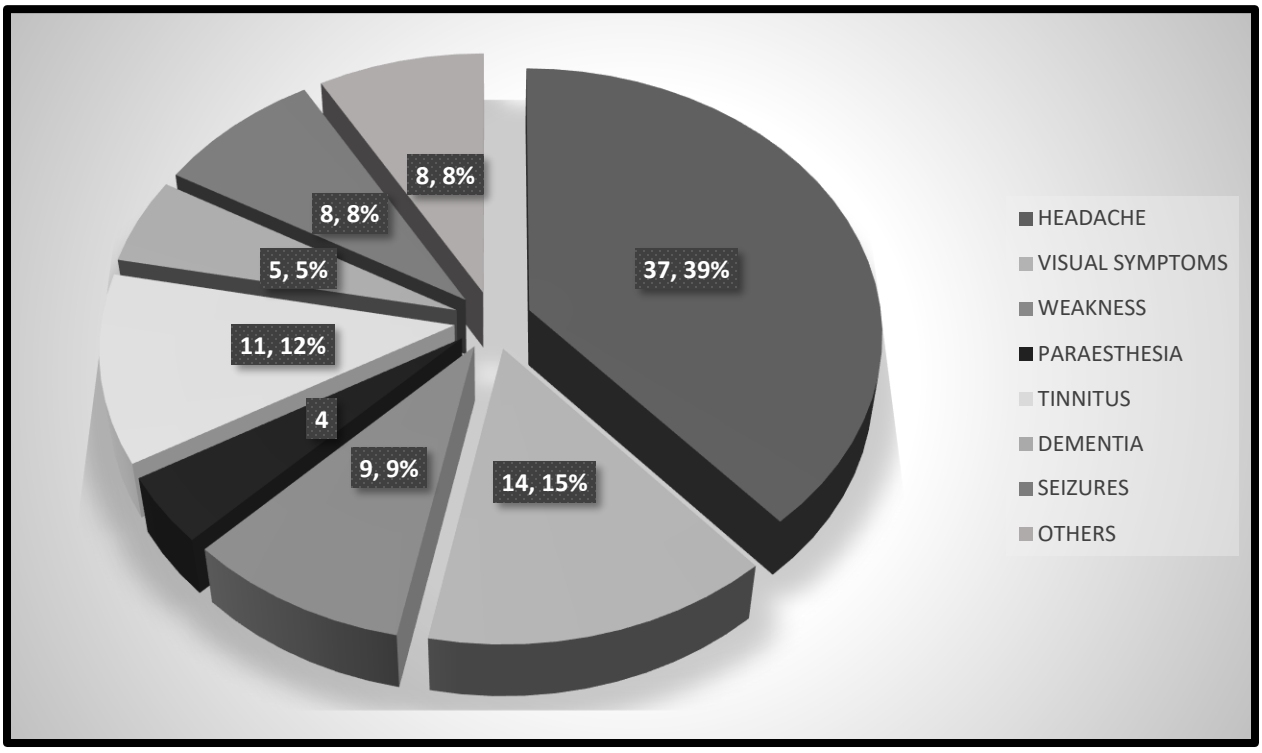


Figure No 2: CLINICAL PRESENTATION

The spectrum of patient symptomatology were classified further into two subgroups: Benign symptoms and aggressive symptoms. 16 patients (36%) presented with aggressive symptoms whereas 30 patients (64%) presented with benign symptoms.

13 patients (28%) presented with prior history of cerebral venous sinus thrombosis (CVT). Some patients had presented with CVT in the past (9 patients, 69%) and had received treatment for it while some others were noted to have chronic CVT on imaging at future presentation (4 patients, 31%). Two patients gave history of prior road traffic accidents with head injuries and two others gave history of prior head and neck surgery for unrelated causes.

13 patients (28%) had associated intracranial haemorrhage including parenchymal, subarachnoid and subdural hemorrhages. Only 3 patients presented as a consequence of the bleed whereas the others were noted to have sequelae of prior haemorrhage on imaging.

49% patients within the cohort were noted to have underlying comorbidities. 14 patients (30%) were found to be hypertensive, 9 (19%) were diabetic. Other comorbidities included coronary artery disease, dyslipidemia, smoking and alcoholism.

ANGIOGRAPHIC FEATURES

DSA identified DAVF in 45 of the 46 patients. One patient was treated previously for a left transverse sinus DAVF with complete obliteration of shunt and no residual shunt on follow up. 30 patients (64%) were noted to have only a single fistulous point whereas the other 16 patients (35%) were seen to have multiple fistulous points.

LOCATION OF FISTULA

The commonest location for site of fistula was in transverse sinus/sigmoid sinus junction and followed by transverse sinus. Considering this transverse sinus region as one entity, it accounted for 66% of all fistula sites in our cohort.

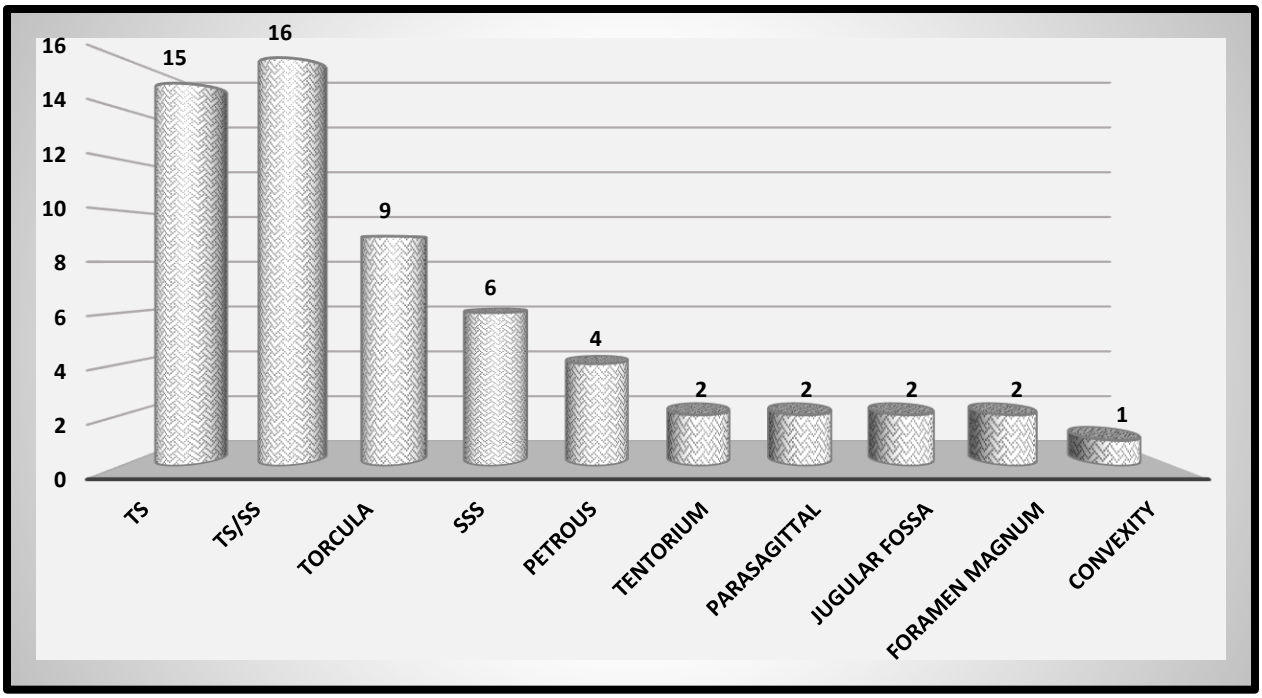


Figure No 3: LOCATION OF FISTULA

GRADING

All the DAVF were graded based on the angioarchitecture according to the Borden as well as the Cognard grading schemes. 12 fistulae (21%) were in the benign group as per Cognard classification and 7 patients (15%) in the benign group as per the Borden classification scheme.

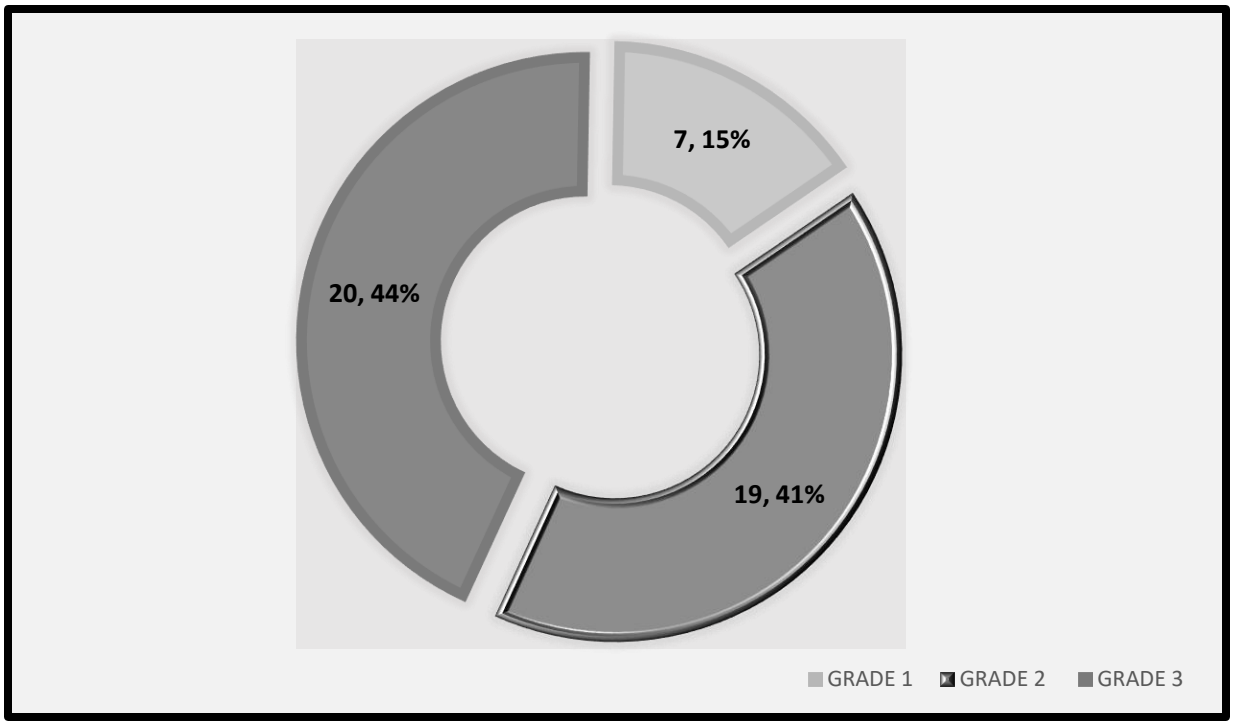


Figure No 4: BORDEN GRADES

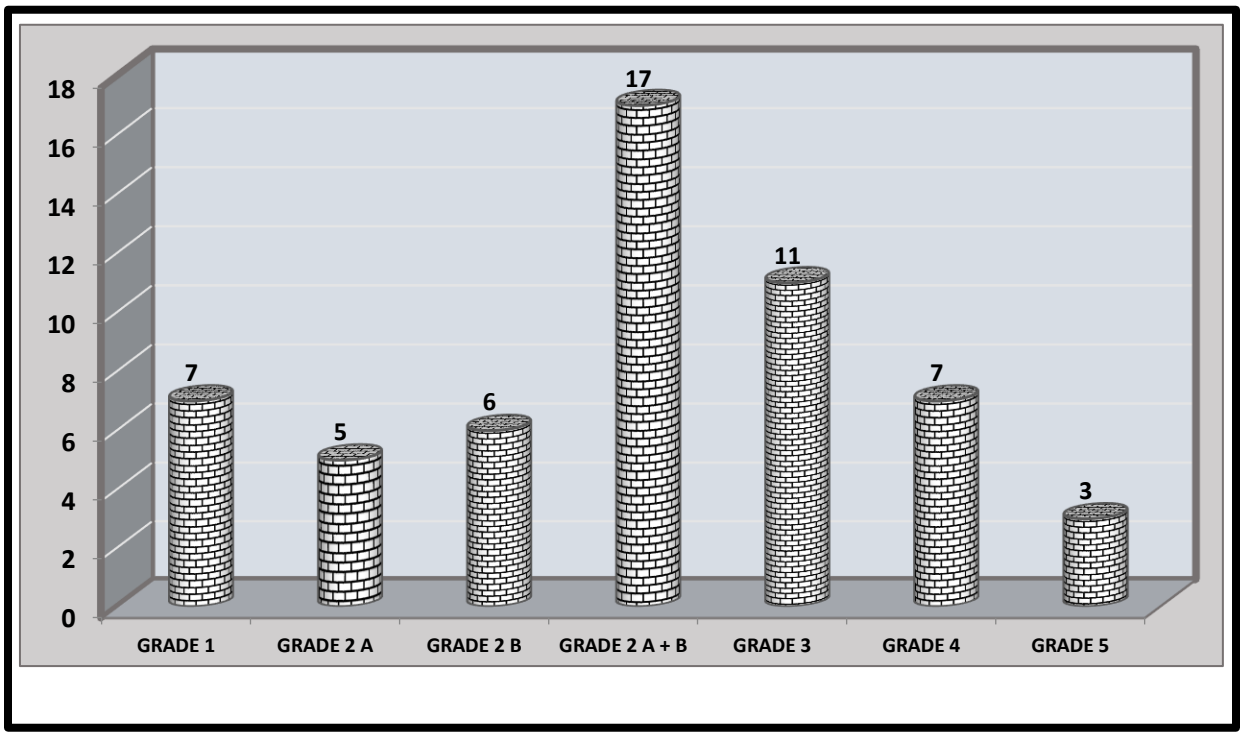


Figure No 5: COGNARD GRADES

CORTICAL VENOUS REFLUX (CVR)

CVR was noted in 34 of 46 patients (74%) with shunt. 12 patients (26%) did not show any angiographic evidence of cortical venous reflux.

Table No 4: Clinical presentation in patients with and without CVR

	CVR present	CVR absent
Benign symptoms	**22**	**7**
Aggressive symptoms	**12**	**5**

PSEUDOPHLEBETIC PATTERN (PPP)

PPP was noted in 33 (72%) patients. This was identified by increased caliber, tortuosity and number of venous channels with significantly increased circulation time in the involved hemisphere.

