To assess the clinico-angiographic profile of patients with brain arteriovenous malformation presenting with native hemorrhage

A thesis submitted for the award of
Doctor of Medicine (D.M.) degree to

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY
TRIVANDRUM -695011, KERALA, INDIA

By

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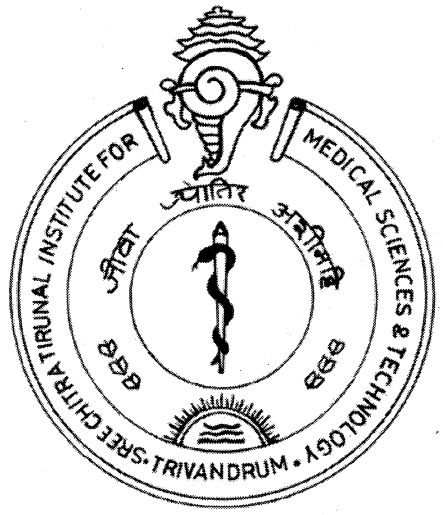

DEPARTMENT OF IMAGING SCIENCES AND INTERVENTIONAL RADIOLOGY

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DEPARTMENT OF IMAGING SCIENCES AND INTERVENTIONAL RADIOLOGY

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CERTIFICATE

This is to certify that this thesis entitled **'To assess the clinico-angiographic profile of patients with brain arteriovenous malformation presenting with native hemorrhage'** has been carried out by Dr. Amit Aslam Khan in this department under my direct supervision and guidance during the year 2006-2009. This study submitted by the candidate, for the award of Doctor of Medicine (DM) degree in Neuroimaging and Interventional Radiology.

This study is a record of the candidate's personal efforts. The work was carried out in the Department of Imaging Sciences and Interventional Radiology, SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY, Trivandrum during his rotatory postings as per schedule, and is to my satisfaction.

1-609

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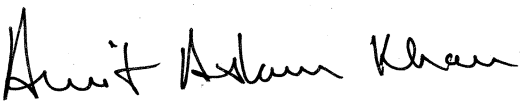
DECLARATION

I, Dr. Amit Aslam Khan, hereby declare that the study titled, **'To assess the clinico-angiographic profile of patients with brain arteriovenous malformation presenting with native hemorrhage'** was carried out by me at SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY, Trivandrum. This study was done under the guidance of Dr. A. K. Gupta, Professor and Head, Department of Imaging Sciences and Interventional Radiology, SCTIMST.



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Amit Aslam Khan

Amit Aslam Khan

Dedicated to

My esteemed Teacher

Late Professor Jayakumar Rockfellar Daniel

his inspiration illuminates me

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Abbreviations

AVM - Arteriovenous malformation

GCS - Glasgow Coma Scale

DVP - Draining vein pressure

ICH - Intracerebral haemorrhage

SAH - Subarachnoid Hemorrhage

IVH - Intraventricular Hemorrhage

SDH - Subdural Hemorrhage

MTT - Mean transit time

PPTA - Persistent primitive trigeminal artery

MCA - Middle cerebral artery

DSA - Digital Subtraction Angiography

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Introduction

An arteriovenous malformation is a tangled cluster of vessels, typically located in the supratentorial part of the brain, in which arteries connect directly to veins without any intervening capillary bed. The lesion may be compact, containing a core of tightly packed arterio-venous loops, or it may be diffuse, with anomalous vessels dispersed among normal brain parenchyma (1).

Arteriovenous malformations account for approximately 11% of cerebrovascular malformations and are more likely than any other types of malformations to be symptomatic. Intracranial vascular malformations are the leading cause of intracerebral hemorrhage in young adults. As shown by Mast et al and Valvanis in separate studies, approximately half of the patients harboring cerebral arteriovenous malformations do present with hemorrhage (2,3).

The presenting ictus of hemorrhage may be fatal, carrying an annual mortality and morbidity rate of 1-4% (4-8).

Relevant factors in the decision to treat an arteriovenous malformation include clinical presentation, patient age, past medical history, neurologic status, patient and family preferences, Spetzler-Martin grade, lesion site and angioarchitecture, and pregnancy. A recent prospective population based study by Miller et al conducted in April 2009 has studied the economic burden of intracranial vascular malformations in adults. They concluded that the costs of healthcare and loss of productivity attributable to intravascular

malformations are considerable, and highest in those aged <65 years, presenting with intracerebral hemorrhage, receiving interventional treatment, and harboring arteriovenous malformations rather than cavernous malformations (9).

Demographic as well as underlying angiographic profile may play a role in defining the cause of cerebral arteriovenous malformations presenting as hemorrhage, thus helping to identify the high risk patients for AVM bleed. Hence defining these factors might help in understanding the disease process better, as well as triaging patients for various modalities of treatment. As the disease is known to affect young individuals in productive age group, and involves considerable cost to the healthcare system, studying the angiographic profile and its associated risk factors becomes of paramount importance.

Keeping the above in mind, we conducted this study to assess the angiographic profile of patients presenting with native hemorrhage due to underlying brain arteriovenous malformation (AVM).

Aim and Objectives

1. To relate the clinical presentation with angiographic findings in patients with brain arteriovenous malformation presenting with native hemorrhage.

2. To correlate the angiographic finding with hemorrhage due to AVM.

Review of Literature

Brain arteriovenous malformations (AVM's) are lesions exhibiting a congenital persistence of primitive arteriovenous shunts. Arrest of vascular development may be the basis for AVM formation. This is substantiated by similarities between AVM morphology and the anastomotic plexuses of developing vasculature in the embryo (10). It is suggested that AVM's form during human embryonic development (40-80 mm length interval) during the sequential formation and absorption of surface veins (11). A discordance of vein formation and resorption may potentially result in the genesis of an AVM.

AVMs consist of 3 components: an arterial feeding component, a nidal sump component consisting of clumps of dysplastic, thin-walled vessels with no intervening cerebral tissue and a venous draining unit. Failure of primitive arteriovenous shunts to evolute to normal intervening capillary networks after the first three months of embryogenesis form the basis for cerebral arteriovenous malformation (4).

Animal model studies conducted by Pile et al with high flow arteriovenous shunts have depicted irregular erosion and thickening of the intima, elastica and muscular layer, resulting in angiopathic irregular thinning and thickening of the arterial walls (12).

Analysis by Mast and Valavanis showed that approximately half of the patients harboring cerebral arteriovenous malformations present with hemorrhage (2,3). Other studies show that the presenting ictus of hemorrhage may be fatal carrying an annual mortality and morbidity rate of 1-4% (4-8).

The hemorrhage can be intraparenchymal, intraventricular, subarachnoid, and subdural or a combination of the same. The presenting ictus of hemorrhage may be fatal carrying an annual mortality and morbidity rate of 1-4%(4-8). Each hemorrhagic episode carries mortality and morbidity rates of 10 to 15% (13) and 20 to 30%, respectively(5,13).

The risk of hemorrhage for AVM's is found to be approximately 2% to 4% per year (7,8) and each hemorrhagic episode to carry mortality and morbidity rates of 10 to 15% (13) and 20 to 30% (5,13).

Clinical series have now established that these lesions pose an annual hemorrhage risk of 2 to 6% (5-8), with quoted yearly morbidity and mortality rates ranging from 1 to 4% (5-7).

Brown and his team have conducted a population-based study of intracranial vascular malformations (IVMS) in Olmsted County, Minnesota. The mean age of patients at first ICH was 38.7 years, which was slightly younger than the mean age at detection for all IVMS (mean 44.2 years, range 3 to 81 years). The peak occurrence of hemorrhage was during the fifth decade of life, and 75% of hemorrhages occurred before the patient reached 50 years of age (14).

Stapf has described brain AVMs as a neurovascular disorder that comes to clinical attention mainly in young adults in their mid-thirties (15). Van Beijnum et al found that the patients with AVM related cerebral bleed were younger, had lower pre-stroke and blood pressure, had a favorable GCS, and were more likely to have a lobar location as compared to the patients with spontaneous bleed. They also reported that the patients in the AVM subgroup had a better outcome. In their opinion, this might have been

partially due to the under diagnosis of AVM in routine clinical practice (16). Although AVM's are more common above the tentorium, in children the ratio of supra to infratentorial AVM is reduced to approximately 3:1 (17). The infratentorial AVM's, particularly cerebellar AVM's have been found to be of importance in children because they carry a very high mortality rate.