Table No 5: Angiographic grades and clinical presentation in patients with and without PPP

	Benign Grade	Aggressive Grade	Benign Presentation	Aggressive Presentation
PPP Present	**0**	**33**	**22**	**11**
PPP Absent	**7**	**6**	**7**	**6**

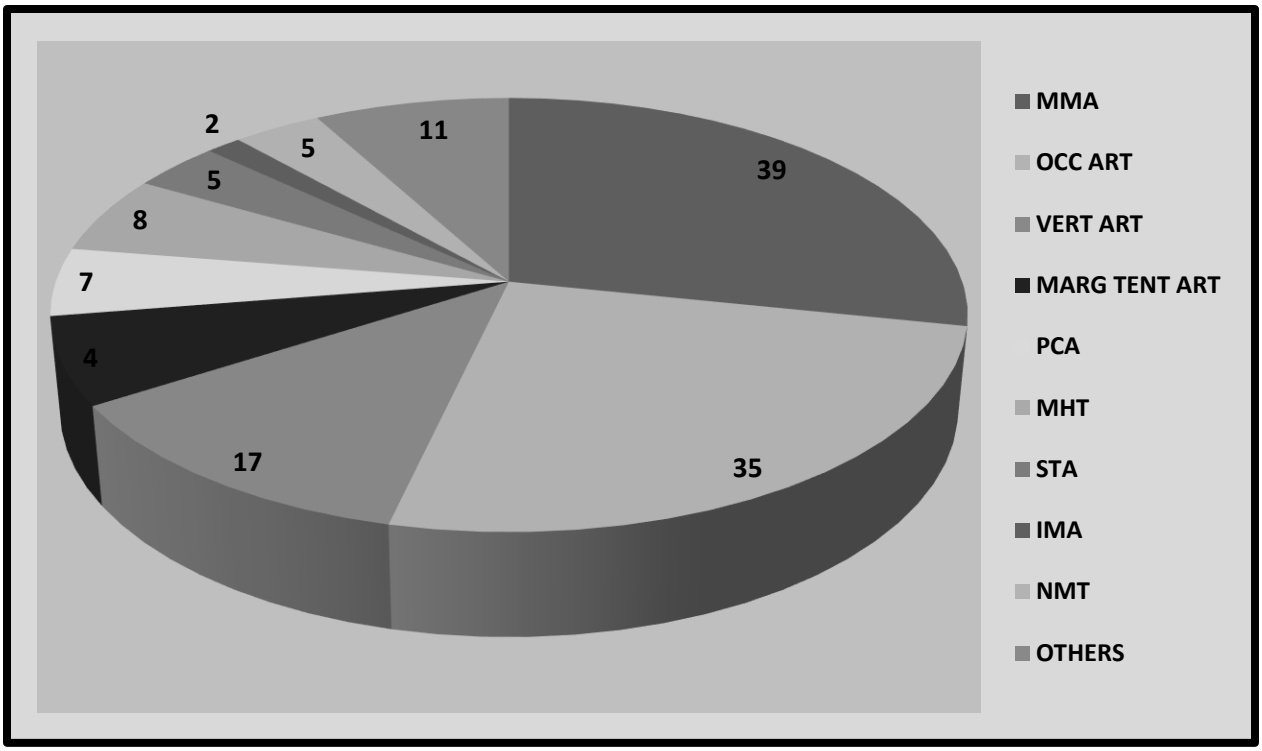


Figure No 6: ARTERIAL FEEDERS

ADVANCED MAGNETIC RESONANCE IMAGING (MRI)

Susceptibility Weighted Angiography

Fistulous point was identified as a focal hyperintensity within a dural sinus or adjacent cortical vein. In 7 cases (15%) no fistulous point could be confidently identified. In the remaining 39 cases (85%) a fistulous point could be identified on SWAN. In 8 patients (17%) multiple fistulae points were noted. In 34 patients (74%) CVR was noted while in 12 patients it was not seen. PPP was absent in 10 patients and present in 36 patients (78%). On evaluation of the grades of fistula, 15 cases (33%) were graded benign by Cognard classification and 7 (15%) were graded benign by Borden classification.

Table No 6: Interobserver correlation of variables assessed in SWAN

Interobserver variable in SWAN	*Kappa Value*
Presence of absence of fistula	**0.49**
Number of sites (Single/multiple)	**0.39**
Presence of CVR	**0.68**
Presence of PPP	**0.67**
Site of Fistula	**0.50**
Cognard grade	**0.68**
Borden grade	**0.72**

Arterial Spin Labeling

Fistulous point was identified as bright signal within a dural sinus or cortical vein. In 2 cases (4%) fistulous point could not be identified. One was in a post embolization patient without residual fistula. In the remaining 44 cases (96%) a fistulous point could be identified. Multiple fistulae were noted in 5 cases (11%). In 26 patients (57%) there was evidence of CVR and in 20 patients (43%) there was no evidence of CVR. Pseudophlebetic pattern could not be assessed by ASL as it could not be confidently differentiated from CVR. 20 cases (43%) were graded benign in Cognard classification and 18 (39%) were graded benign in Borden classification.

Table No 7: Interobserver correlation of variables assessed in ASL

Interobserver variable in ASL	*Kappa Value*
Presence of absence of fistula	**0.48**
Number of sites (Single/multiple)	**0.73**
Presence of CVR	**0.74**
Site of Fistula	**0.48**
Cognard grade	**0.73**
Borden grade	**0.76**

Combined SWAN and ASL evaluation

After the individual assessment of SWAN and ASL by the two readers, after an interval of 4 weeks, a consensus reading of SWAN and ASL combined was done by the same two readers. This was taken as the final MRI data which was then evaluated against DSA data which was considered the gold standard.

Fistulous point could be identified in all 45 patients. One patient was post embolization without a residual shunt. Multiple fistulae were identified in 4 cases, 31% of overall multiple fistulae on DSA could be correctly identified. CVR could be identified in 33 of the 34 cases. PPP was overestimated with 38 cases noted to have PPP on MRI compared to 33 on DSA . The fistula was graded benign by Cognard grading in 11 cases of the 12 on DSA and by Borden grading in 11 compared to 7 on DSA. The Kappa correlation was calculated for interobserver agreement between the consensus MRI reading and DSA. Taking into account the fact that identifying higher grades

of fistula is more important in management, weighted Kappa with higher weighting for higher grades of fistula was also calculated.

Table No 8: Intermodality correlation between MRI and DSA (Fistula characteristics)

Intermodality variable	*Kappa value*	*Sensitivity*	*Specificity*	*PPP*	*NPV*	*Accuracy*
Presence of fistula	**0.66**	**97.8**	**100**	**100**	**50**	**97.9**
Presence of CVR	**0.69**	**88.9**	**88.9**	**97**	**66.7**	**88.9**
Presence of PPP	**0.62**	**84.2**	**100**	**100**	**53.8**	**86.7**

Table No 9: Intermodality correlation between MRI and DSA (Fistula Grading)

Intermodality variable	*Kappa value*	*Weighted Kappa value*	*Sensitivity*	*Specificity*	*PPP*	*NPV*	*Accuracy*
Cognard Grade	**0.41**	**0.58**	**84.6**	**87.5**	**97.1**	**53.8**	**85.1**
Borden Grade	**0.54**	**0.59**	**86.8**	**85.7**	**97.1**	**54.5**	**86.7**

Table No 10: Intermodality correlation for location of fistula

Location of fistula	*Kappa value*
Superior Sagittal Sinus	**0.19**
Transverse Sinus	**0.51**
Transverse sinus/Sigmoid sinus junction	**0.51**
Torcula	**0.43**
Foramen Magnum	**0.65**
Petrous	**0.37**
Others	**0.47**
Transverse sinus region	***0.91***

REPRESENTATIVE CASES

REPRESENTATIVE CASES

CASE NUMBER 1

Cognard Type I DAVF in right sigmoid sinus region

HISTORY

35 year old male patient presented with complaints of chronic occipital headache of 1 year duration and tinnitus of 3 months duration. He gave history of prior surgery for cervical spondylosis after which he developed CVT involving right transverse sinus and sigmoid sinus and was treated for the same. He was diagnosed to have DAVF while being imaged for evaluation of his headache and referred to SCTIMST for definitive management.

Clinical examination

He was averagely built and nourished. General condition was good. GCS was 15/15. There was no focal neurological deficit. Bruit was noted in right mastoid region. Other systems were unremarkable.

MRI

SWAN revealed focal hyperintensity in the right distal sigmoid sinus region. There was no evidence of similar hyperintensity in transverse sinus on right side. No evidence of CVR or PPP was seen in the rest of the brain parenchyma.

ASL revealed focal high signal intensity seen within the right sigmoid sinus in jugular fossa. There was no evidence of increased signal in any of the other dural venous sinuses or cortical veins.

This was suggestive of DAVF in right sigmoid sinus with normal antegrade flow in the venous channels- Cognard Grade 1

DSA

Angiograms revealed a Cognard Grade I fistula in right transverse and sigmoid regions, fed predominantly by transosseous branches form occipital artery with antegrade venous outflow into right transverse and sigmoid sinuses without any retrograde flow or CVR.

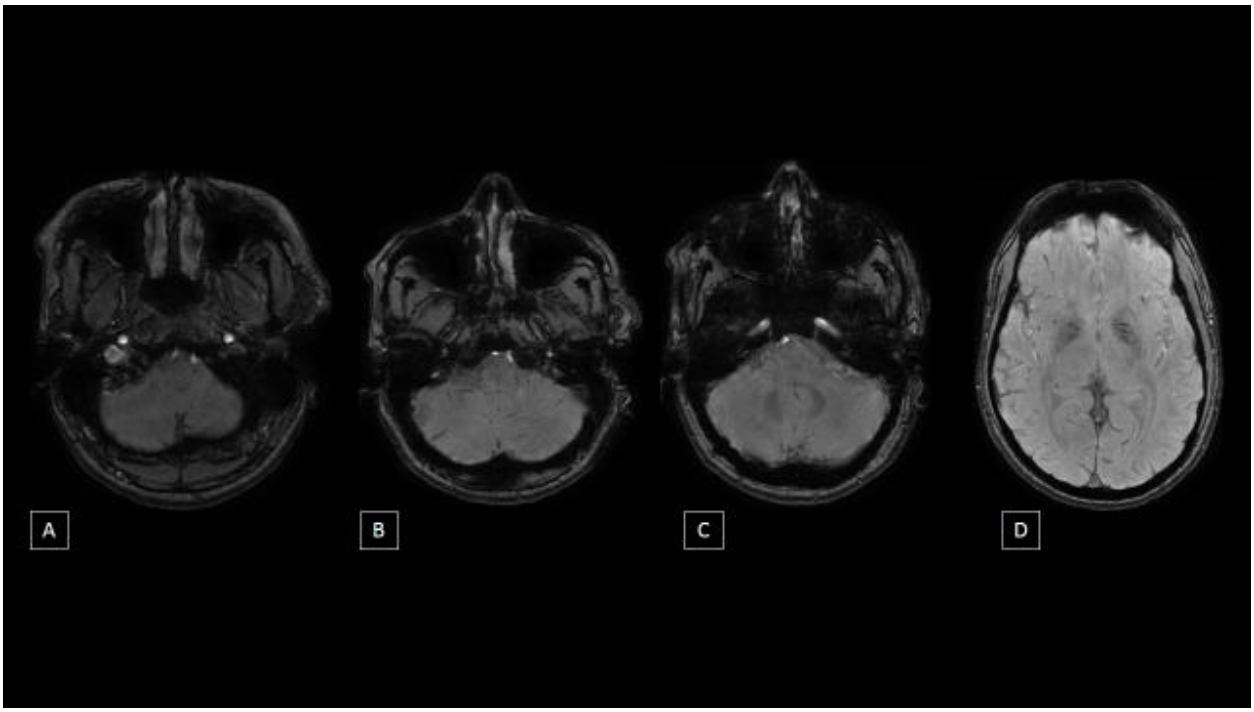


Figure No 7: Axial SWAN images. (A) and (B) Focal hyperintensity in right sigmoid sinus/Jugular fossa region. (C) No Hyperintensity in transverse sinus or torcula (D) No evidence of CVR or PPP

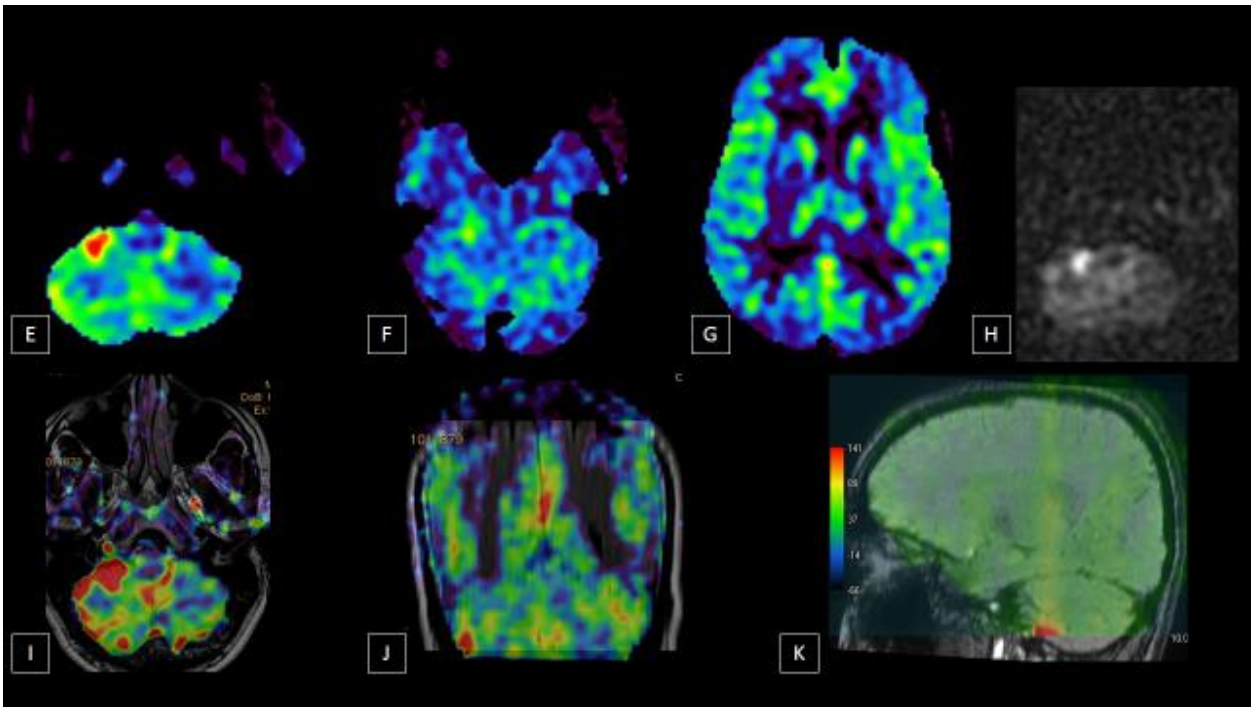


Figure No 8: ASL Images. (E) (H) Bright signal within right sigmoid sinus/jugular fossa region (F) No abnormal signal in transverse sinus or torcula (G) No CVR (I), (J) and (K) ASL/FLAIR fusion multiplanar images showing site of fistula with no retrograde venous flow

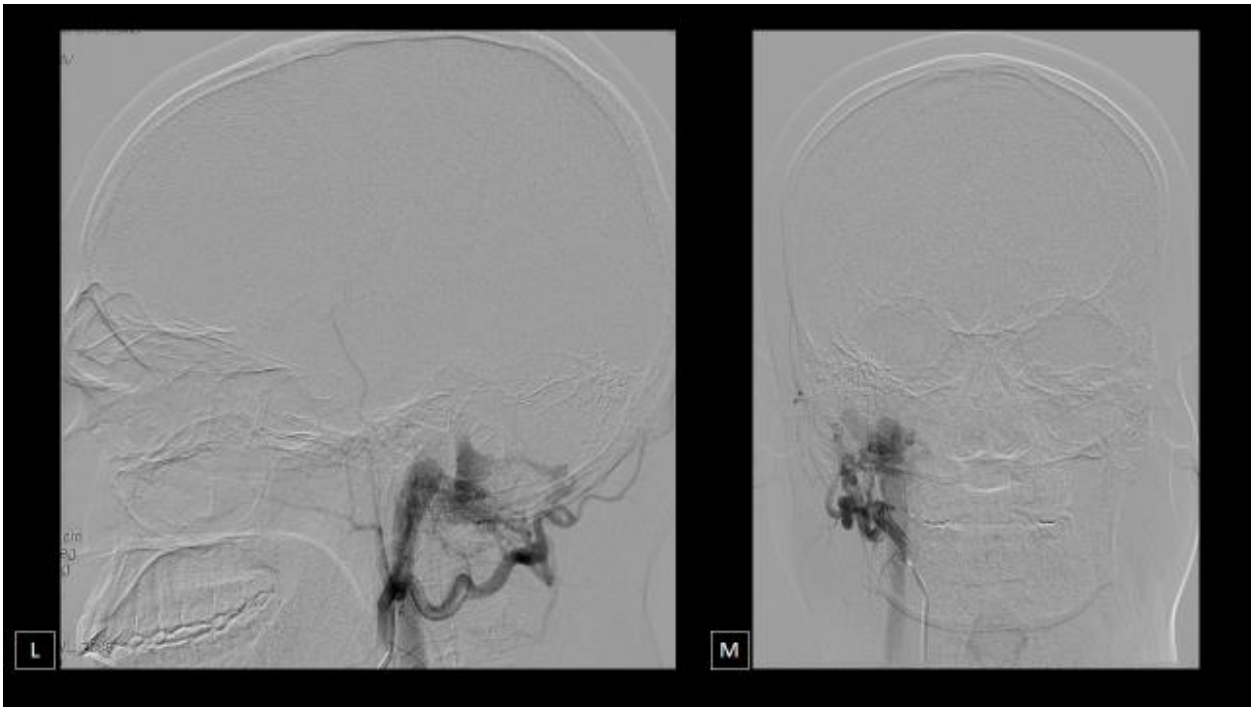


Figure No 9: (L), (M) DSA Lateral and frontal views. Cognard type I DAVF in right sigmoid sinus region without retrograde flow or CVR

CASE NUMBER 2

Cognard Type IIa DAVF in posterior Superior Sagittal Sinus

History

37 year old male patient, a known smoker and alcoholic, presented with complaints of a single episode of generalized tonic clonic seizure. He denied any complaints of headache, tinnitus or visual problems. There was no prior episode of seizure, loss of consciousness or any weakness or paraesthesia. He underwent neuroimaging for evaluation of seizure episode which was suspicious for DAVF and he was referred to SCTIMST for further evaluation and management.