Hartmann et al have reported that the morbidity associated with hemorrhage from an AVM is much lower than was reported earlier (18). They showed that 47% of patients with cerebral AVM did not develop neurological deficits, another 37% were able to continue living independent lives after the insult, and only 16% were moderately or severely disabled after suffering hemorrhaged. Perret and Nishoika in their cooperative study of intracranial aneurysms and subarachnoid hemorrhage found an incidence of neurological deficit to be 58% (13). However, Graf et al who studied the natural history of cerebral AVMS that bled documented an incidence of 81% for the same(8). In a cooperative study based on 6368 cases, the incidence of re-hemorrhage following the first incidence was found to be lower in cerebral arteriovenous malformations when compared to patients with ruptured intracranial aneurysms (19).

Separate studies conducted by Kader et al and Spetzler et al have shown that larger AVM's present mostly with seizures (20,21). Also, infratentorial hemorrhages have been found to be less likely to cause seizures, as shown by Khaw et al in their study on the association of infratentorial brain AVM's with hemorrhage at initial presentation (22). Turjman et al in multivariate analysis of angioarchitectural characteristics in patients with epilepsy harboring an AVM have found 6 parameters to be predictors of epilepsy viz., cortical location of the AVM; feeding by the

middle cerebral artery (MCA); cortical location of the feeder; absence of aneurysms; presence of varices in venous drainage; and finally the association of varix and absence of intranidal aneurysms (23).

Aneurysms associated with AVMs

Hemodynamic overload may result in aneurysms being associated with arteriovenous malformations, as shown by various studies(20,24-27). This is supported by the fact that there is great disparity between the incidence of feeding artery aneurysms in patients with intracranial arteriovenous malformations and otherwise (28). Nornes and Grip who studied the hemodynamic aspects of cerebral AVMS, have demonstrated that there is rapid flow velocity (70cm/sec) in large arteries, however highest velocities for smaller arteries was found in several patients (29).

Lasjaunias et al reviewed the case records of 101 patients with cerebral AVM and found an incidence of 23% with general association of aneurysm and cerebral AVM. They classified aneurysms into 3 types, based on their angiographic assessment viz 1. distal or intralesional aneurysms (19%); 2. proximal aneurysms on vessels directly supplying the AVM (57%); and 3. remote or dysplastic, which are unrelated to the inflow vessels (24%) (26). In addition, Perata et al have defined the pedicle aneurysm as those along the course of the feeding artery, but remote from the Circle of Willis and AVM itself. Knowledge about the pedicle aneurysm is important as they represent a significant indicator of hemorrhage source and also pose a risk of recurrent hemorrhage (30).

Regression of these feeding artery aneurysms is known following complete obliteration of the arteriovenous malformation (26,31). The distal

flow related aneurysms tend to regress more (80%) in comparison to proximal aneurysms (4%) on complete obliteration of the cerebral arteriovenous malformation (32).

Gao et al have found that the pressure and flow changes are more aggressive distally near the nidus while quite meek at the circle of Willis (33). They used a computer simulation model to estimate the magnitude of pressure changes along the vascular tree during stepwise occlusion of an AVM. Prior to AVM obliteration, there is a progressive decrease in arterial pressure along feeding artery pedicles. As the AVM is occluded and flow decreases, the mean arterial pressure increases in a nonlinear fashion, with 70 to 90% occlusion being required to increase the pressure halfway to the eventual maximum value. As the AVM is gradually occluded, the blood velocity and shear stress decrease while the arterial pressure increases. Furthermore, the pressure and flow changes near the circle of Willis are relatively minor, although they are quite profound in distal vessels near the AVM nidus.

In the systematic review conducted by Rinkel et al on the prevalence and risk of rupture of intracranial aneurysms, the prevalence of saccular aneurysm is 2% in the adult population, with majority being small in size and having a annual risk of rupture of less than 1% (34). However, aneurysms associated with intracerebral arteriovenous malformations have a reported wide variation of prevalence between 10%-58% (5,8,13,23,26,27,31).

Predisposing factors for hemorrhage

Within a population of patients with AVMs there may exist subgroups that have either higher or lower risks of hemorrhage. Identifying at the outset into which subgroup a patient fits would be beneficial in planning management of the lesion.

There have been studies to assess the higher or lower risks of hemorrhage. The coexistence of intranidal or perinidal aneurysms, the presence of deep venous outflow restriction, or the finding of high feeding artery pressures are features that have been shown to correlate with a higher risk of hemorrhage (21,35-37). However, many patients with AVMS do not have lesions exhibiting these overt predictive features but still suffer an intracerebral hemorrhage (ICH).

Langer et al have predicted hypertension as one of the risk factors to be associated with the risk of hemorrhagic presentation of cerebral arteriovenous malformation (38). In contradiction, Szabo et al have not found hypertension to be a risk factor for spontaneous intracranial hemorrhage (39).

Hemodynamic risk factors are also thought to play important roles in hemorrhage associated with AVM's, and high-perfusion arterial pressure has been shown to represent an especially high risk factor (20,21,38,40-42).

The coexistence of intranidal or perinidal aneurysms, the presence of deep venous outflow restriction, or the finding of high feeding artery pressures are features that have been shown to correlate with a higher risk of hemorrhage (21,35-37). Studies of intravascular pressure have revealed that

it was higher in the feeding arteries of ruptured than unruptured AVM's (20,21,40-42).

There has not been any consensus on the relationship between draining vein pressure (DVP) and the risk for hemorrhage. Nornes and Grip who have studied the hemodynamic aspects of cerebral AVM's have reported that average DVP tended to be higher in AVM patients with hemorrhage than in those without hemorrhage (29). However, their sample size had been small, and their results have been inconclusive. Kader et al (20) have found no difference in DVP between ruptured and unruptured AVMs.

More recently, Miyasaka et al (42) have demonstrated that the pressure in draining as well as feeding vessels is significantly higher in AVM's with than without hemorrhage. Furthermore, in their study population, DVP was inversely related to the number of draining veins and the size of the AVM's. Several studies have found that DVP elevation may be attributable to the presence of a central venous drainage pattern, stenotic or occlusive involvement of the venous drainage system, or a low number of draining veins (36,38,42,43).

Out of the associated factors to be taken into consideration in case of bleed, size and location of the AVM are found to be important. Small cerebral arteriovenous malformations are found to present more frequently with hemorrhage. This has been concluded in separate studies by Graf et al and Guidetti B (8,44). However, Stephani MA et al have found that large and deep brain AVM's are more prone to hemorrhage. They argued that small AVM's tend to present with hemorrhage, as they do not tend to

produce dangerous symptoms of seizures or bruits in contrast to their larger counterparts (45).

Turjman et al in a series of 100 patients with AVM's treated between 1987 and 1990 found that the basal ganglia was the only significant location associated with hemorrhagic presentation. Temporal and occipital locations have also been identified as risk factors for bleeding. Deep seated cerebral arteriovenous malformations as well as certain sites in the neuroparenchyma like cerebellum, brain stem, temporal lobe, insular, callosal and periventricular region are susceptible for hemorrhage as studied by Stephani MA et al in their study of angioarchitectural factors in brain arteriovenous malformations (45).

Small nidus size (20,21,38,41,42,46) and deep seated location of AVM (36,43,47); pathomorphological changes viz presence of arterial aneurysms (32,36,47); venous drainage (single draining vein) (41,42,45) and impaired venous drainage (41,43,48) have been proven to be the angiographic predisposing factors for hemorrhage in multitude of studies.