Examination

He was averagely built and nourished. General condition was good. GCS was 15/15. Visual acuity was 6/6 in both eyes. There was no focal neurological deficit. Other systems were unremarkable.

MRI

SWAN revealed bright signal within the posterior part of SSS extending towards the torcula. There was no similar hyperintensity seen in the anterior aspect of SSS. No hyperintensity could be seen in adjacent cortical veins in the frontal or parietal regions. No evidence of CVR as seen. Mild PPP was seen.

ASL revealed bright signal in the mid and posterior segments of SSS with extension anteriorly as well as posteriorly towards the torcula. No evidence of CVR was seen.

These findings were indicative of a DAVF in the posterior SSS with both antegrade as well as retrograde venous outflow- Cognard Grade 2a.

DSA

Angiograms revealed a Cognard grade 2a DAVF in posterior third SSS fed by arterial feeders from bilateral MMA, STA and occipital arteries. There were feeders also noted from ophthalmic artery and left vertebral artery also. Retrograde as well as antegrade venous outflow was noted. The circulation time was prolonged at 6.5sec. In a subsequent sitting, the patient was embolized with 11.5ml Squid via right MMA route with venous balloon protection with complete obliteration of fistula.

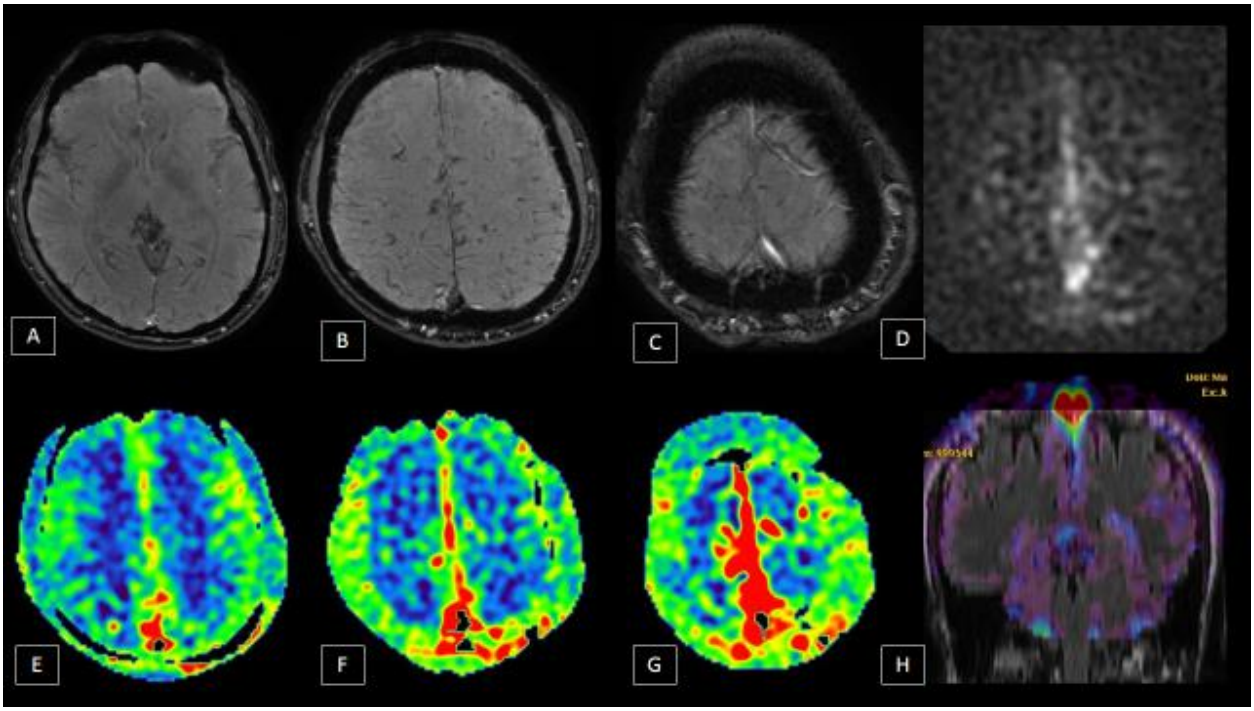


Figure No 10: (A) to (D) Axial SWAN images showing hyperintensity in posterior SSS region. No CVR is seen. Mild PPP is noted.
(E) to (H) ASL images showing signal in mid and posterior SSS without CVR

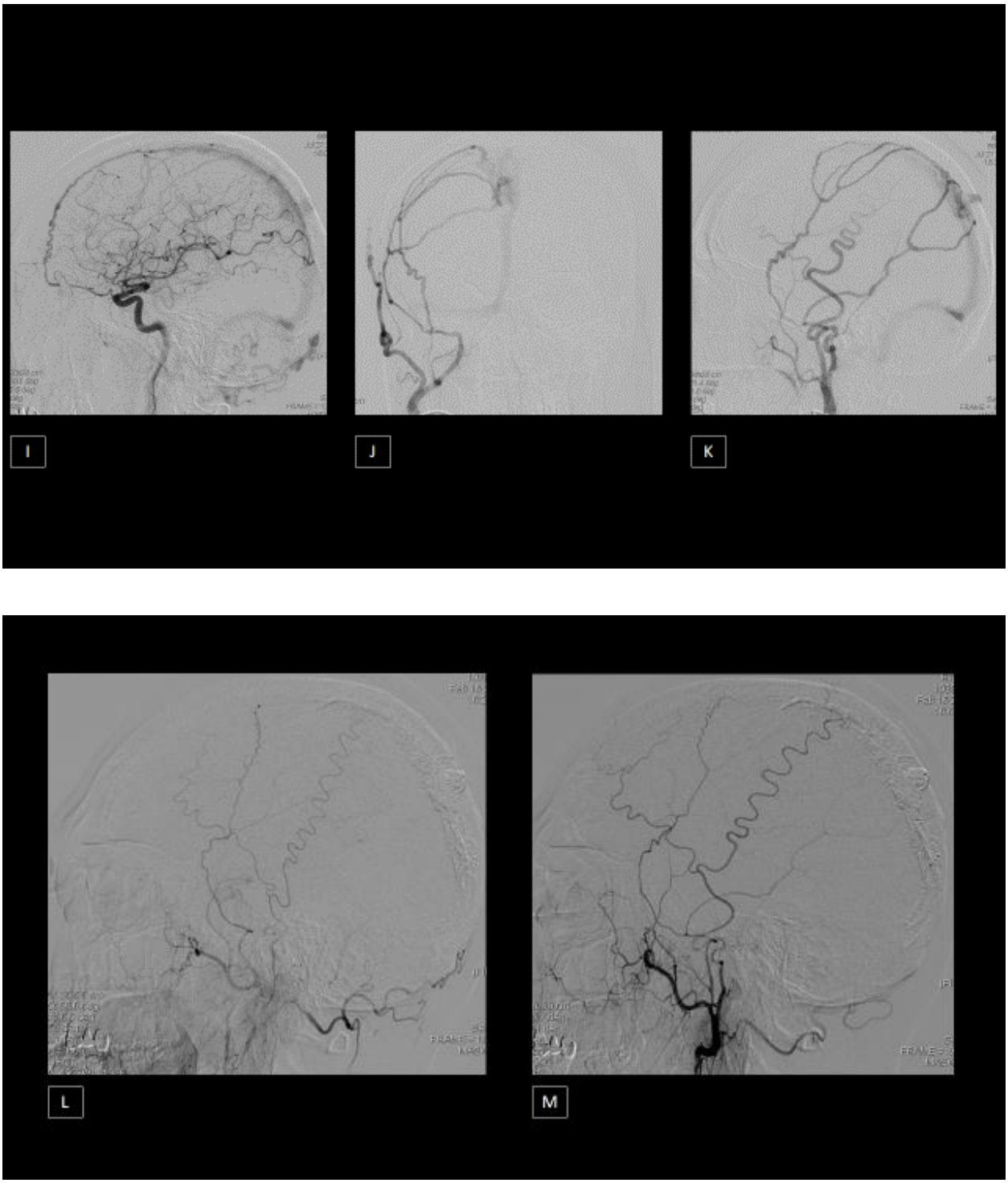


Figure No 11: (I) (J) (K)- Frontal and lateral DSA images showing Cognard type IIa DAVF in posterior SSS
(L) (M) – Post embolization status with complete obliteration of fistula

CASE NUMBER 3

Cognard Type 2b DAVF in left transverse sinus

History

34 year old male patient presented with history of gait ataxia of 2 months duration. He denied any complaints of headache, tinnitus or visual problems. There was no prior episode of seizure, loss of consciousness or any weakness or paraesthesia. He underwent neuroimaging for evaluation of ataxia which was suspicious for presence of DAVF and he was referred to SCTIMST for further evaluation and management.

Examination

He was averagely built and nourished. General condition was good. GCS was 15/15. Visual acuity was 6/6 in both eyes. The IOP was 17 in right eye and 14 in left eye. There was evidence of horizontal nystagmus. There was no focal neurological deficit. Other systems were unremarkable.

MRI

SWAN revealed presence of a large DVA in left cerebellar hemisphere with an enlarged collector vein in left ponto-medullary region. There was evidence of hyperintensity noted in left transverse and sigmoid sinus region as well as hyperintensity seen within the cortical veins in the left occipital and posterior parietal regions suggestive of CVR. Minimal PPP was seen in the posterior fossa and posterior temporal veins on left side.

ASL revealed bright signal within the left transverse and sigmoid sinuses as well as within the cortical veins on the left posterior parietal and posterior temporal regions consistent with CVR. These findings were suggestive of Cognard grade 2b at the left transverse sinus region.

DSA

Angiogram revealed a Cognard grade 2b DAVF in left transverse sinus/sigmoid sinus region, with arterial feeders from bilateral MMA, left occipital artery, left STA and bilateral vertebral arteries. The venous outflow was antegrade along the sigmoid sinus and IJV with CVR into adjacent cortical veins.

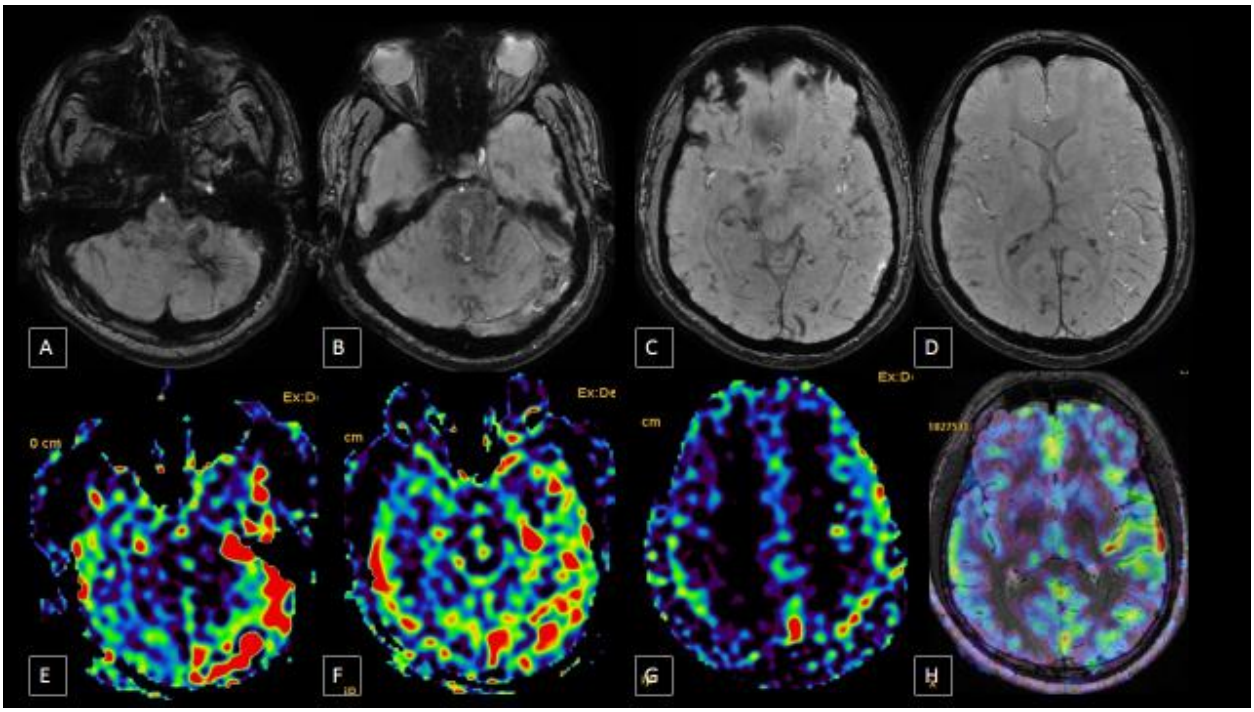


Figure No 12: Axial SWAN images. (A) and (B) Shows a large DVA in left cerebellar hemisphere. Focal hyperintensity in left transverse sinus region. (C) and (D) Show hyperintensity within cortical veins in left posterior parietal and occipital areas suggestive of CVR. Mild PPP is also noted

(E) to (H) ASL images showing bright signal within left transverse sinus region and in cortical veins on left side suggestive of left transverse sinus DAVF, Cognard type 2b

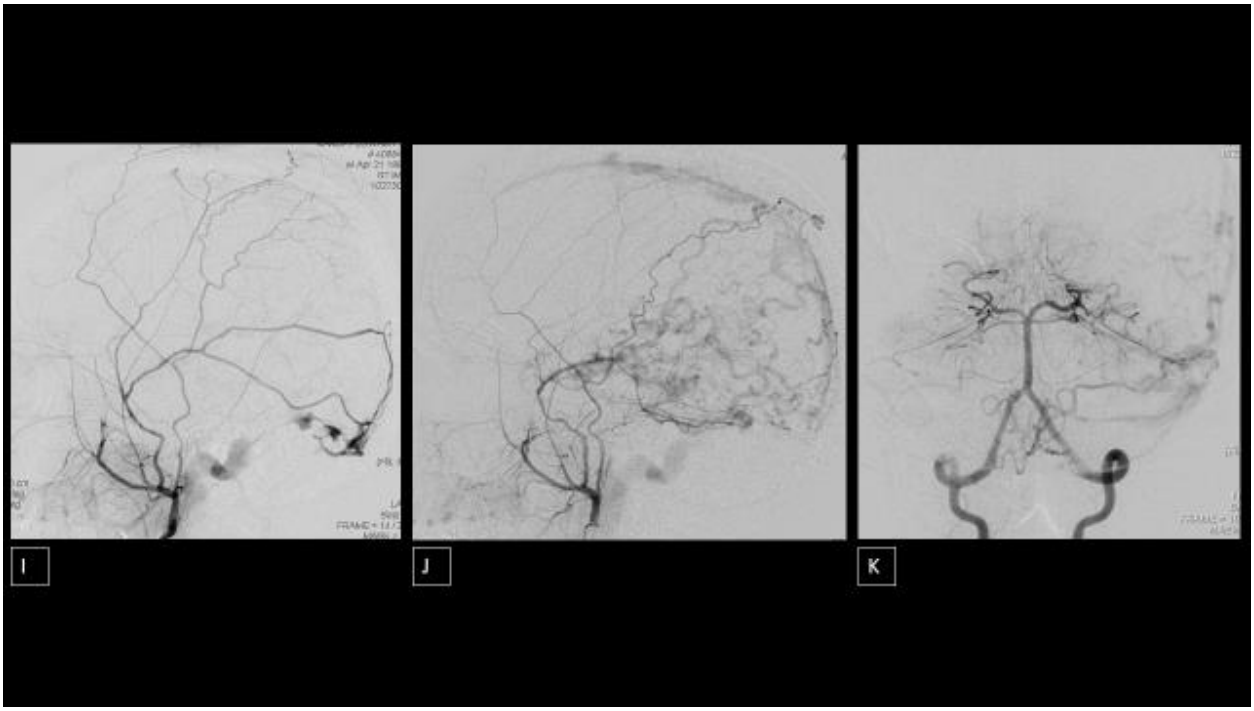


Figure No 13: DSA images (I) to (K) Lateral and Frontal views showing left transverse sinus DAVF with antegrade sinus flow and cortical venous reflux with moderate PPP

CASE NUMBER 4

Cognard Type 2a+b DAVF in Tentorial region

History

49 year old female patient with associated comorbidities of diabetes as well as hypertension presented with complaints of left sided chronic headache of 1 year duration. She also complained of worsening gait ataxia. There were no complaints of seizures, LOC, focal neurological deficits. She was imaged for her headache and then referred to SCTIMST for further management.

Examination

She was averagely built and nourished. General condition was good. GCS was 15/15. Visual acuity was 6/6 in both eyes. There was no focal neurological deficit. Other systems were unremarkable.

MRI

SWAN images revealed gross PPP with dilated tortuous veins noted in both hemisphere. There was evidence of focal hyperintensity noted in the region of the tentorium in the vicinity of falcotentorial junction with extension of hyperintensity seen along SSS and straight sinus. There was hyperintensity seen in the adjacent cortical veins also suggestive of CVR.

ASL images revealed bright signal in the region of tentorium as well as along bilateral transverse sinuses and SSS. Foci of bright signal were also noted within the peripheral cortical veins in both hemispheres.

These findings were suggestive of Cognard grade 2a+b DAVF in the tentorium.

DSA

Angiogram revealed a tentorial DAVF Cognard grade 2a+b, with arterial feeders from bilateral MMA branches, bilateral occipital arteries and from bilateral PCAs. The venous drainage was noted into persistent falcine sinus and posterior SSS. CVR was also noted. Gross PPP was seen with significant prolongation of circulation time.

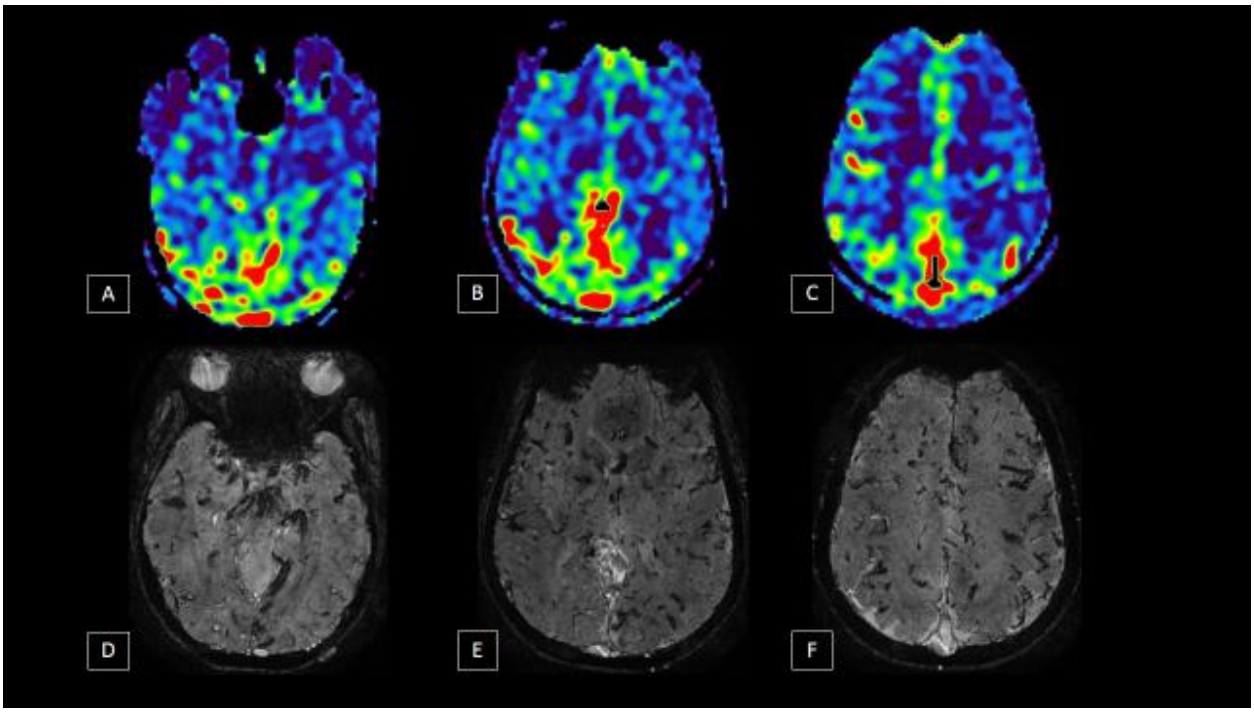


Figure No 14: ASL images (A) (B) (C) showing bright signal in midline in tentorial region, along straight sinus and torcula with similar signal in adjacent cortical veins

SWAN axial images (D) (E) (F) showing gross PPP with hyperintensity in region of falcotentorial junction, along straight sinus and torcula. Similar hyperintensity is also seen in adjacent cortical veins. Tentorial DAVF Cognard type 2 a+b

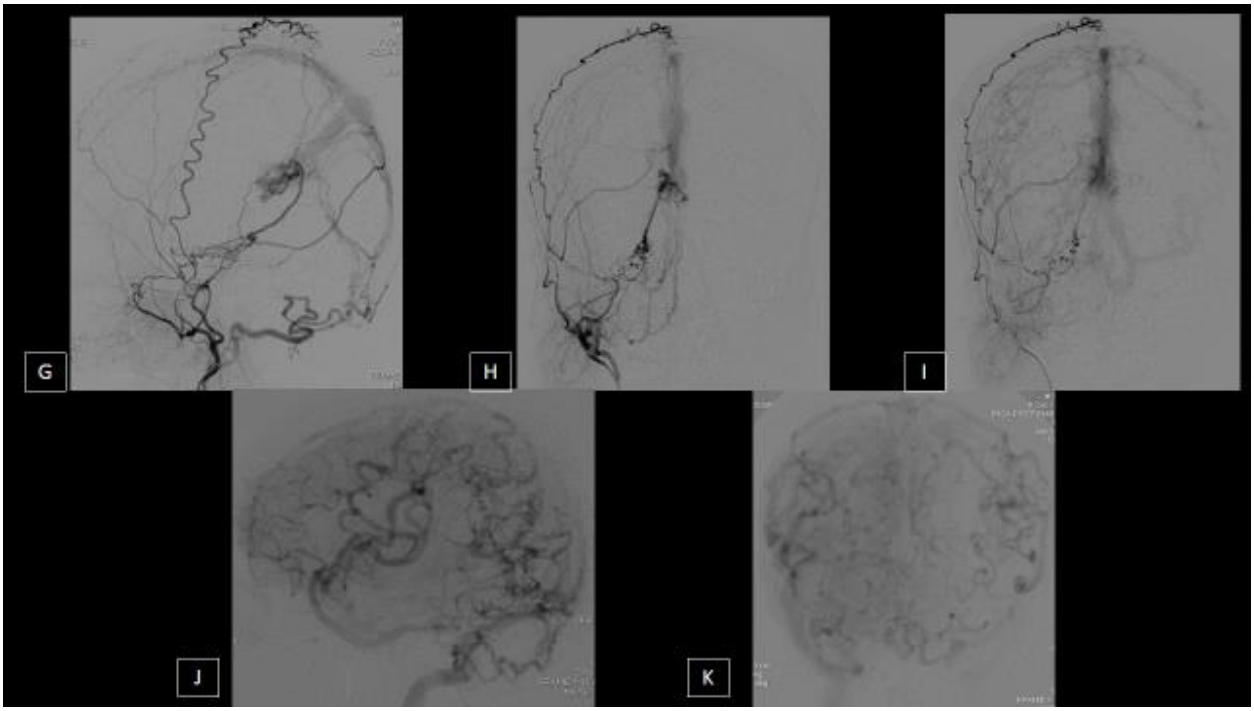


Figure No 15: DSA frontal and lateral images (G) to (K) showing Tentorial DAVF Cognard type 2a+b with CVR and severe PPP and prolonged circulation time and venous delay suggestive of venous hypertension.

CASE NUMBER 5

Cognard Type 2a+b DAVF in left transverse sinus region

History

35 year old female patient presented with complaints of 2 months history of left temporal headache. She also complained of tinnitus in her left ear for the same duration. For the last 1 months she noticed a sensation of giddiness and had experienced multiple episodes of transient weakness in her right upper limb with facial deviation in the last 3 weeks. She was evaluated at nearby hospital. Neuroimaging had revealed possibility of DAVF for which she was referred to SCTIMST.

Examination

She was averagely built and nourished. General condition was good. GCS was 15/15. Visual acuity was 6/6 in both eyes. There was no focal neurological deficit. There was evidence of bilateral occipital and posterior temporal region bruits. Other systems were unremarkable.

MRI

SWAN revealed features of PPP involving both hemispheres. There was bright signal noted within the left transverse sinus as well as within the SSS and straight sinus. Foci of hyperintensity was also noted within cortical veins in occipital, posterior temporal and posterior parietal regions.

ASL images showed bright signal within bilateral transverse sinuses, torcula, parts of SSS and also within peripheral cortical veins in the right occipital and posterior parietal regions.

These findings were suggestive of Cognard grade 2a+b extensive DAVF in left TS region.

DSA

Angiograms showed Cognard 2a+b DAVF in left transverse sinus and torcula with arterial feeders from bilateral MMA, occipital arteries, marginal tentorial artery from ICA and also from left PCA, SCA and PICA. Venous drainage was seen retrogradely into SSS with significant CVR. There was PPP with significant delay in circulation time at 6 and 5.8sec in right and left sides respectively.

Patient underwent transarterial squid embolization via left MMA branch. There was intraprocedural haemorrhage due to rupture of a transosseous branch of left STA which was occluded with squid and NBCA. There was significant SDH and EDH which was subsequently surgically evacuated. Patient made a slow recovery and has remained MRS 4

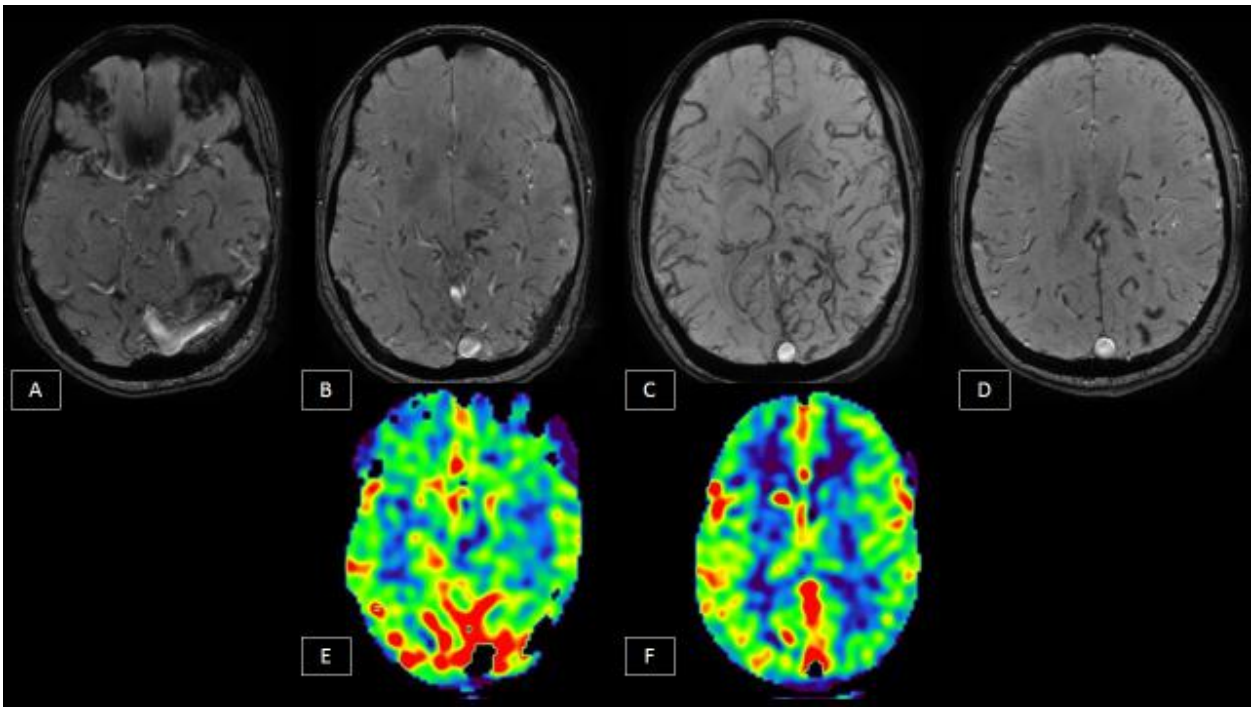


Figure No 16: Axial SWAN images. (A) to (D) Focal hyperintensity in left transverse sinus region, torcula and straight sinus. Hyperintensity also seen within adjacent cortical veins. Severe PPP is also noted

(E) (F) ASL images showing bright signal in bilateral transverse sinuses, torcula and part of SSS along with signal in adjacent cortical veins

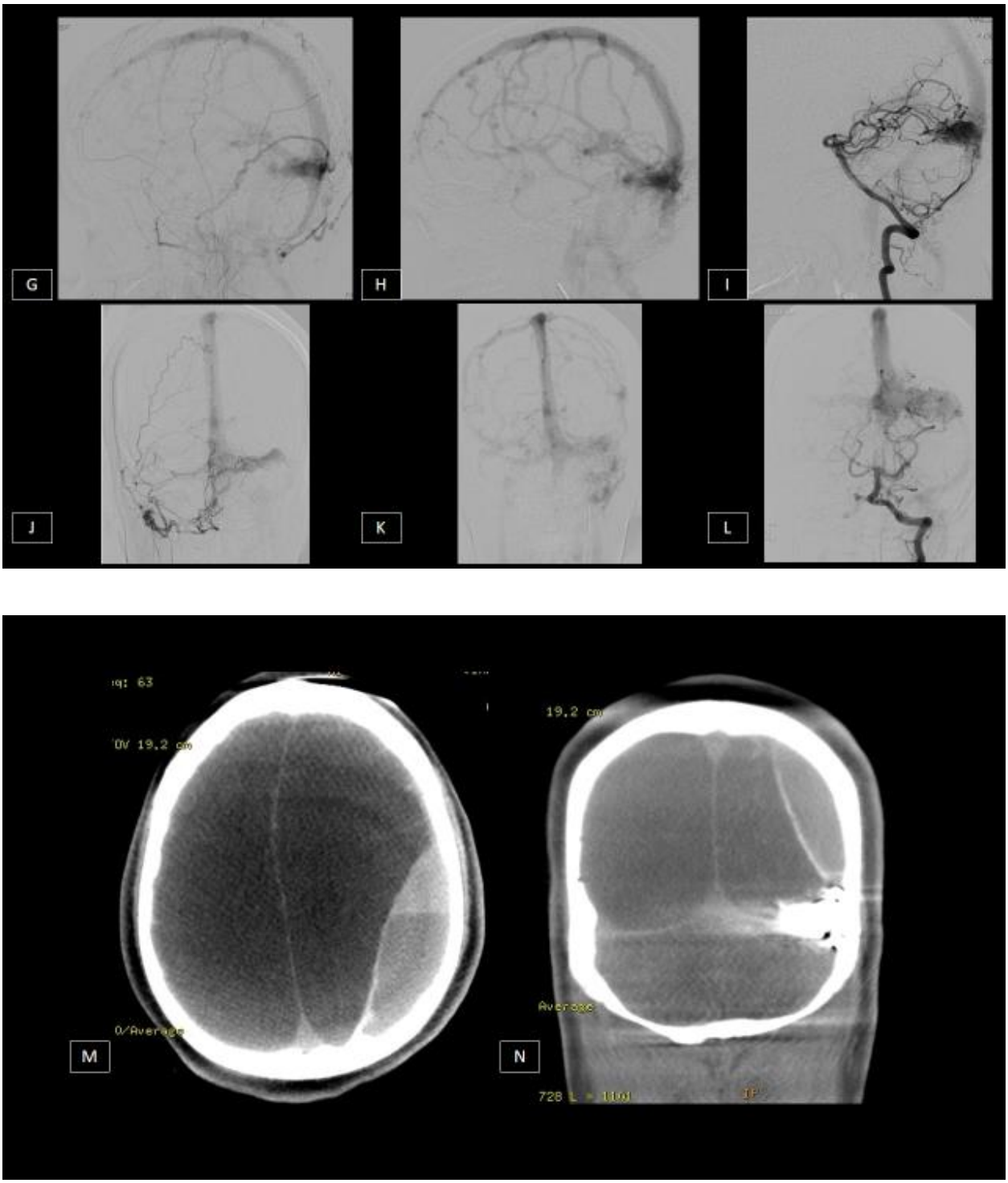


Figure No 17: DSA images (G) to (L) reveal Cognard type 2a+b DAVF in left transverse sinus region with CVR, retrograde venous drainage and mild PPP