However not all patients harboring underlying cerebral arteriovenous malformations presenting with hemorrhage have the above angiographic factors. Studies have been done comparing cerebral AVM patients presenting with hemorrhage and otherwise. Short mean transit times (MTT) were found in feeding arteries of patients presenting with hemorrhage, thus predisposing them to high pressures. In a study by Todaka et al, who analyzed the mean transit time of contrast in ruptured and unruptured arteriovenous malformations, a short mean transit time with smaller vessel diameters did result in higher feeding artery pressures in small cerebral

arteriovenous malformations. The small size of the AVM would also predispose to hemorrhage as they have a short mean transit time as demonstrated by Todaka et al (49). Stephani et al found that fast nidal inflow and a high MTT ratio of drainers to feeders are risk factors for hemorrhage in patients with AVMs. A high MTT ratio of drainers to feeders is the most reliable and feeder-to-drainer ratio is not an independent risk factor, but a numerical expression of the degree of mismatch between nidal inflow and outflow, which are affected by nidus size, number and stenotic status of drainers, and drainage pathway (45).

Spetzler et al have analyzed 24 AVM's, in which they measured the feeding artery pressures intraoperatively. Ten of the patients had presented with hemorrhage, and the other 14 experienced other neurological symptoms. Patients with hemorrhages had mean feeding artery pressures of 90% of systolic blood pressure compared with 47% of systolic in those with other symptoms. The mean feeding artery pressures were higher in the smaller AVM's regardless of the mode of presentation and that there was no fluctuation in the systemic arterial pressure. By comparison, larger AVM's did demonstrate lower resistance, high-flow shunts, and presented with neurological symptoms secondary to surrounding ischemia from the proximal steal or "suck" of the shunt. Evidence from various studies shows that large, high-flow AVM's are fed by low-pressure arteries (21).

Various innovative and risk stratifying methods have been employed to explore the other possible underlying causes leading to hemorrhage, of which hemodynamic risk factors like feeding arterial pressures are foremost (20,21,38,40-42).

Young et al have tried to measure the pressure gradients across the nidus of an AVM to delineate any relationship with the deep venous pressures. In 21 patients there was positive correlation between feeding arterial pressures and draining venous pressures associated with the AVM, particularly when the head (as opposed to the heart) was the reference point. These authors noted that changes in the systemic mean arterial and central venous pressures affect the AVM arterialized draining veins more as venous structures than arterial (50).

Spetzler et al showed that AVM's exhibiting long contrast material uptake and/or dilution times possess either increased capacitance or increased resistance to blood flow. The latter would be manifest as increased feeding artery pressures compared with mean systemic pressure, as directly demonstrated by Spetzler et al (21). On angiographic studies, the hold up of blood at the nidus would be apparent as a delay in contrast material passing through the nidus and reaching the venous phase.

Hirai et al have shown that the presence of intranidal aneurysms and venous stenosis does contribute to risk of hemorrhage in cerebral AVM's (51). Flow related (41%) and intranidal (63%) aneurysms were seen in patients presenting with cerebral AVM's and hemorrhage (32). The feeding arteries have been found to be the favored site of aneurysm in the study by Brown et al (35). In contradiction, only 5 aneurysms were detected in association with cerebral AVM's in 154 patients in the statistical analysis on the location of aneurysms associated with intracranial AVM's conducted by Okamoto et al (28).

Nornes and Grip have demonstrated that there is rapid flow velocity (70cm/sec) in large arteries, however highest velocities for smaller arteries

were found in several patients (29). This high velocity gives rise to shear stress in the vessels, causing weakening of the vessel wall, which gives rise to the formation of aneurysms.

While Redekop documented that 0.8% of unrelated vessels revealed aneurysms in patients with cerebral arteriovenous malformation (32) no association was seen between presentation as initial hemorrhage in patients with cerebral arteriovenous malformation and aneurysm (45,52).

In the systematic review conducted by Rinkel et al on the prevalence and risk of rupture of intracranial aneurysms, the prevalence of saccular aneurysm was found to be 2% in the adult population, with majority being small in size and having a annual risk of rupture of less than 1% (34). However, aneurysms associated with intracerebral arteriovenous malformations have a reported wide variation of prevalence between 10%-58% (5,8,13,26,27,31,53).

Turjman et al have found that intranidal or perforating vessels contributed to 70% of the aneurysms associated with cerebral AVMS (53). The venous drainage compartment of an AVM plays a role in hemorrhagic incidence of a cerebral arteriovenous malformation. Over time the draining veins too change in their in-situ pressures and become arterialized. These arterialized veins are susceptible to changes in the systemic mean arterial and central venous. Thus, a sudden rise in systolic arterial pressure may increase the in-situ venous pressures. As a result factors contributing towards venous hypertension have also been implicated in the hemorrhagic incidence in patients with cerebral AVM. Thus, it is no surprise that deep venous pressures are inversely related to the number of draining veins and size of the arteriovenous malformation (37). However Turjman et al did not

find lone venous drainage to be a factor responsible for hemorrhage. They felt that the discrepancy could be due to selection bias in recruitment of the patients (54). A series of 340 patients described by Duong et al had deep venous drainage as a significant factor for hemorrhagic presentation in a multivariate analysis (40).

Venous ectasia was defined as "a markedly ectatic vein" or as "pouches," usually associated with a stenotic draining vein. Reduction of 50% or more of the vein diameter defined venous stenosis (45,54). Venous stenosis in high flow draining veins was suggested by Hademenos and Massoud as a risk factor for hemorrhage (48).

Mathematical models relying on electrical network analysis have studied the effects on the different compartments of an AVM (21,37,48). Hademenos et al used a biomathematical model based on network analysis to qualitatively and quantitatively investigate the altered hemodynamic of venous drainage impairment of an intracranial AVM and the corresponding risk of hemorrhage. The model was designed to accurately characterize anatomic landmarks and features clinically observed in human AVMS. Since they found the reduction of 50% diameter of vein to be a non uniform definition of venous stenosis, hence they investigated the effects of various (0% to 100%) degrees of narrowing in the draining veins on the risk of nidus rupture. On the basis of biomechanical properties of the intranidal vessels, it is possible that the rupture occurs when the cumulative hemodynamic stresses of the vessel wall exceed its elastic modulus. The site of a typical AVM rupture has been postulated to occur at the venous end of the nidus. The mechanisms responsible for this in the presence of venous drainage impairment have been thought to occur because of retrograde venous

hypertension yielding regional intranidal hypertension with consequent rupture of delicate AVM vessels. The presence of significant prestenotic draining vein hypertension has been confirmed by Miyasaka et al during intraoperative measurements in three patients with marked segmental stenosis and a history of AVM rupture. Stenosis or occlusion of a high-flow draining vein induces a significant redistribution of blood into the weak plexiform vessels of the opposing region of the nidus, causing a hemodynamic overload and an increased risk of rupture.

In a study by Willinsky et al, stenosis was seen in cerebral arteriovenous malformations presenting as hemorrhage in young adult females (47). Previous studies show that deep venous or hindered venous drainage in the form of stenosis or occlusion and presence of a lone draining vein does contribute towards increasing the deep venous pressure resulting in hemorrhage (36,38,41,43,52,55). However, the report of Turjman et al describes selective investigation in all of the 100 patients seen. They found no association between venous stenosis and initial bleeding (54).

Perforating feeding vessels and periventricular location of the AVM also lead to an increase in the incidence of hemorrhage as shown by Turjman et al (54).

Persistent primitive trigeminal artery (PPTA) has been found as the most common anomaly of the carotid-basilar anastomosis and is usually an incidental finding with an incidence of 0.1-0.6%. However, the reported incidence of association of PPTA with cerebral AVM is 4.5% (56).

Risk Stratification

Grading systems have been devised to study the morbidity and mortality associated with the treatment of AVM's. The Spetzler and Martin grading system attempts to predict the risk of surgical morbidity and mortality by assigning points to an arteriovenous malformation on the basis of its size, the eloquence of the adjacent brain, and the pattern of venous drainage. The grade of a lesion is determined by summing the points given in each of the 3 categories. Surgical treatment of a grade I arteriovenous malformation, therefore, presents little risk of morbidity and mortality. By contrast, a grade V lesion is associated with significant risk (57).

Patients and Methods

We conducted a retrospective cross sectional study of patients with underlying brain arteriovenous malformation (AVM), presenting with native hemorrhage to SCTIMST, Trivandrum. A total of 112 patients (72 males, 40 females; median age 28 years, age range 4 to 58 years) were recruited in this study after they met the required inclusion criteria from January 2001 to December 2008 were reviewed.

Inclusion Criteria:

- Patients consenting to the procedure.
- Patients presenting with hemorrhage.
- Belonging to all age groups.
- All patients who could undergo imaging.

Exclusion criteria:

Absolute:

- Patients who did not consent to the procedure.
- Patients who did not suffer from hemorrhage.
- Patients who could not undergo imaging.

Relative:

- Coagulopathy

The clinical data of the patients was obtained by reviewing their case sheets obtained from the Medical Records Department (MRD) & the imaging data was obtained from the DSA lab records. From these, the data regarding clinical presentation, angiographic characteristics were obtained.

Clinical Assessment

Demographic data included the age and sex of the patient. The date of admission, the time since ictus and the details of clinical presentation, including the Glasgow Coma Scale were recorded. A thorough history noting the past and present complaints, social and family history, history of underlying disorders and risk factors, details of treatment were recorded.

Investigations

Appropriate hematological, biochemical and serological investigations were done, including complete blood count, prothrombin time, activated partial thromboplastin time, blood glucose, renal function tests, liver function tests, lipid profile, serum electrolytes and screening for HIV and Hepatitis B infection.

Imaging

The patients underwent computerized tomography (CT) scan, magnetic resonance imaging (MRI), and digital subtraction angiography (DSA), as per the requirements of the case. Cross sectional imaging was performed if the patient consented for the same.

CT Brain

CT of the brain was acquired using GE High Speed single slice series – CT/i. A plain scan of the brain was obtained with the patient supine and head within the head holder. The symmetry of the position was adjusted using laser localizers. Initially a lateral scanogram was obtained and slices planned along a line passing through the external auditory meatus and the outer canthus of orbit. The slice thickness was 3 to 5 mm for the posterior fossa and 7 to 10 mm for the supratentorial compartment depending on the expected site of the cerebral AVM.

The patients presenting in the chronic phase of ictus without hemorrhage were subjected to hand injected contrast study using 40 ml Omnipaque through a 20 gauge peripheral cannula with adjustment of the mA factor

Patients were referred for CT Angiography due to patient presenting with subarachnoid hemorrhage. A CT angiogram was performed using a helical scanning mode with slice thickness of 1mm; FOV of 20 cm, a maximum pitch of 1.4 with standard reconstruction using 120 kV and 230 mA having acquisition time of 0.8 second. A pre-group delay of 15 seconds was given (depending on patient's heart rate) and 60-100 ml of Omnipaque contrast was injected using ENVISION CT pressure injector with a flow rate of 4 ml/second at 300 psi.

MRI Brain

MRI examinations were performed on 1.5 T MR System (Avanto; Siemens, Erlangen, Germany) and a 12-channel phased array head coil. After scout view MRI, the examination protocol consists of pre-contrast conventional MRI followed by DWI, SWI and post-contrast T_1 weighted images. Conventional MR images were obtained with T_1 [spin echo (SE), 442/15] and turbo T_2 [turbo spin echo (TSE), 3510/110] weighted spin echo sequences (both with a 382 x 512 matrix, 5 mm slice thickness and 1 average). DWIs were acquired using single-shot echo-planar imaging (EPI) sequence at multiple levels. About 20 slices of 5 mm thickness were obtained [repetition time (TR) 3,500 ms, echo time (TE) 105 ms, field of view 230 x 230, matrix size 191 x 192, b values of 0 and 1,000 mm^2 s-1] in three orthogonal directions. The SWI sequence parameters were: TR (repetition time), 48 ms; TE (echo time), 40 ms; flip angle, 20°; bandwidth, 80 kHz; section thickness, 2 mm, with 56 sections in a single slab; matrix size, 512 x 256. A TE of 40 ms was chosen to avoid phase aliasing, and a flip angle of 20° was used to avoid nulling the signal from pial veins located within the cerebral spinal fluid (CSF). The acquisition time was 2.58 min with the use of iPAT factor-2. After post-processing nine to 12 thick MIP slabs are generated and were performed along the z direction. CE MRA was done using a FLASH 3D sequence with the following parameters were TR/TE – 2.8/1 ms, flip angle of 30°, slice thickness of 1 mm, a matrix size of 205 x 384 with a total acquisition of 15 seconds. A total volume of 15 ml of Gd- DTPA (Omniscan; GE Healthcare) contrast followed by 15 ml saline at a flow rate of 0.8-1.1 ml/sec was injected using a pressure injector with care bolus technique. T1WI with fat saturation post contrast were obtained using a 2D spin echo sequence with flow compensation using the following

parameters: TR of 850 ms, TE-110 ms, flip angle of 90°, slice thickness of 5 mm and a matrix of 156 x 256.

The cross sectional data was assessed with regard to the location, size and extent of the AVM and associated features of hemorrhage, edema, mass effect, hydrocephalous and atrophy.

DSA

Informed consent was obtained for the same in all patients. DSA was performed using ADVANTEX LCV single plane floor mounted C arm digital subtraction angiography unit by GE (GE Milwaukee, USA) with a 125 KV, 1000 mA capacity tube. It has a 12 inch with 4 zoom options, maximum frame rate of 8frames/sec and LIH, road map, re masking and edge enhancement facilities.

Anesthesia

The procedure was done under local anesthesia through the femoral route using single or double wall puncture technique after premedication (Injection Pethidine 50mg I.M. & Inj. Phenergan 25mg I.M. for adults and as per body weight for children). Arterial line was inserted for continuous monitoring of blood pressure and if hypotensive anesthesia was used. Central venous line was inserted for guiding fluid management in case of blood loss. Premedication with an opoid or benzodiazepine, followed by intravenous induction using a suitable agent and non-depolarizing muscle relaxant was employed to facilitate intubation of trachea. Controlled ventilation was employed intraoperatively, which also helped in controlling

intracranial pressure. Hypotension was induced if required by the use of vasodilators. Brain bulk was reduced by hypotension, hypocapnia, hypothermia and barbiturates. Blood loss was managed vigilantly, as was brain edema. The patient was managed in the intensive care unit, with special care to avoid brain edema, manage blood loss, monitor intracranial pressure, neurological status and hemodynamics.

A detailed six vessel diagnostic cerebral DSA consisting of bilateral vertebral, internal and external carotid artery hand injections in A-P, lateral and oblique views with magnification and high frame rate was performed.

The angiograms were acquired using the following factors in the various projections.

Table 1: DSA Tube Factors In Different Projections

PROJECTIONS	KV	MA
AP	75	320
LAT	60	250
OBLIQUE	75	360

The feeding artery was imaged, along with the venous segment and the results noted, along with the flow characteristics of the AVM. The name of the artery or arteries feeding the malformation and the extent of these feeders were noted. The presence of an underlying aneurysm as well as the AVM was studied in detail.

Venous Morphology: Venous ectasia was defined as "a markedly ectatic vein" or as "pouches," usually associated with a stenotic draining vein. Reduction of 50% or more of the vein diameter defined venous stenosis (45,54).

The imaging features noted were:

The site, size, involvement of the eloquent cortex, details of the hemorrhage (site, size, age of bleed).

The location was classed as:

Supra and infratentorial; parenchymal, periventricular, intraventricular; superficial versus deep; right versus left dexterity; and involvement of eloquent cortex.

The AVM was classified as:

Small (< or = 3 cm's), medium (3-6 cm's), and large (> 6 cm's).

The same dimensions were used to grade the size of hemorrhage as well.

Post-hemorrhage features and the time to DSA since ictus were recorded.

Grading

Finally, after imaging studies, the AVM was graded. The patients were graded in five categories according to the Spetzler-Martin grading system.

Table 2: Spetzler Martin Grading of Brain AVM		
Variables		Points
Size		
	< 3 cm	1
	3-6 cm	2
	>6 cm	3
Venous Drainage		
	Superficial	0
	Deep	1
Brain Region		
	Non Eloquent	0
	Eloquent	1

Statistical Analysis

Descriptive statistics were used to summarize the data. Data for different age groups (pediatric, young and middle aged) were analyzed separately. Statistical analysis was done using the SPSS software.