3D CT images (M) (N) reveal intraprocedural bleed with EDH. Post embolization squid cast is also noted in left transverse sinus

CASE NUMBER 6

Cognard Type III DAVF in right transverse sinus region

History

47 year old female patient, a known diabetic on treatment, presented with acute onset sudden severe headache with nausea, vomiting and vertigo. This was followed in a few minutes by one episode of generalized tonic clonic seizures followed by post ictal confusion. She was taken to a nearby hospital, stabilized and then underwent neuroimaging as part of evaluation of her seizures. Imaging done outside revealed right parieto-occipital haemorrhage with sulcal SAH and strong suspicion of underlying DAVF. She was then referred to SCTIMST for further management.

Examination

She was thin built and averagely nourished. General condition was good. GCS was 15/15. She was found to have right homonymous hemianopia on VA/VF charting. There was no other focal neurological deficit. Other systems were unremarkable.

MRI

SWAN images revealed sequelae of haemorrhage with blooming in right parieto-occipital region. Bright signal was noted within the right transverse sinus without extension along the sigmoid sinus or torcular region. Similar bright signal suggestive of CVR was noted in the adjoining cortical veins in parieto-occipital region. PPP was also noted in this region.

ASL images revealed reduced perfusion in the region of the haemorrhage. Focal increased signal was note within the small segment of right transverse sinus and within adjacent cortical veins

suggestive of direct CVR from an isolated sinus segment. Coronal reformatted ASL image reveals intense cranio-caudaly directed smearing artefact from the isolated sinus segment.

These features were suggestive of Cognard grade 3 DAVF in right transverse sinus with isolated transverse sinus segment and direct CVR.

DSA

Angiograms showed Cognard grade 3 DAVF at right transverse sinus with isolated sinus segment. The arterial feeders were noted to be from right MMA and right occipital artery. There was direct CVR from the isolated sinus segment noted. There was no evidence of PPP or prolonged circulation time.

This patient was planned for definitive transarterial squid embolization but was noted to have had spontaneous occlusion of fistula on follow up.

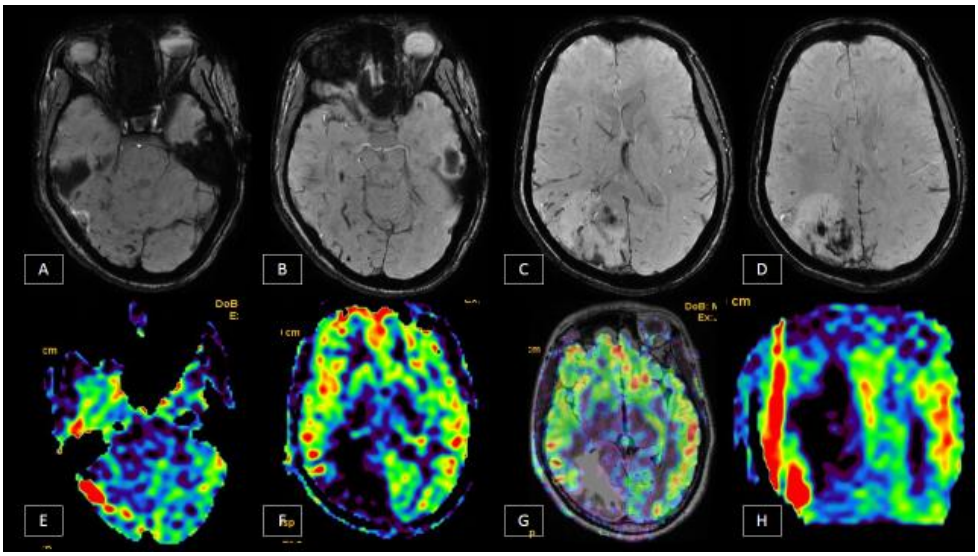


Figure No 18: Axial SWAN images. (A) to (D) Focal hyperintensity in right transverse sinus without similar signal in sigmoid sinus or torcula. CVR is noted with signal in adjacent cortical veins. Sequelae of prior bleed is noted in right parieto occipital region

ASL images show bright signal in right transverse sinus and cortical veins with smearing artefact adjacent to sinus suggestive of isolated sinus segment

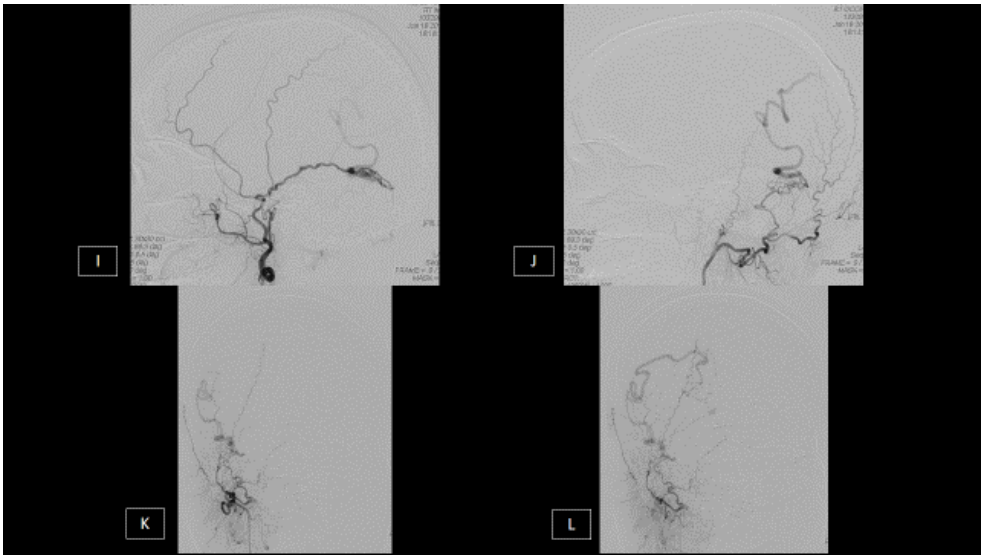


Figure No 19: DSA images (I) to (L) frontal and lateral views show Cognard type III DAVF in right transverse sinus region with isolated sinus segment and CVR. Moderate PPP is also noted.

CASE NUMBER 7

Cognard Type III DAVF in left transverse sinus

History

48 year old male patient, a known case of CAD on medical management presented with 1 month history of severe holocranial headache and 1 week history of left sided tinnitus. He then had a sudden onset acute episode of nausea, vomiting and confusional state. He was taken to nearby hospital and evaluated. Imaging was suggestive of DAVF and he was referred to SCTIMST for definitive management.

Examination

He was well built and averagely nourished. General condition was good. GCS was 15/15. He was found to have left hemianopia on VA/VF charting. The IOP was noted to be 20.6 in both eyes. There was no other focal neurological deficit. Other systems were unremarkable.

MRI

SWAN images revealed sequelae of haemorrhage in right posterior temporal region and also along the right posterior para falcine region. There was evidence of focal bright signal noted within the distal aspect of left transverse sinus with no similar signal seen within the sigmoid sinus or torcular region. There was hyperintensity in adjacent cortical veins of left posterior temporal region suggestive of CVR. Minimal PPP was seen in left side. ASL images also revealed focal bright signal within a part of the left transverse sinus with signal seen within adjacent cortical veins suggesting CVR. Coronal reformatted images show the prominent vertically directed smearing

artefact originating from the isolated TS segment. These findings were suggestive of Cognard grade 3 DAVF in left transverse sinus with isolated sinus segment and direct CVR.

DSA

Angiograms showed a Cognard grade 3 DAVF in left TS with feeders from left MMA, bilateral occipital arteries, left posterior auricular artery and MHT from ICA with venous outflow into isolated left transverse sinus segment and further CVR into adjacent cortical veins.

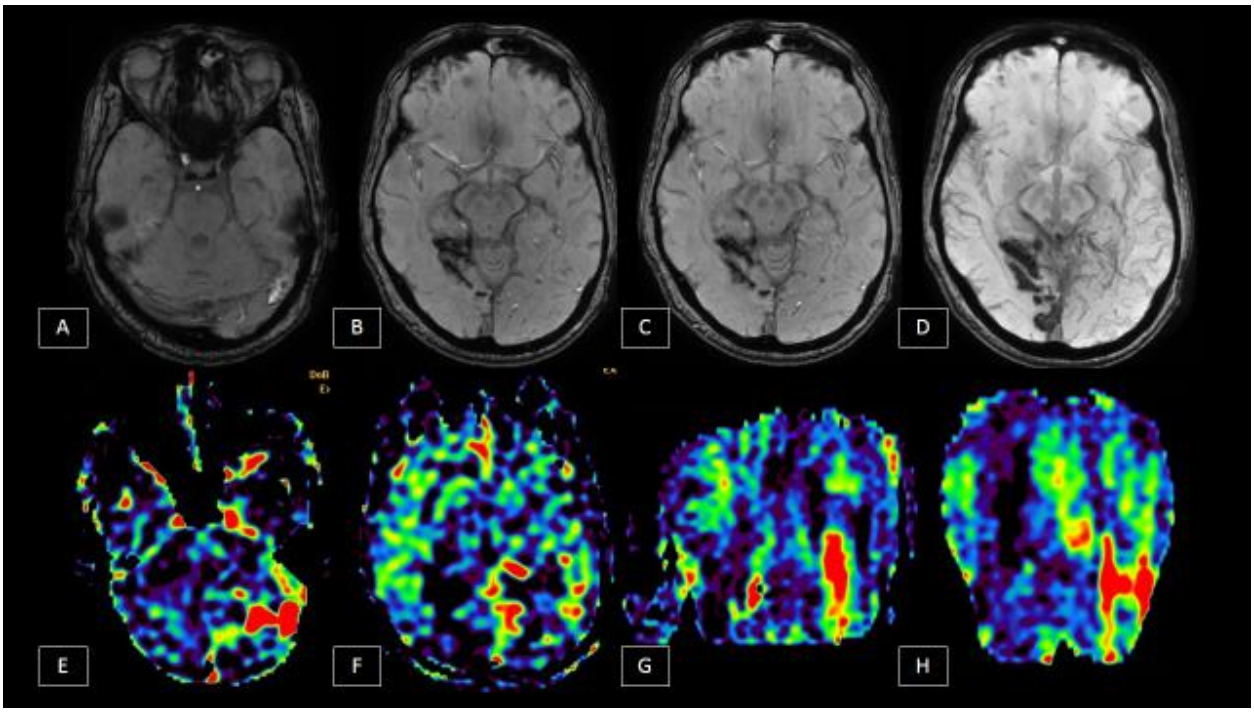


Figure No 20: Axial SWAN images. (A) to (D) Focal hyperintensity in left transverse sinus without signal in torcula or sigmoid sinus. CVR is noted with bright signal in adjacent cortical veins. Sequelae of prior bleed is also noted adjacent to right side of tentorium

ASL images (E) to (H) reveal bright signal in left transverse sinus region and adjacent CVR with smearing artefact along the left isolated transverse sinus segment.

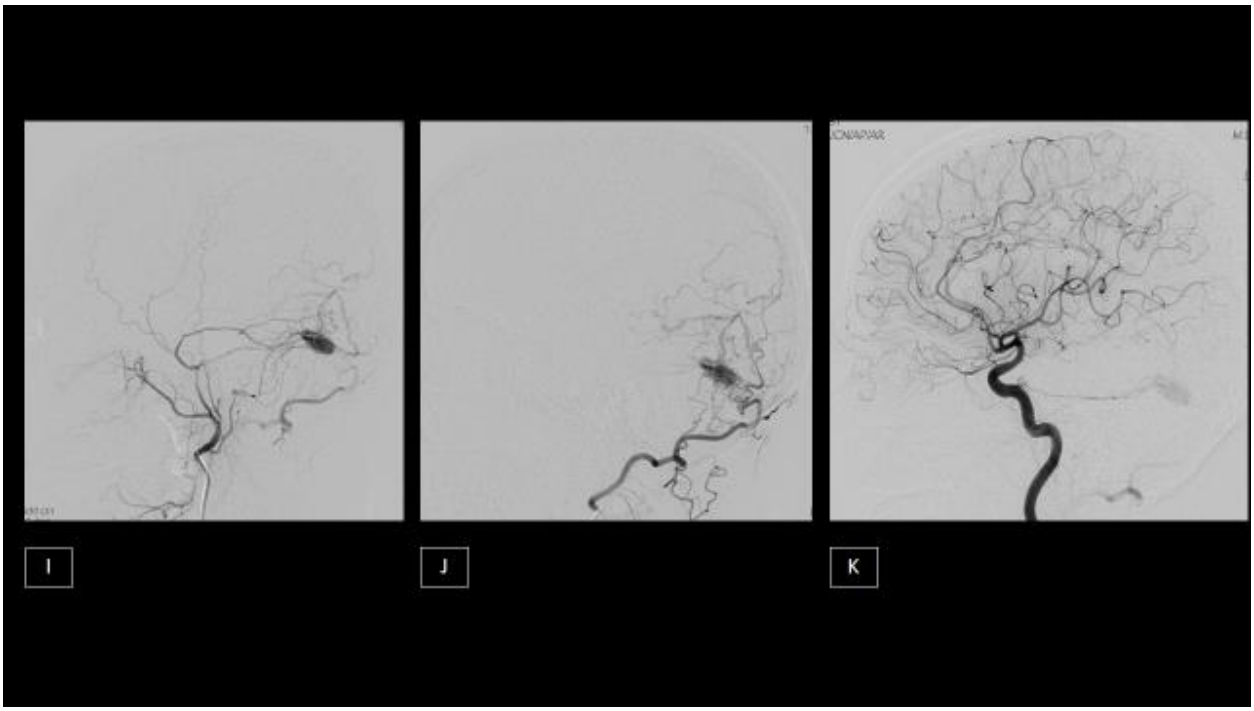


Figure No 21: DSA images (I) to (K) Frontal and lateral images show Cognard type III DAVF in left transverse sinus with CVR

CASE NUMBER 8

Cognard Type IV DAVF in right Superior Petrosal Sinus region

History

53 year old male patient presented with history of chronic holocranial headache of 7 years duration. He also complained of 4 month history of right facial pain suggestive of trigeminal neuralgia. Due to his worsening symptoms he sought medical attention and underwent neuroimaging which revealed DAVF. He was then referred to SCTIMST for definitive management.