RESULTS

A total of 112 patients were recruited in the present study of native hemorrhage with underlying brain arteriovenous malformations.

Age:

The minimum age group of patients recruited was 4 years with the maximum being 58 years with a mean age of 29 years. Demographically, 55 (49.1%) were young adults, 32 (28.6%) were pediatric and adolescents while 25 (22.3%) were middle aged (Table 3).

Table 3. Age of 112 Patients recruited	
Minimum Age of patients	4 years
Maximum Age of patients	58 years
Median Age	28 years
Number of patients in 0-19 years age group	32 (28.6%)
Number of patients in 20-39 years age group	55 (49.1%)
Number of patients in 40-59 years age group	25 (22.3%)

Gender:

Predominantly included were males 72 (64.3%) with females being 40 (35.7%). Thirty six (50%) of the males were young adults, 16 (22.2%) were children or adolescents while 20 (27.8%) were middle aged. Nineteen (47.5%) of females were young adults, 16 (40%) were children or adolescents while only 5 (12.5%) were middle aged (Table 4).

Table 4. Gender Distribution	Males	Females
Gender of 112 patients recruited	**72** (64.3%)	**40** (35.7%)
Gender of patients in 0-19 years age group	16 (22.2%)	16 (40%)
Gender of patients in 20-39 years age group	36 (50%)	19 (47.5%)
Gender of patients in 40-59 years age group	20 (27.8%)	5 (12.5%)

Time of presentation:

Of the 112 patients, 22 (19.65%) presented in the acute period (1-3 days), 20 (17.9%) in the sub acute period (8-30 days) while majority 70 (62.5%) in the chronic timeframe. 16 patients presented after 1 year of ictus. Thrice as many patients had a chronic presentation, as compared to acute onset.

Clinical presentation:

Seven (6.3%) of patients Glasgow Coma Scale (GCS) was not defined at admission. Majority of the patients 94 (83.9%) had a favorable GCS (13-15), 5 (4.5%) were in the borderline GCS (7-12) while 6 (5.4%) were critical GCS (4-7).

Headache was present in 92 (82.1%) of the patients, followed by vomiting 74 (66.1%), in 49 (43.8%) and altered sensorium 42 (37.5%) (Table 5).

Table 5. Clinical presentation of 112 patients		
S.No.	Symptom	Number (Percentage)
1.	Headache	92 (82.1%)
2.	Altered Sensorium	42 (37.5%)
3.	Loss of consciousness	49 (43.8%)
4.	Vomiting	74 (66.1%)
5.	Recent memory loss	3 (2.7%)
6.	Paresis	40 (35.7%)
	Hemiparesis	30 (26.8%)
	Monoparesis	7 (6.3%)
	Quadriparesis	3 (2.7%)
7.	Aphasia	6 (5.4%)
8.	Impaired vision	18 (16.1%)
9.	Diplopia	3 (2.7%)
10	Giddiness	7 (6.3%)
11.	Seizures	26 (23.2%)
12.	Imbalanced gait	13 (11.6%)
13.	Dysarthria	9 (8%)
14.	Neck Pain	6 (5.4%)
15.	Hiccups	1 (0.9%)
16.	Sensory Loss	3 (2.7%)
17.	Facial Palsy	14 (12.5%)

Risk Factor:

Only two patients (1.8%) had hypertension as an underlying risk factor, they belonged to the younger age group.

Investigations:

Table 6: Positive Investigations of 112 patients		
S.No.	Investigation	Number(Percentage)
1.	HIV	1 (0.9%)
2.	Dyslipidemia	12 (10.7%)
3.	Anemia	16 (14.3%)
4.	Leukocytosis	25 (22.3%)
5.	Leukopenia	2 (1.8%)
6.	Elevated ESR	24 (21.4%)
7.	Hyperglycemia	10 (8.9%)
8.	Abnormal Liver Function Tests	5 (4.5%)

***Imaging* (Tables 7-29):**

The neuroparenchyma was most commonly involved site (Table 7). Majority of arteriovenous malformations out of the 112 patients studied were in the supratentorial compartment 100 (89.3%) [Table 8], while 12 (10.7%) were in the infratentorial compartment [Table 9]. Parenchymal distribution was predominant in both supra and infratentorial region, contributing 84% and 91.7%, respectively. Thirteen (11.6%) patients had lesions in deep grey matter; only one (3.1%) pediatric patient had involvement of deep grey matter.

***Site of AVM*:**

Majority of AVM were supratentorial 100 (89.3%) while 12 (10.7%) were in the infratentorial compartment.

Table 7: Location of AVM in 112 patients		
S.No.	Location of AVM	Number(Percentage)
1.	Parenchymal	95 (84.8%)
2.	Periventricular	13 (11.6%)
3.	Intraventricular	4 (3.6%)

In the supratentorial compartment:

Table 8: Location of AVM in the Supratentorial Compartment		
S.No.	Supratentorial Location (n= 100)	Number(Percentage)
1.	Parenchymal	84 (84%)
2.	Periventricular	13 (13%)
3.	Intraventricular	3 (3%)

In the infratentorial compartment:

Table 9: Location of AVM in the Infratentorial Compartment		
S.No.	Infratentorial Location (n= 12)	Number(Percentage)
1.	Parenchymal	11 (91.7%)
2.	Intraventricular	1 (8.3%)

13 (11.6%) were present in the deep grey matter.

Table 10: Hemispheric Distribution of AVM		
S.No.	Dexterity of AVM	Number(Percentage)
1.	Right	49 (43.8%)
2.	Left	57 (50.9%)
3.	Midline	5 (5.4%)

Involvement of Eloquent Cortex:

Thirty eight (33.9%) of 112 patients had involvement of eloquent cortex (Table 11).

Table 11:	**Eloquent Cortex involvement**	
S.No.	Site of eloquent cortex	Number(Percentage)
1.	Sensorimotor	14 (12.5%)
2.	Basal Ganglia	8 (7.1%)
3.	Thalamus	7 (6.3%)
4.	Hypothalamus	3 (2.7%)
5.	Visual	3 (2.7%)
6.	Brainstem	2 (1.8%)
7.	Cerebral Peduncle	1 (0.9%)

Size of AVM:

Ninety one patients had small malformations of less than 3 cm's size, 20 were medium sized and only one had a malformation of greater than 6 cm, respectively (Table 12).

Table 12:	**Size of AVM in 112 patients**	
S.No.	Size of AVM	Number(Percentage)
1.	Small < 3 cm's	91 (81.3%)
2.	Medium 3-6 cm's	20 (17.9%)
3.	Large >6cm's	1 (0.9%)

Hemorrhage:

All patients presented with hemorrhage in the brain. Large sized hemorrhage measuring more than 6 cm's was seen in 57 (50.9%) of

patients (Table 13). Hemorrhage was limited to the brain parenchyma in 52 (46.4%) of patients. Hemorrhage involving the deep grey matter was seen in 9(8%) patients (Table14).

Table 13: Size of hemorrhage in 112 patients		
S.No.	Size of hemorrhage	Number(Percentage)
1.	Small < 3 cm's	43 (38.4%)
2.	Medium 3-6 cm's	12 (10.7%)
3.	Large >6cm's	57 (50.9%)

Table 14: Compartmentalization of hemorrhage in 112 patients		
S.No.	Compartmentalization of hemorrhage	Number(Percentage)
1.	Parenchymal	52 (46.4%)
2.	Parenchymal + Intraventricular	28 (25%)
3.	Intraventricular (IVH)	16 (14.3%)
4.	Subarachnoid (SAH)	6 (5.4%)
5.	Parenchymal + Intraventricular + SAH	3 (2.7%)
6.	Parenchymal + SAH	3 (2.7%)
7.	SAH + IVH	2 (1.8%)
8.	Parenchymal + IVH + SAH + SDH	1 (0.9%)
9.	Parenchymal + SAH + SDH	1 (0.9%)

Table 15: Age of Hemorrhage in 112 patients		
S.No.	Age of hemorrhage	Number(Percentage)
1.	Acute	24 (21.4%)
2.	Sub acute	17 (15.2%)
3.	Chronic	71 (63.4%)

Imaging features post hemorrhage:

Atrophy of the brain parenchyma was present in 22 (19.6%) of patients, edema surrounding the hematoma in 42 (37.5%), post- hemorrhage

hydrocephalus in 39 (34.8%) and mass effect due to hematoma in 3 (33%), respectively (Table 16).