Examination

He was well built and averagely nourished. General condition was good. GCS was 15/15. He was noted to have right Vth nerve palsy with reduced power in muscles of mastication. Loss of corneal reflex was also noted. There was no other focal neurological deficit. Other systems were unremarkable.

MRI

T2 axial images revealed large bilocular flow void in the right CP angle region with indentation of the pons. SWAN images showed small areas of bright signal adjacent to petrous region. Bright signal was also noted within the large venous sacs as also within a few posterior fossa veins in the vicinity suggestive of CVR. No PPP was seen.

ASL images showed bright signal in the petrous region suggestive of shunt along with signal within the venous sacs and adjacent cortical veins suggesting CVR. Intense smearing artefact in cranio caudal direction was noted from within the venous sacs.

These MRI findings were suggestive of DAVF in right petrous region with direct CVR and adjacent venous sacs consistent with Cognard grade 4 fistula.

DSA

Angiograms showed a Cognard grade 4 DAVF in right SPS region with arterial feeders from right MMA, occipital artery, AICA and ICA. Venous outflow was noted into 2 large venous sacs with further egress into posterior fossa veins with CVR. There was also prolongation of circulation time which was noted with mild PPP also seen.

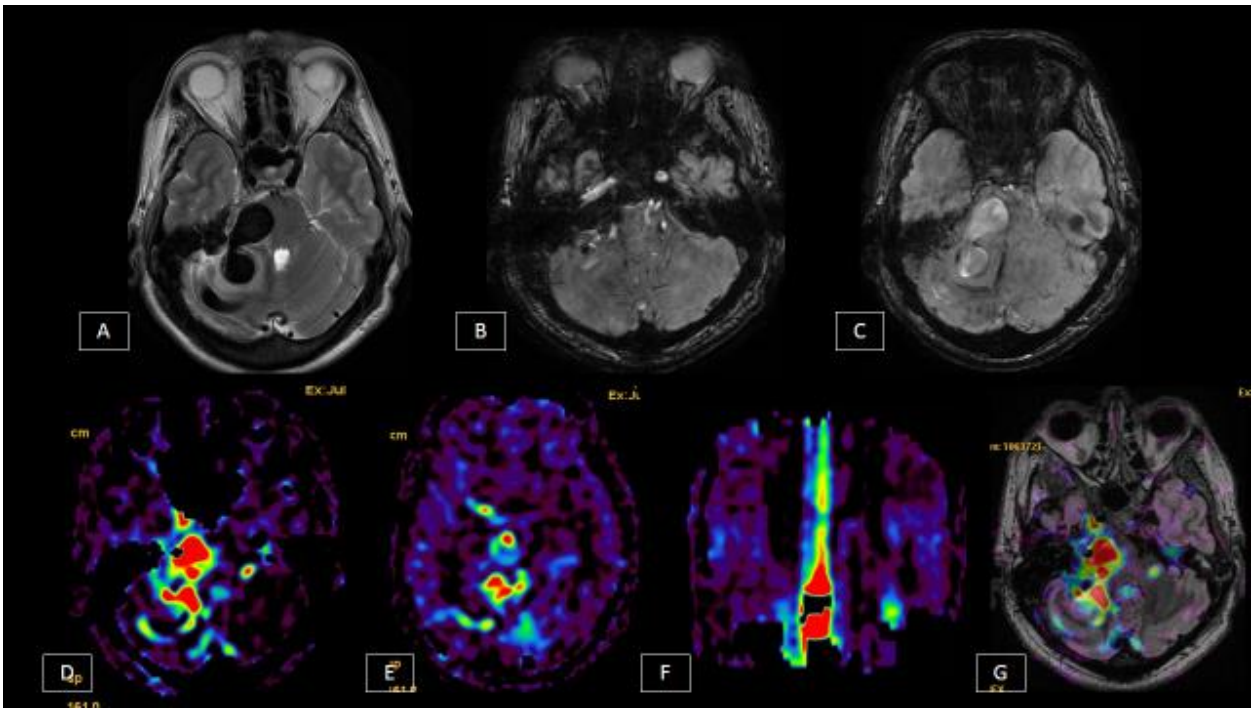


Figure No 22: Axial T2 image (A) shows a bilocular flow void in right petrous region with indentation of Pons. Axial SWAN images (B) (C) show hyperintensity in right petrous region and also within the large venous sacs.

ASL images (D) to (G) showing bright signal in right petrous region and also in large venous sacs and cortical veins with smearing artifacts seen to arise from location of sacs.

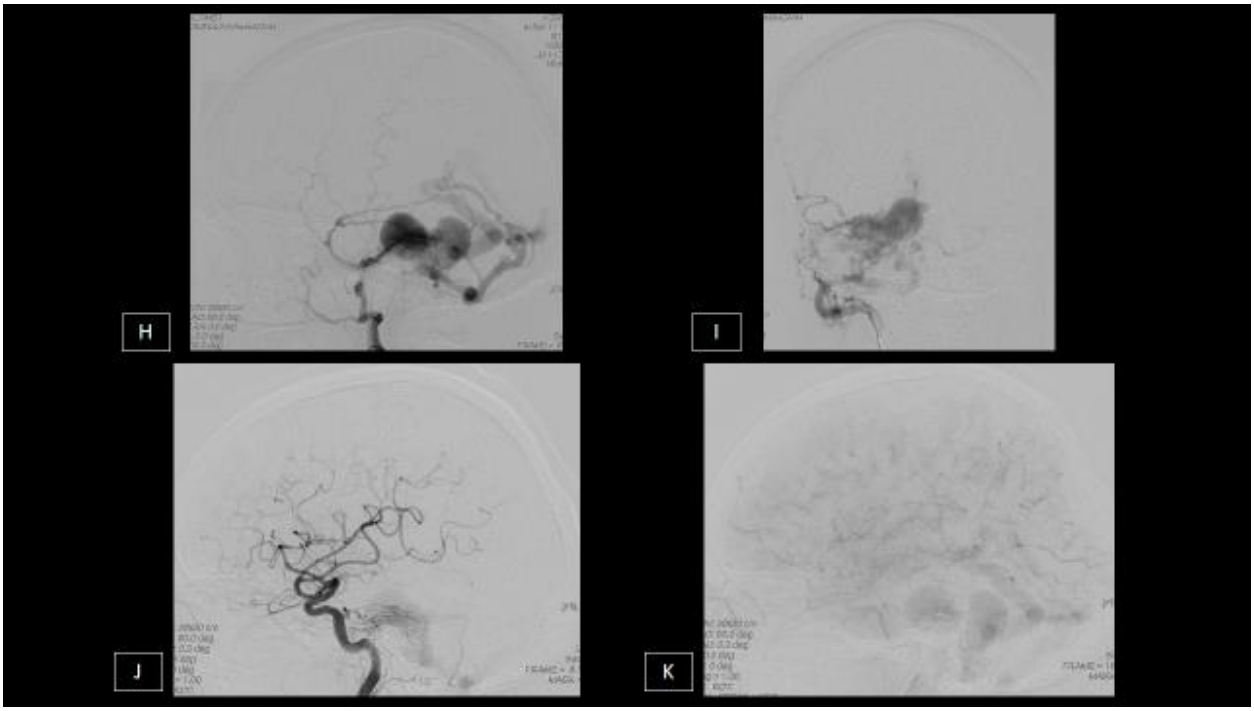


Figure No 23: DSA images (H) to (K) frontal and lateral views show right SPS Cognard type IV DAVF with large venous sacs and CVR with gross PPP and venous delay

CASE NUMBER 9

Cognard Type V DAVF at foramen magnum

History

42 year old female patient presented with history of paresthesias involving both feet for 1 year duration. Slowly the paresthesias increased and ascended till the trunk level. She did not take any treatment for these complaints. She then presented with sudden onset paraparesis with urinary retention for which she was evaluated in outside hospital and then referred to SCTIMST for definitive management.

Examination

She was averagely built and averagely nourished. General condition was good. GCS was 15/15. She was noted to have total paraparesis with grade 0/5 power in both lower limbs. DTRs were not elicitable in either leg. There was a sensory level noted at T6 level. There was no other focal neurological deficit. Other systems were unremarkable.

MRI

T2 sagittal image of the cervical spine revealed cord hyperintensity below C6 vertebral level. Multiple vascular flow voids were noted both anterior and posterior to the cervical cord. SWAN images and post contrast T1 images show hyperintensity in left side of foramen magnum with focal enhancement and multiple vascular channels along the cervicomedullary junction extending inferiorly.

ASL images reveal bright signal within the above mentioned vascular channels with extension into the cervical spinal canal. The supratentorial brain does not reveal any abnormal signal.

DSA

Angiograms revealed Cognard grade 5 DAVF in posterior border of foramen magnum with arterial feeders from left vertebral artery and venous outflow into perimedullary venous channels in the cervical region. There was no evidence of PPP or supratentorial CVR.

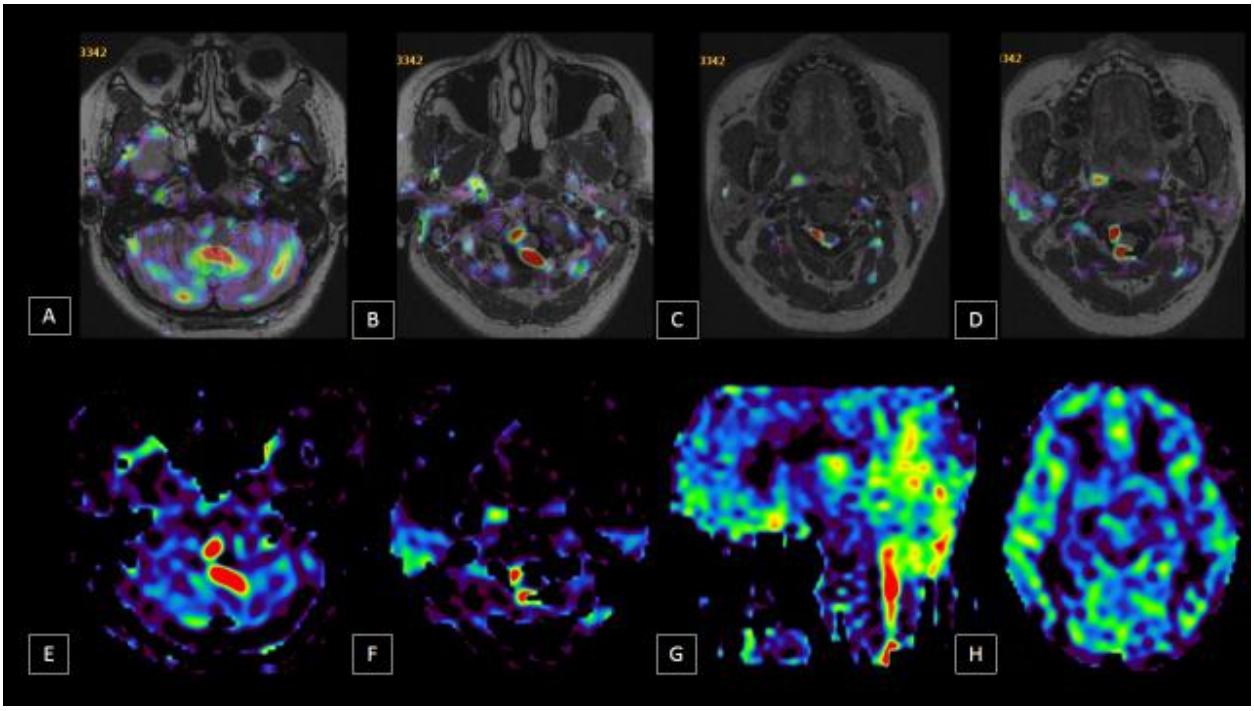


Figure No 24: ASL images (A) to (H) showing focal bright signal posteriorly at foramen magnum level with extension of this signal inferiorly into spinal canal both anterior and posterior to cervical cord. No supra tentorial abnormal signal is seen.

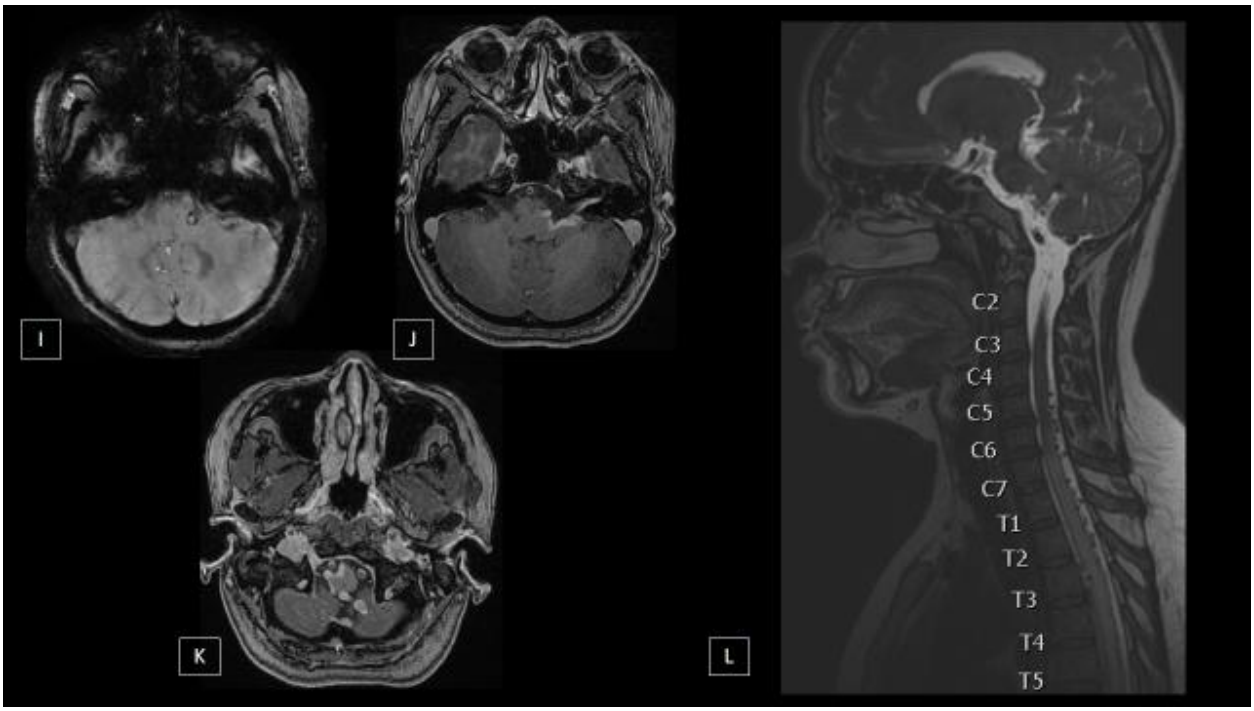


Figure No 25: Axial SWAN and post contrast T1 images (I) to (K) showing focal hyperintensity and enhancement in foramen magnum region on left side. Sagittal T2 image (L) showing cervical cord hyperintensity and multiple flow voids in cervical spinal canal

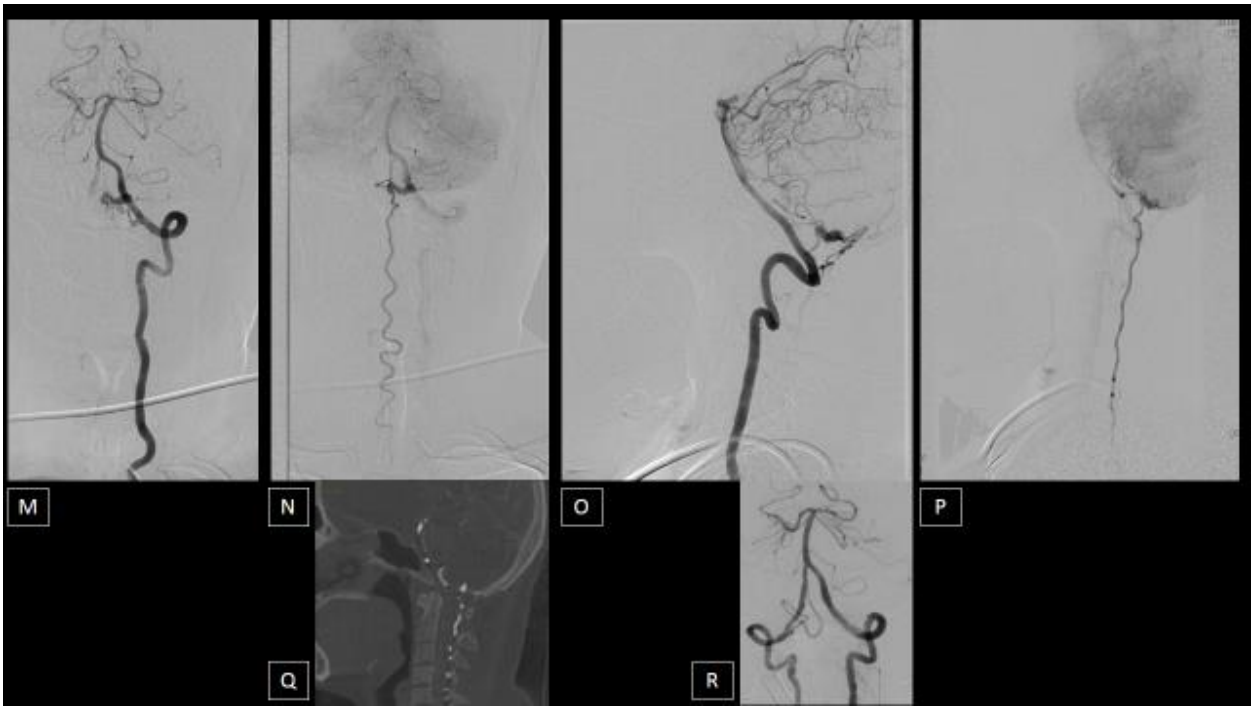


Figure No 26: DSA images (M) to (R) showing Cognard type V DAVF at foramen magnum level with perimedullary venous drainage into cervical spinal canal.