Table 16: Hemorrhagic sequelae		
S.No.	Imaging features post hemorrhage	Number(Percentage)
1.	Edema surrounding hematoma	42 (37.5%)
2.	Hydrocephalus post hemorrhage	39 (34.8%)
3.	Mass effect caused by hematoma	37 (33%)
4.	Atrophy of brain parenchyma	22 (19.6%)

In 112 patients recruited, in majority of the cases (n=74), DSA was done after 30 days of ictus. Only in 14 patients was the DSA done within 0-7 days of presentation. Forty (35.7%) patients underwent DSA 100 days after the ictus (Table 17).

Table 17: Time of DSA since Ictus		
S.No.	Timing of DSA since ictus	Number(Percentage)
1.	Acute (0-7 days)	14 (12.5%)
2.	Sub acute 8-30 days	24 (21.4%)
3.	Chronic >30 days	74 (66.1%)

On digital subtraction angiography, 80.4% of the arteriovenous malformations had compact nidus. Venous ectasia and presence of steal was seen in 49.1% of patients. Kinking of the draining vein was seen in 42 % of patients while 13.4% had presence of venous sac in the draining vein (Table 18).

Table 18: Angiographic features on DSA		
S.No.	Angiographic features	Number(Percentage)
1.	Compact nidus	90 (80.4%)
2.	Presence of steal	55 (49.1%)
3.	Presence of intranidal arteriovenous fistula	5 (4.5%)
4.	Presence of angiomatous change	3 (2.7%)
5.	Stenosis of draining vein	1 (0.9%)
6.	Venous ectasia	55 (49.1%)
7.	Kinks in draining vein	47 (42%)
8.	Presence of venous sac in draining vein	15 (13.4%)
9.	Occlusion of draining vein	1 (0.9%)
10.	Presence of venous reflux	1 (0.9%)
11.	Presence of straight sinus anomaly	1 (0.9%)

Table 19: Associated Findings on DSA		
S.No.	Associated Findings on DSA	Number(Percentage)
1.	Presence of Persistent Trigeminal artery	1 (0.9%)
2.	Presence of distant 2 AVM nidus	2 (1.8%)
3.	Presence of Dural AVF	1 (0.9%)
4.	Presence of Falcine sinus	1 (0.9%)
5.	Presence of Occipital sinus	2 (1.8%)

In 53.6% of the cases the arteriovenous malformation was being fed from the anterior circulation or a combination of anterior and posterior circulation as in 29.5%. A single feeding artery was seen in 45.5% of the total patients

while 31.3% had double and the remaining had three or more feeding arteries, respectively (Table 20).

Table 20: Feeding artery on DSA		
S.No.	Feeding artery on DSA	Number(Percentage)
1.	From Anterior Circulation	60 (53.6%)
2.	From Posterior Circulation	19 (17%)
3.	From Anterior and Posterior Circulation	33 (29.5%)
4.	Single feeder	51 (45.5%)
5.	Two feeders	35 (31.3%)
6.	3 or > 3 feeders	26 (23.2%)

The middle cerebral artery or its branches in isolation or with other arteries was the most commonly recruited in 62 (55.3%) patients, followed by anterior cerebral artery 45 (40.1%) and posterior cerebral artery 44 (39.2%) respectively (Table 21).

Table 21: Name of feeding artery on DSA		
S.No.	Name of feeding artery on DSA	Number(Percentage)
1.	MCA	62 (55.3%)
2.	ACA	45 (40.1%)
3.	PCA	44 (39.2%)
4.	Anterior Choroidal	7 (6.3%)
5.	SCA	7 (6.3%)
6.	PICA	5 (4.5%)
7.	AICA	3 (2.7%)
8.	ICA	3 (2.7%)
9.	ECA	3 (2.7%)
10.	Basilar	2 (1.8%)
11.	Vertebral	1 (0.9%)

Cortical feeders were seen in 73 out of 112 patients, 12 had cortical and perforators, while 23 patients had perforators on angiography (Table 22).

Table 22: Type of arterial feeders on DSA		
S.No.	Type of arterial feeders on DSA	Number(Percentage)
1.	Cortical	73 (65.2%)
2.	Perforators	23 (20.5%)
3.	Cortical + Perforators	12 (10.7%)
4.	Pial + Dural	2 (1.8%)
5.	Perforators + Dural	1 (0.9%)
6.	Cortical + Perforators + Pial	1 (0.9%)

AVM's with associated underlying aneurysms were found in 19 (17%) of patients. Out of these, 12, majority, had feeding artery aneurysm and 6 had intranidal aneurysm (Table 23).

Table 23: Presence of underlying aneurysm on DSA		
S.No.	Presence of underlying aneurysm on DSA (n=19)	Number
1.	Feeding artery aneurysm	12
2.	Intranidal aneurysm	6
3.	Unrelated aneurysm	1

Flow characteristics within the AVM:

Defining the cerebral AVM's according to their hemodynamics, 63.4% had high flow within. In the residual number of patients, 26.8% had moderate flow, 7.1% had mild flow and 2.7% had low flow, respectively (Table 24).

Table 24: Flow characteristics within the AVM on DSA		
S.No.	Flow characteristics within the AVM on DSA	Number(Percentage)
1.	High	71 (63.4%)
2.	Moderate	30 (26.8%)
3.	Mild	8 (7.1%)
4.	Low	3 (2.7%)

Venous Drainage of AVM:

Superficial venous drainage was seen in 43.8% of patients, while deep venous drainage and a combination of both superficial and deep venous drainage was seen in 29.5% and 26.8% of patients respectively. Thus 56.3% of the patients recruited deep veins for their drainage (Table 25). A single draining vein was seen in 46.4% of patients, 17% had two and 36.6% had three or more draining veins, respectively (Table 26).

Table 25: Venous Drainage of AVM on DSA		
S.No.	Venous Drainage of AVM on DSA	Number(Percentage)
1.	Superficial	49 (43.8%)
2.	Deep	33 (29.5%)
3.	Superficial and Deep	30 (26.8%)

Table 26: Number of veins draining the nidus on DSA		
S.No.	Number of veins draining the nidus on DSA	Number(Percentage)
1.	Single draining vein	52 (46.4%)
2.	2 draining veins	19 (17%)
3.	3 or > 3 draining veins	41 (36.6%)

In 59 patients, a single vein reached the sinus, while in 36 patients three or more veins reached the sinus (Table 27).

Table 27: Number of veins reaching the sinus on DSA		
S.No.	Number of veins reaching the sinus on DSA	Number(Percentage)
1.	Single vein reaching sinus	59 (52.7%)
2.	2 veins reaching sinus	17 (15.2%)
3.	3 or > 3 veins reaching sinus	36 (32.1%)

Table 28: TYPE OF AVM		
S.No.	Type of AVM	Number(Percentage)
1.	Type A – constriction or stenosis of draining vein	2 (1.8%)
2.	Type B- Presence of incidental feeder or intranidal aneurysm	14 (12.5%)
3.	Type C- Periventricular location	38 (33.9%)
4.	Type A + Type C	2 (1.8%)
5.	Type B + Type C	1 (0.9%)
6.	Venous Aneurysm	1 (0.9%)
7.	None of the above	53 (47.3%)

Maximum numbers of our patients were in grade 2 of Spetzler- Martin grading system (Table 29). Only one patient had a grade of 5.

Table 29: Spetzler-Martin Grading of AVM		
S.No.	Spetzler-Martin Grading of AVM	Number
1.	Grade 1	29
2.	Grade 2	47
3.	Grade 3	31
4.	Grade 4	4
5.	Grade 5	1

Findings in the paediatric age group (Tables 30-32):

The total number of cases included was 32 with equal males (16) and females (16). In children the incidence of seizures was only 5 (15.6%).