CASE NUMBER 10

Cognard type V DAVF at foramen magnum

History

62 year old female patient, a known hypertensive on treatment with adequate control, presented with complaints of chronic holocranial headache of 4 years duration. She had a sudden acute severe episode of headache with nausea, vomiting and altered sensorium for which she was taken to nearest medical college hospital. While at hospital she developed transient right lower limb weakness. She was managed conservatively and when neuroimaging was suggestive of SAH with perimedullary flow voids, she was referred to SCTIMST for definitive management.

Examination

She was averagely built and averagely nourished. General condition was good. GCS was 15/15. She was noted to have grade 4/5 power in right lower limb. There was no other focal neurological deficit. Other systems were unremarkable.

MRI

T2 axial and SWAN images revealed multiple flow voids around the upper cervical cord. Focal hyperintensity was noted within these flow voids located posterior to cord suggestive of shunting lesion.

ASL images reveal bright ASL signal within these venous channels with extension into the cervical spinal canal. No similar signal was seen in the supratentorial brain.

These features were suggestive of foramen magnum DAVF with perimedullary spinal venous drainage.

DSA

Angiograms showed Cognard grade 5 DAVF at ophisthion at foramen magnum level with arterial feeders from bilateral vertebral arteries and venous outflow into perimedullary venous channels along the cervical spinal canal.

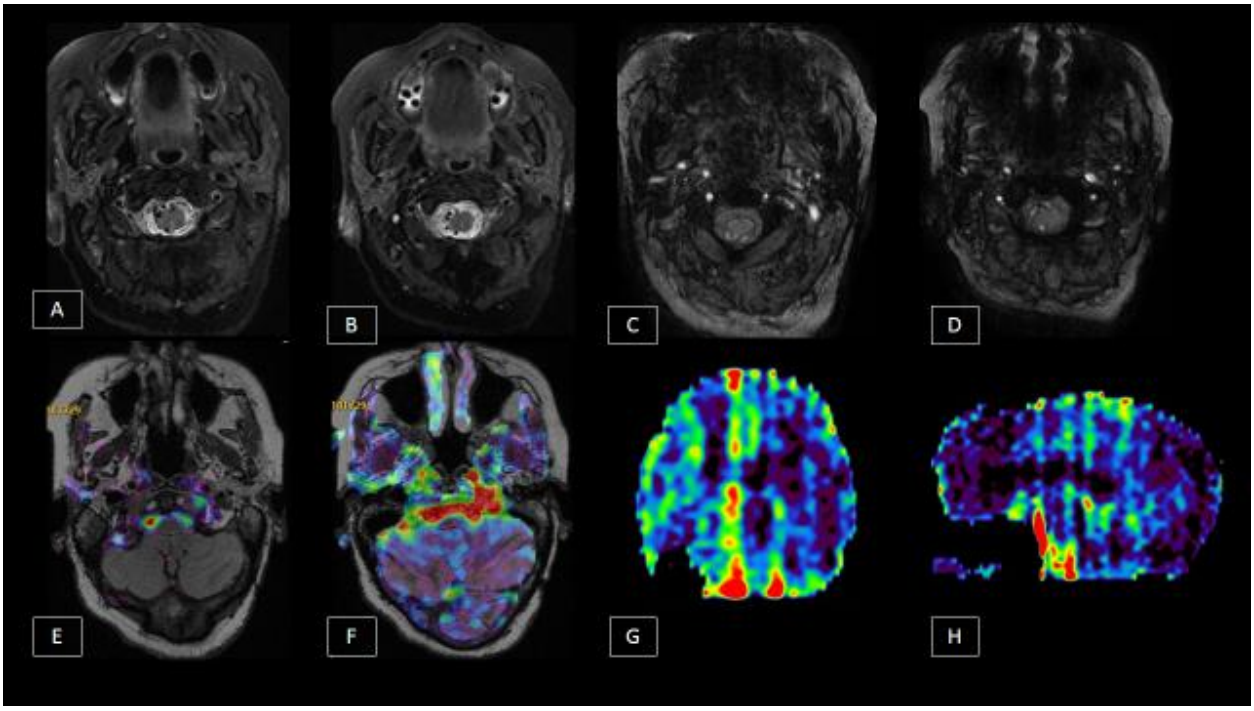


Figure No 27: Axial T2, SWAN images (A) to (D) showing focal hyperintensity and vascular flow voids in foramen magnum region around cervical cord.

ASL images (E) to (H) shows bright signal at foramen magnum fistula site and around the cervicomedullary junction

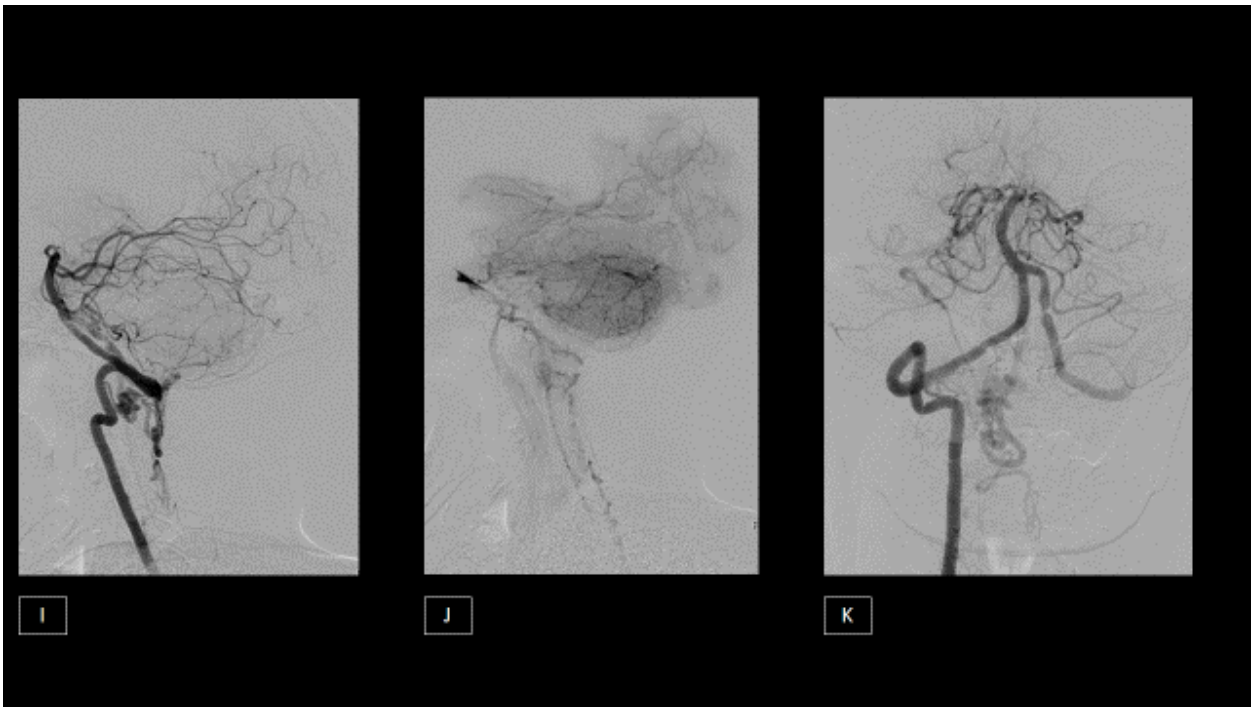


Figure No 28: DSA images (I) to (K) show Cognard type V DAVF at foramen magnum with perimedullary venous drainage into cervical spinal canal.

DISCUSSION

DISCUSSION

DAVF is not an uncommon disease entity and with more widespread availability of diagnostic modalities, there has been in increasing trend in diagnosis of this illness. The gold standard in diagnosis of DAVF is DSA and the modality of choice for treatment is transarterial or transvenous embolization. It has been documented that inspite of complete occlusion of fistula, recurrences are common and upto 14% recurrence has been seen with time and follow up angiography has been recommended. (36) The follow up of patients is also based on diagnostic angiograms done at predefined intervals based on the institution protocols. The patient is thus bound to undergo multiple DSA examinations, each with its own procedural risks and the added radiation exposure hazards. A reliable noninvasive diagnostic test and follow up tool could potentially limit the need for additional diagnostic tests to selected patients, on whom suspicion is high. (74) (6). Our study evaluated whether advanced MRI sequences could be used as a reliable noninvasive diagnostic modality and also in noninvasive follow up of patients with intracranial DAVF. For this purpose, primary as well as previously treated DAVF were included in the analysis.

The demographic features in our cohort were similar to other larger studies in literature dealing with presentation, natural history and follow up of DAVF. (31)(32)(88)(4) The commonest presentation of our patients was with chronic headache. Aggressive symptoms were noted in 36% of patients whereas 64% patients presented with benign symptoms. The symptom distribution in our study is similar to other prior studies. Baltsavias et al in their study cohort of 116 patients had 67% benign presentation and 33% aggressive presentation. Oh et al too observed aggressive clinical presentation in approximately 30% of their cases.

30 patients had only a single fistula site whereas 16 patients had multiple fistula sites. An overwhelming 66% of all cases were located in the transverse sinus region. Cavernous sinus

fistulae, seen as indirect CCF, were not included in this study as the etiopathogenesis, presentation and management was quite different compared to the other intracranial DAVF. Our results generally seem to mirror that already available in literature. Jain et al reported 17 out of 33 (52%) cases in the transverse sigmoid region. (62) Piippo et al had 67% cases located in the transverse and sigmoid sinus regions amongst their cohort of 227 patients.(90) Baltsavias et al noted approximately 22% cases, in their study group of 170 patients, had the fistula in transverse sinus second only to cavernous sinus. An additional 18% cases were seen to have fistula in the transverse- sigmoid sinus region. (89)

In our study, the fistula was analysed based on both Cognard as well as Borden classification systems to enable comparison with available literature, where different authors have used the two systems variably. Most studies in literature have used the simpler Borden grading. Cognard grading being more elaborate and more closely associated with aggressive features was considered in our study.

There were 15% cases noted in the benign group in Borden system (Grade I) and 21% noted in the benign group among the Cognard grading (Grades I and IIa). The commonest grade of fistula amongst the whole group was II a+b with 17 cases followed by grade III with 11 cases. Amukotuwa et al described 35% Borden grade 1 cases amongst their cohort of 34 patients in a retrospective study. Grade II was the commonest grade in this study. (74) Oh et al reported 50% cases of Borden II, 36% cases of Borden I and 14% cases of Borden III in their series of 95 cases with DAVF. (23) Gross et al reported 39% cases in their group of 260 patients who were in Borden grade I.

Our series had a much smaller component of patients in Borden grade I compared to other authors. This could be attributable to a relatively smaller sample size and referral bias in a tertiary care situation.

CVR was noted in 34 of 46 patients (74%). Out of the 34 patients with CVR, 12 patients (35%) had aggressive presentation and of the 12 patients without CVR, 5 patients (42%) had aggressive type of presentation. Sato et al in their series of 56 patients with DAVF, reported 73% cases displaying CVR. In this cohort 36% cases with CVR showed aggressive presentation and 38% cases with CVR presented without aggressive features. Our series also shows comparable data. (64). Van Rooij et al studied 91 patients with DAVF and noted 32% cases with CVR in this series. Out of the 29 patients with CVR, 22 patients (76%) presented with aggressive symptoms. These results were in variance with most studies which showed a higher percentage of cases with CVR. (91)

Pseudophlebitic pattern was noted in 72% patients in our cohort. PPP was always associated with aggressive grade of fistula and none of the benign grade fistula revealed PPP. Of the 33 patients with PPP, 11 patients (33%) presented with aggressive clinical features. It was noted that higher grade of fistula was associated with more severe PPP and correspondingly increased circulation time. In amongst the earlier studies on DAVF, Willinsky et al in their series of 122 patients with intracranial DAVF, documented PPP in 42% of their cases. They also noted that 73% cases had an aggressive presentation compared to the ones without PPP. They opined that this angiographic feature is a prognostic indicator and should feature in treatment decision making. (40)

Imaging evaluation using advanced MRI

SWAN

In our study, SWAN could identify the fistulous point in 85% of the cases. Multiple fistulae were identified in 50% of the overall multiple fistula cases. The kappa values showed moderate agreement between the two observers in identifying the presence and location of fistulous point. In 74% cases, CVR could be identified and there was good interobserver agreement with kappa value of 0.68. This suggest that SWAN could be a reliable tool in identifying CVR.

Jain et al demonstrated that SWI could correctly identify 75% of fistulous points and 90% cases with CVR with sensitivity of 85%. They also noted that SWI underperforms with multiple fistulous points, probably owing to variable flow dynamics and fistula sizes at different fistula sites. They also acknowledged the limitation of fistula site and CVR identification in vicinity of susceptibility artefacts. (62)

In a small study by Guillon et al, fistulous point could be identified fistulous point in 5 out of 6 patients. The authors noted that SWI under performed at identification of CVR and attributed this to slow flow at fistula or dilution of bright oxyhaemoglobin signal with large quantity of deoxyhaemoglobin in the venous side. (59)

In our study good interobserver agreement with kappa value of 0.7 was obtained for both Cognard as well as Borden grading of fistula on SWAN. The correlation was noted to be better with Borden grading, probably due to its simpler classification system.

ASL

ASL could identify a fistulous point in 96% cases, which was higher that the detection rate by SWAN. Multiple sites of fistula were identified in 31% of the overall multisite fistula cases. For the identification of presence and site of fistula there was moderate interobserver correlation, whereas for identification of multiple sites there was significant correlation. The identification of fistula at base of skull, petrous regions and also at SSS near vertex was hampered by lower ASL signal and at times due to lack of complete coverage. Thus planning of FOV in all cases should be meticulous and should include all the relevant anatomy.

CVR was identified in 57% cases as presence of bright signal within the adjacent venous structure. Pseudophlebetic pattern could not be assessed using ASL as it was difficult to differentiate between CVR, venous rerouting and PPP. There was good interobserver agreement between readers when it came to identifying CVR or in grading of the fistula with kappa value > 0.70

43% cases were seen to be of benign Cognard grade (I and IIa) and 39% cases were seen to be of benign Borden grade (Grade I). The interobserver agreement between the two readers for grading of fistula was seen to be good with kappa value >0.7. When compared to the gold standard ie DSA, it was seen that ASL often under graded the fistula, which was likely due to inability to identify cortical venous signal amidst normal parenchymal CBF signal.

Noguchi et al in their small series of 16 patients demonstrated the value of identifying venous signal on ASL in DAVF cases. They could identify dural sinus venous signal in all Borden I cases and cortical venous signal in all Borden III cases but could identify cortical venous signal in only 25% of Borden II cases. This led them to conclude that to identify Borden I from Borden II cases additional imaging is warranted. (69)

Amukotuwa et al in 2016 retrospectively assessed the role of 3D ASL in a group of 34 patients with DAVF. CVR was seen in 65% cases. They noted that ASL had >90% sensitivity and specificity in identifying CVR with interobserver Kappa value >0.8. The interobserver Kappa value in identifying the Borden grade was also noted to be >0.8. They concluded that ASL is of value in diagnostic evaluation of intracranial DAVF. (74)

Noguchi et al had previously demonstrated that Borden grade III fistulae were well identified and the cortical venous signal was easy to pick up. (57) We also noted that cortical venous signal was very prominent in higher grade fistulae.

Another interesting feature which was seen consistently was that in all Cognard type III fistulae with fistula site opening into an isolated sinus segment, the CVR signal was prominent but there was also evidence of a cranio-caudally aligned smearing artefact noted to arise from the isolated sinus segment. This appeared similar to the smearing artefact causing blurring as demonstrated and described in a case of ICA aneurysm by Amukotuwa et al who attributed this artifact to the 3D stack of spiral acquisition. (72) This artefact is probably caused by swirling of signal tagged blood within the isolated sinus prior to exit into the cortical veins. Similar findings were also noted at sites of significant retrograde venous flow, again likely due to retention of spin in the region. Identification of this artifact could prove useful in grading of the fistula and estimating the direction of venous flow but further focused evaluation would be necessary to validate these findings.

Combined SWAN and ASL assessment

Using combined SWAN and ASL evaluation, the presence of fistula could be identified in all the cases. Multiple fistulae were correctly identified in 31% cases amongst the overall cases with

multiple fistulae. CVR could be identified in 72% cases and PPP in 83% cases. 24% cases harbored benign Borden grade fistula whereas 76% had aggressive grade fistula. Combined evaluation greatly improved the detection of multiple fistula sites and PPP and the identification rates of CVR and grading of fistula was maintained.

In identification of fistula, presence of CVR and presence of PPP; combined evaluation of SWAN and ASL was seen to perform well with good intermodality agreement and kappa value >0.6. But in the grading of fistula by either Cognard or Borden grading, MRI was seen to have only moderate intermodality agreement with kappa value 0.4 to 0.5. When analysed with increased weighting for higher fistula grades, the intermodality correlation was seen to improve mildly. When analyzing the performance of MRI in accurate localization of site of fistula, a moderate intermodality agreement was seen with kappa value >0.4 There was significant subjective variation noted when evaluating site of fistula in transverse sigmoid region. When all the fistulae in transverse sinus, transverse sinus-sigmoid sinus junction were taken together, the intermodality agreement was seen to be excellent with kappa value >0.9. Localization of fistulae in SSS and petrous regions was found to be inadequate. This was due to poor spatial resolution adjacent to bony structures and base of skull as also in the highest sections near the vertices where SNR was low.

In identification of presence of fistula combined ASL and SWAN MRI revealed a sensitivity of 97.8%, specificity of 100% and positive predictive value of 100%. This compared favorably with the results of Hodel et al who evaluated the presence of shunting lesions in 63 patients in which 10 were cases of DAVF. They noted a sensitivity of 98%, specificity of 97% and a high kappa value of 0.9. (61)

This study has demonstrated that when used together, ASL and SWAN augment each other by overcoming their respective limitations to some extent. SWAN was noted to underperform at

identification of fistula but this down side was overcome with ASL which performed exceedingly well at identifying presence of a shunt. Similarly where ASL could not reliably identify PPP, SWAN was seen to be very efficient at identifying PPP in most cases.

Even though the results of MRI in totality appear encouraging there were a few limitations which were encountered. The spatial resolution attained in ASL was not always satisfactory and often precluded confident identification of fistula site or cortical venous drainage. The restricted temporal resolution of ASL also prevented accurate assessment of direction of flow and presence or absence of retrograde venous flow and delineation between two grades of fistula. Small shunts with limited flow was difficult to identify owing to minimal signal variation in the vicinity. SWAN evaluation of venous signal was hampered in presence of susceptibility artifacts of prior haemorrhage or in fistula location adjacent to bony structures or skull base.

LIMITATIONS

Even though this was a prospective study with inclusion of consecutive cases of intracranial DAVF presenting to our institute there were a few limitations in this study.

1. The number of patients included in the study was 46 which was limited in number and did not afford the statistical power to analyse the various data points.
2. Only patients with DAVF were included in the study and thus an inherent bias existed in evaluation of the MRI and DSA data.
3. Inspite of a time gap between reading of SWAN and ASL and even after blinding of data, there would still be a bias owing to the small number of cases.

CONCLUSION

CONCLUSION

This study with prospective evaluation of 46 patients represents the largest available prospective cohort of DAVF in literature and perhaps the only study to evaluate the role of both SWAN as well as ASL in understanding the nuances of the disease.

A combined use of both ASL and SWAN is useful in identifying presence of fistula, locating the site of fistula, identifying CVR and PPP and also in assigning a grade to the disease. This study demonstrated a sensitivity of 97.8%, specificity of 100% and accuracy of 97.9% in identification of fistula and also displayed a good intermodality agreement in identification of CVR and PPP. In localizing the fistula to the transverse sinus-sigmoid sinus region the intermodality agreement was excellent.

Even though the results of this study are encouraging, a combination of SWAN and ASL still cannot replace DSA in diagnosis. However, it could be considered in the long term follow up of treated DAVF patients in whom suspicion of DAVF remains low.

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ANNEXURES

Appendix A

TITLE OF THE STUDY: THE ROLE OF ADVANCED MAGNETIC RESONANCE IMAGING SEQUENCES ARTERIAL SPIN LABELING, DIFFUSION WEIGHTED IMAGING AND SUSCEPTIBILITY WEIGHTED IMAGING IN NON INVASIVE ASSESSMENT OF INTRACRANIAL DURAL ARTERIO VENOUS FISTULAE

Study number: IEC/808

There is a clinical suspicion that you have an abnormal connection between arteries and veins in your brain (which is called Dural Arterio Venous Fistula), for which, you have undergone or will be undergoing a digital subtraction angiography (DSA) test and Magnetic Resonance Imaging (MRI) as a part of clinical evaluation of your disease to plan the treatment.

You are being requested to participate in a study to see the role of advanced magnetic resonance imaging sequences in assessment of Dural Arterio Venous Fistula. Participating in this study, in which only data from the investigations you have undergone for your treatment will be used, will in no way influence treatment decisions. If the study is found useful then during subsequent reviews you can be evaluated just by non invasive MRI rather than undergo a more invasive DSA.

What are DSA and MRI and do they have any harmful effects?

DSA is an advanced imaging technique where the blood flow to your brain will be evaluated by injecting a dye into the arteries to the brain through a small tube which will be inserted through the artery in your thigh. X Rays will be obtained during the procedure which will clearly show the abnormal connections between arteries and veins if they exist. You will not experience much pain as an injection will be given on your thigh prior to the procedure to make it numb. You will not feel any pain during the rest of the procedure. In rare cases some people may have allergic reaction to the dye. There is also a very small risk of injury to the blood vessel and slight chance of bleeding at site of puncture. This test is vital in diagnosis of your condition and is also the means of treatment if planned subsequently.

MRI is an advanced imaging technique which uses certain waves and magnetic fields to image body part. It does not involve any ionizing radiation. There will be no administration of any type of drug or medicine during the study. Some patients may develop claustrophobia (Fear of closed spaces etc.) due to closed space and noise. This investigation is not to be done for patient with metallic implants, pacemakers. This MRI is being done as a part of clinical evaluation of your disease; however certain data from this study will be used

for research purpose to compare with the DSA study which you have already undergone/ will undergo shortly.

If you take part what will you have to do?

This study will only analyze the results of the routinely ordered imaging investigations you will undergo during treatment and follow up of your illness. You will not be required to do anything apart from the regular follow up that will be advised to you.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

This study only analyzes the results of your investigation and treatment details and thus we do not expect any injury to happen to you but if you do develop any side effects or problems due to the study, these will be treated at this institute by the experienced team of medical professionals. We are unable to provide any monetary compensation, however.

Will you have to pay for the study?

The study will only analyze the results of the investigations and treatment which you will undergo in natural process of your treatment at this institute and no extra cost will be borne by you for this particular study.

What happens after the study is over?

You may or may not benefit from this study. If the study is found useful then during subsequent reviews you can be evaluated just by non invasive MRI rather than undergo a more invasive DSA.

Will your personal details be kept confidential?

The results of this study may be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask Dr. Manoj Gopinath (tel: 9400408866) or email: drmanojg@sctimst.ac.in

Participant's name: Date of Birth / Age (in years): I_____ _____, son/daughter of _____ (Please tick boxes) •

Declare that I have read the above information provide to me regarding the study the role of advanced magnetic resonance imaging sequences in non invasive assessment of intracranial Dural Arterio Venous Fistulae and have clarified any doubts that I had. [ ] • I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights [ ] I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access [ ] • I understand that my identity will not be revealed in any information released to third parties or published [ ] • I voluntarily agree to take part in this study [ ] • I received a copy of this signed consent form [ ]

Name: Signature: Date: Name of witness: Relation to participant: Date:

(Person Obtaining Consent) I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

_____ _____

Name and Signature of Person Obtaining Consent

Appendix B

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY

PROFORMA FOR DAVF STUDY

General Instructions

Please fill in all the questions

Write Yes / No/NA wherever applicable

If the response is not known please write UK

If additional info is available please elaborate

Please use separate proforma for each admission

If admission is for a post operative / intervention complication please go to section E after completing the general information

A.PROFORMA SERIAL NUMBER:

B.CLINICAL DETAILS

Mode of Presentation [Bleed/ Tinnitus/headache/incidental/others]

For patients presenting with bleed

Date of Thunder clap headache ± vomiting :

Duration of headache :

LOC/Altered sensorium & duration :

Seizures :

Limb weakness (if yes specify) :

Visual disturbances, if any :

Any other symptoms :

No of days of admission :

Any specific treatment given :

Improvement in above symptoms :

For incidental

How was the DAVF detected :

(Reason for imaging)

Examination findings

On initial examination

GCS :

Vitals (BP/PR) :

Vision (VA/VF) :

Extraocular movements :

Cranial nerve palsy (if yes, specify)

Weakness (if yes, specify)

Bruit

Any other neurological findings :

C. INVESTIGATIONS

Magnetic resonance Imaging (MRI) including ASL SWI and DWI-

Presence of SAH:

Site:

Feeding artery:

Venous drainage:

Venous reflux:

Pseudophlebetic pattern

Parenchymal damage

Angiogram [DSA]

Site :

Feeding artery:

Venous drainage:

Venous reflux

Type :

Pseudophlebetic pattern

D. Management

1) Type of Treatment:

2) Reasons for type of treatment method adopted :

3) Date of procedure:

4)Brief description of procedure:

5) Intra-procedural complications (if any):

6) 2nd procedure on the same lesion (if any):

E. COMPLICATIONS (elaborate if needed)

Postoperative electrolyte imbalance : (if yes, specify)

Neurological deficit :

Response to treatment : Complete recovery/ partial recovery/
No improvement/ worsened

Other Complications :

Total Hospital Stay:

In case of Death :

- Time from initial presentation:
- Direct cause of death:
- Pre-treatment or post treatment:
- Whether death due to treatment related complication:
- If yes , elaborate the complication and duration of survival after treatment:

Clinical Follow Up:

At Discharge :

At six weeks :

At six months :

At one year :

At 2 years :

PRINCIPAL INVESTIGATOR MASTER KEY PROFORMA

PROFORMA SERIAL NUMBER:

1.1 Name

1.2 Age

1.3 Sex

1.4 Hospital No

1.5 Address

1.6 Phone number

1.7 Mobile

1.8 Email id

1.9 Date of admission

1.11 Date of discharge/death

Appendix C

ABBREVIATIONS

(In order of appearance in text)

DAVF- Dural Arterio Venous Fistula

CT- Computed Tomography

CTA- Computed Tomography Angiography

MRI- Magnetic Resonance Imaging

MRA- Magnetic Resonance Angiography

DSA- Digital Subtraction Angiography

SWI- Susceptibility Weighed Imaging

ASL- Arterial Spin labelling

ECA- External Carotid Artery

ICA- Internal Carotid Artery

SCTIMST- Sree Chitra Tirunal Institute for Medical Sciences and Technology

MDCT- Multi Detector Computed Tomography

ICU- Intensive Care Unit

CVR- Cortical Venous Reflux

PPP- Pseudo Phlebetic Pattern

NHFND- Non Haemorrhagic Focal Neurological deficit

SAH- Sub Arachnoid haemorrhage

ICH- Intra Cerebral Haemorrhage

NCCT- Non Contrast Computed Tomography

AVM- Arterio Venous Malformation

TOF- Time Of Flight

BOLD- Blood Oxygen Level Dependent

DSC- Dynamic Susceptibility Contrast

DWI- Diffusion Weighted Imaging

ADC- Apparent Diffusion Coefficient

SOV- Superior Ophthalmic Vein

PET- Positron Emission Tomography

CBF- Cerebral Blood Flow

CBV- Cerebral Blood Volume

OEF- Oxygen Extraction Fraction

NBCA- N Butyl Cyan Acrylate

EVOH- Ethylene Vinyl Alcohol

IS & IR- Imaging Sciences and Interventional Radiology

SWAN- Susceptibility Weighted Angiography

CFA- Common Femoral Artery

CCA- Common Carotid Artery

IMA- Internal Maxillary Artery

Appendix D

SNO	DSAFISTULA	ConsFISTULA	SW1BTFISTULA	SW2FISTULA	ASL1FISTULA	ASL2FISTULA	SITE1	SITE2	SITE3	SITE4	SITE5	SITE6	SSS1	SSS2	SSS3	SSS4	SSS5	SSS6	TS1	TS2	TS3	TS4	TS5	TS6	TSSS1	TSSS2	TSSS3	TSSS4	TSSS5	TSSS6	TORCULA1	TORCULA2	TORCULA3	TORCULA4	TORCULA5	TORCULA6	FMAGNUM1	FMAGNUM2	FMAGNUM3	FMAGNUM4	FMAGNUM5	FMAGNUM6	PETROUS1	PETROUS2	PETROUS3	PETROUS4	PETROUS5	PETROUS6	OTHERS1	OTHERS2	OTHERS3	OTHERS4	OTHERS5	OTHERS6
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SNO	COG1	COG2	COG3	COG4	COG5	COG6	COG2A1	COG2A2	COG2A3	COG2A4	COG2A5	COG2A6	COG2B1	COG2B2	COG2B3	COG2B4	COG2B5	COG2B6	COG2AB1	COG2AB2	COG2AB3	COG2AB4	COG2AB5	COG2AB6	COG31	COG32	COG33	COG34	COG35	COG36	COG41	COG42	COG43	COG44	COG45	COG46	COG51	COG52	COG53	COG54	COG55	COG56	CVR	CVR_A	CVR_B	CVR_C	CVR_D	CVR_E	PPPNOT	PPPNOT_B	PPPNOT_C	PPPNOT_A	BORDEN1	BORDEN2	BORDEN3	BORDEN4	BORDEN5	BORDEN6
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