Location of Brain AVM:

In the pediatric age group the supratentorial and infratentorial involvement was 29 (90.6%) and 3 (9.4%), respectively (Table 30). Only one (3.1%) pediatric patient had involvement of deep grey matter while involvement of eloquent cortex was seen in 6 (18.8%) patients. Chronic post hemorrhagic sequel, in the form of atrophy, was present in 7 (22%).

Table 30:	**Site of AVM in Pediatric age group**	
Site	Number	Percentage
Supratentorial	29	90.6%
Infratentorial	3	9.4%
Total	32	100%

Feeding artery recruited:

In children, the MCA 8 (25%) and anterior cerebral artery 7 (22%) were recruited almost equally.

Table 31:	**Feeding arteries recruited in Paediatric age group**	
Feeding artery	Number	Percentage
MCA	8	25%
ACA	7	21.9%
Remaining alone or in combination	17	53.1%
Total	32	100%

Aneurysm:

Children in our study showed almost equal prevalence of feeding artery (2 out of 32) and intranidal aneurysms (3 out of 32) [Table 32].

Table 32: Aneurysms associated with AVM in Pediatric age group		
Location	Present	Percentage
Feeding artery	2/32	6.3%
Intranidal	3/32	9.4%
Total	5/32	15.6%

Venous Ectasia:

Venous ectasia was seen in 9 (28.1%) out of 32 patients.

Findings in patients presenting with seizures **(Tables 33-37):**

The total number of patients presenting with seizures were 26 in number (Table 33). Seizures when present, were more common in young adults 15 (57.7%), and were associated with headache in 17 (65.4%), vomiting, and loss of consciousness in 15 (57.7%) and weakness in nearly half of the patients presenting with the same. Although, only one patient presented with a large arteriovenous malformation, the presenting symptom of seizures was seen in 26 (23.6%) number of patients. 21 (80.8%) of the patients who presented with seizures had a small size AVM. Three (11.5 %) of these patients who presented with seizures with hemorrhage harboring an AVM, had an infratentorial location (Table 34). In patients presenting with seizures, 11 out of 26 (42.3%) had small size hemorrhage, and 12 out of 26 (46.2%) had large size hemorrhage, respectively (Table 35).

Table 33: Age of presentation of Patients with Seizures		
Age	Number	Percentage
Paediatric	5	19.3%
Young adults	15	57.7%
Middle aged	6	23.0%
Total	26	100%

Table 34: Location of AVM in patients presenting with Seizures		
Site	Number	Percentage
Supratentorial	23	88.5%
Infratentorial	3	11.5%
Total	26	100%

Table 35: Size of hemorrhage in patients presenting with Seizures		
Size	Number	Percentage
<3 cm	11	42.3%
3-6 cm's	3	11.5%
>6 cm's	12	46.2%
Total	26	100%

Table 36: Post hemorrhagic sequel in patients with seizures		
Sequel	Number	Percentage
Atrophy	7/26	26.9%
Hydrocephalus	14/26	53.8%
Oedema	13/26	50%
Mass effect	13/26	50%

***Angiographic features*:**

MCA was recruited in 31% of the cases presenting with seizures.

Table 37: Angiographic features in patients with seizures		
Feature	Number	Percentage
Compact Nidus	20/26	76.9%
Aneurysm of artery	4/26	15.4%
Steal	16/26	61.5%
Venous ectasia	14/26	53.8%

***Findings in Middle Aged Group* (Tables 38 to 41):**

Total numbers of patients recruited within the middle age group (40-59years) were 25. The majority of patients had an AVM in the supratentorial compartment (Table 38). Involvement of deep grey matter was seen in 3 (12%) and in 8 (25%) patients the AVM was situated in a eloquent cortex.

Table 38: Location of AVM in the middle age group		
Location	Number	Percentage
Supratentorial	22	88%
Infratentorial	3	12%
Total	25	100%

Table 39: Size of hemorrhage in the middle age group		
Size	Number	Percentage
<3 cm	11	44%
3-6 cm's	0	0%
>6 cm's	14	56%
Total	25	100%

Table 40: Post-hemorrhagic sequel in the middle age group		
Sequel	Number	Percentage
Atrophy	6/25	24%
Hydrocephalus	8/25	32%
Oedema	6/25	24%
Mass effect	6/25	24%

***Angiographic features*:**

In the middle aged, MCA was recruited in 2 (8%) cases. All the aneurysms associated with AVM in the middle aged group were located on the feeding artery 8 (32%) [Table 41]. Venous ectasia was seen in 19 out of 25 (76%) middle aged patients.

Table 41: Angiographic Features in the middle age group		
Feature	Number	Percentage
Feeding artery aneurysm	8/25	32%
Intranidal aneurysm of artery	0/25	0%
Steal	18/25	72%
Venous ectasia	19/25	76%

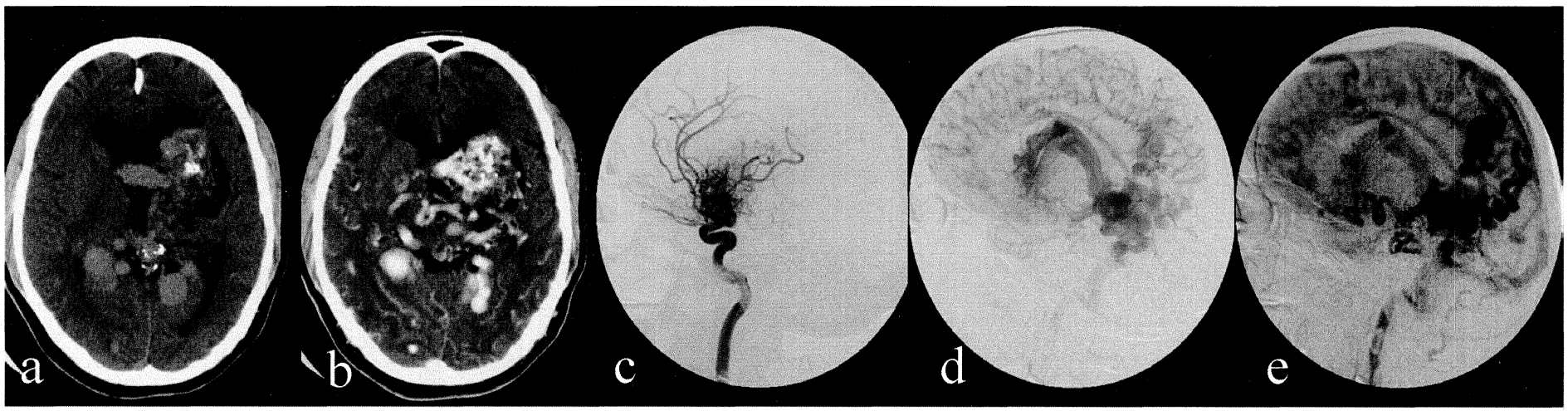

Figure 1. 28 year old male presented with right hemiparesis with altered sensorium in 1996, diagnosed to have left capsuloganglionic AVM, SM Grade IV. Plain (a) and CECT (b) Head show the compact AVM nidus involving left basal ganglia and thalamus with hydrocephalous. Left ICA lateral angiogram (c to e): Venous drainage is to the deep venous system. However , there is stenosis and occlusion of the straight sinus (d). Hence multiple tortuous, dilated collateral venous channels seen draining into the superficial venous system on the delayed venous phase (e).

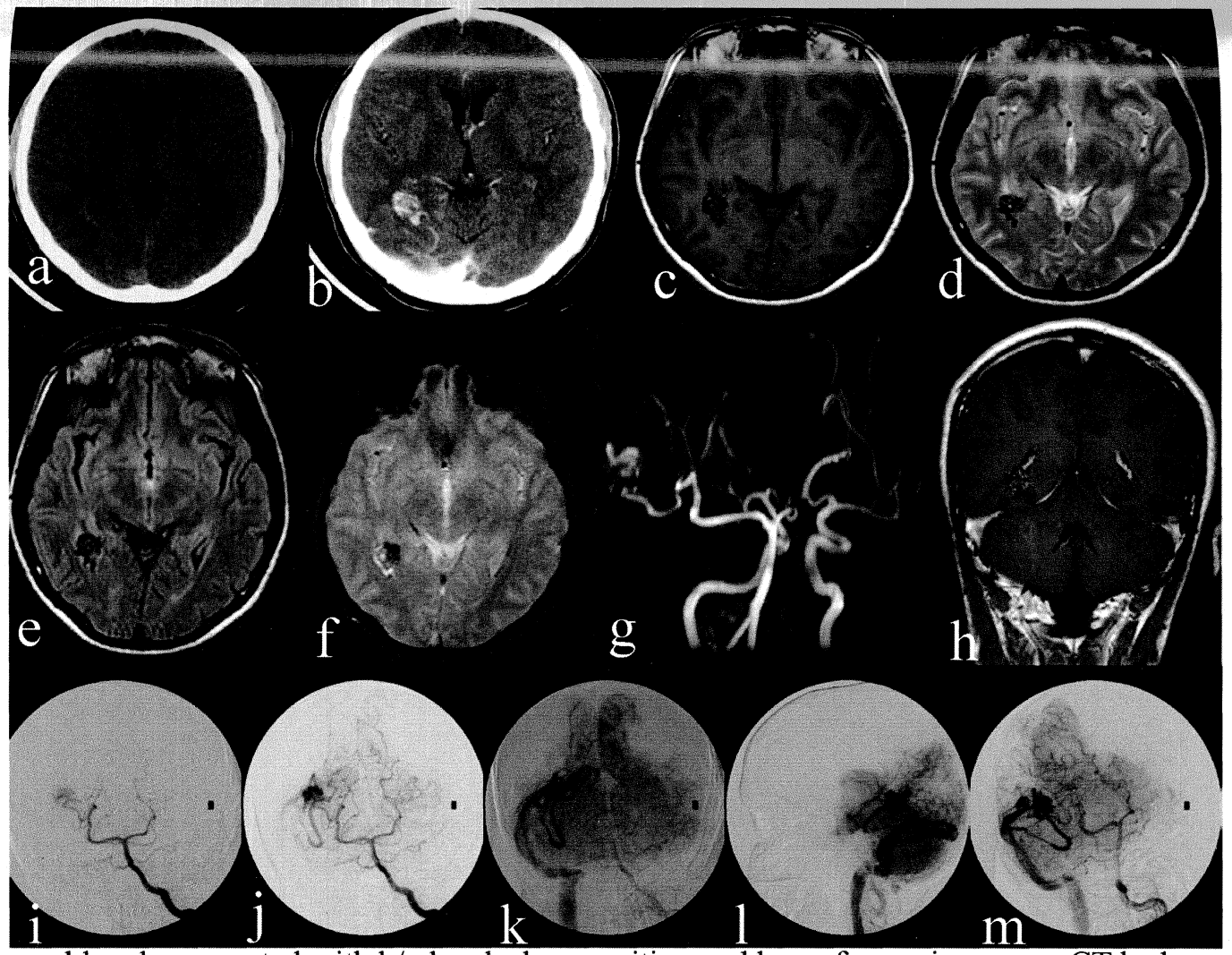

Figure 2: 23 year old male presented with h/o headache, vomiting and loss of consciousness. CT had revealed right tempero-occipital and intraventricular bleed. Present NCCT Brain (a) does not reveal any e/o ICH, IVH or hydrocephalous. CECT (b) show e/o right peritrigonal AVM. However MRI reveals a e/o subtle perinidal gliosis (e) with chronic parenchymal hemosiderin staining on routine (c-e) and gradient (f) sequences in the right trigonal region. The AVM is visualized on TOF MRA MIP (g) fed by right PCA and draining into the deep venous system. The nidus is well defined on post contrast T1WI (h). DSA (i-m) reveals a small compact AVM fed by the posterior temporal branch of right PCA, draining into the straight and transverse sinus. There is e/o stenosis of the draining vein.

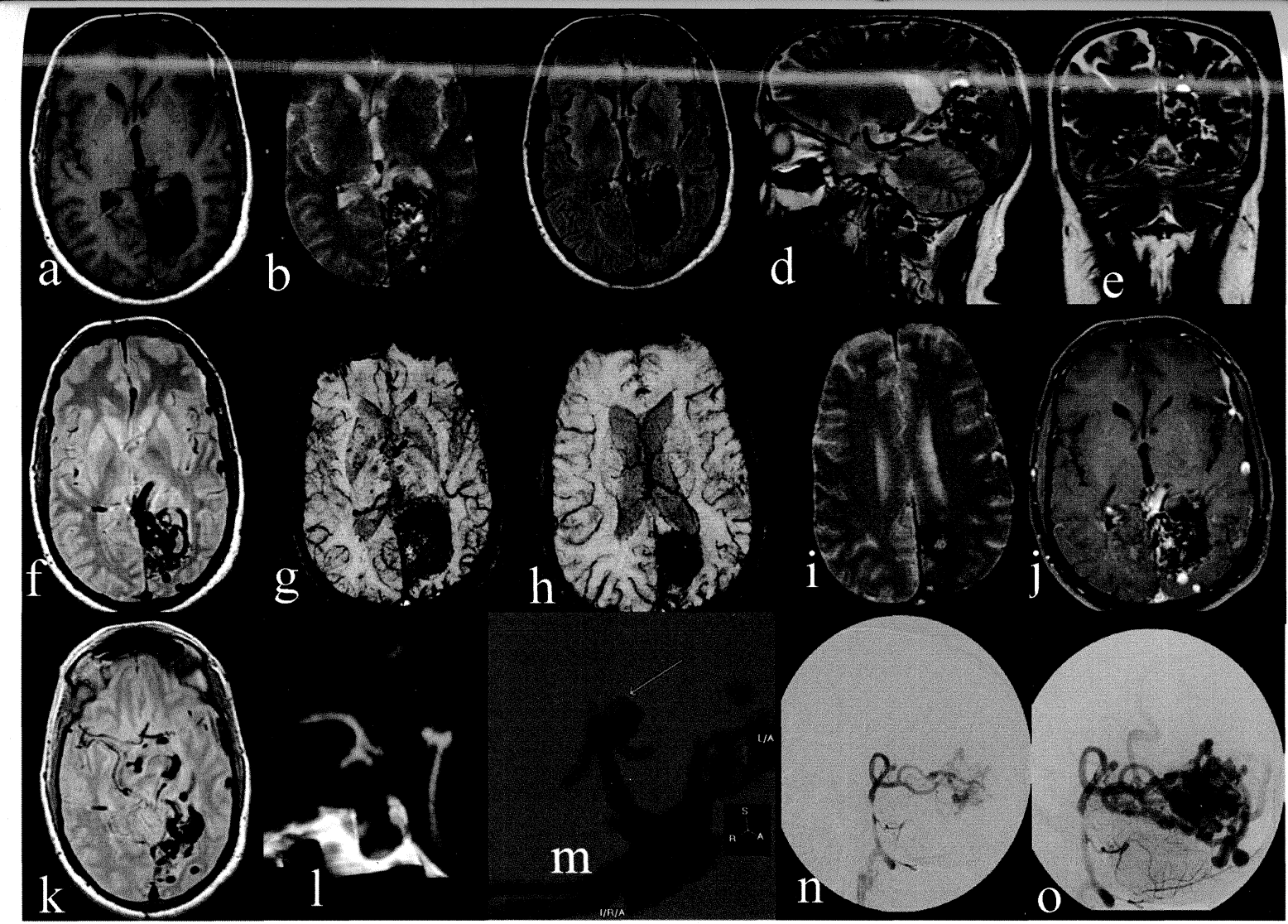

Figure 3: 46 year old gentleman, non hypertensive presented with sudden loss of consciousness, papilledema and right homonymous superior quadrantonopia. CT revealed Lt medial occipital hematoma with SAH. MRI routine(a-f), SWI (g, h), 2D GRE (i), and Post contrast Fat saturation T1WI (j) showed a compact nidus in left cuneus and precuneus, fed by left PCA with dilated tortuous veins draining to superficial and deep veins. There was e/o chronic SAH and ICH in left parietal lobe on SWI (g, h). Proton Density axial MRI (k), CTA 3D reconstruction(l, m) and DSA (n, o) revealed the above morphology as well as a saccular flow related basilar top aneurysm.

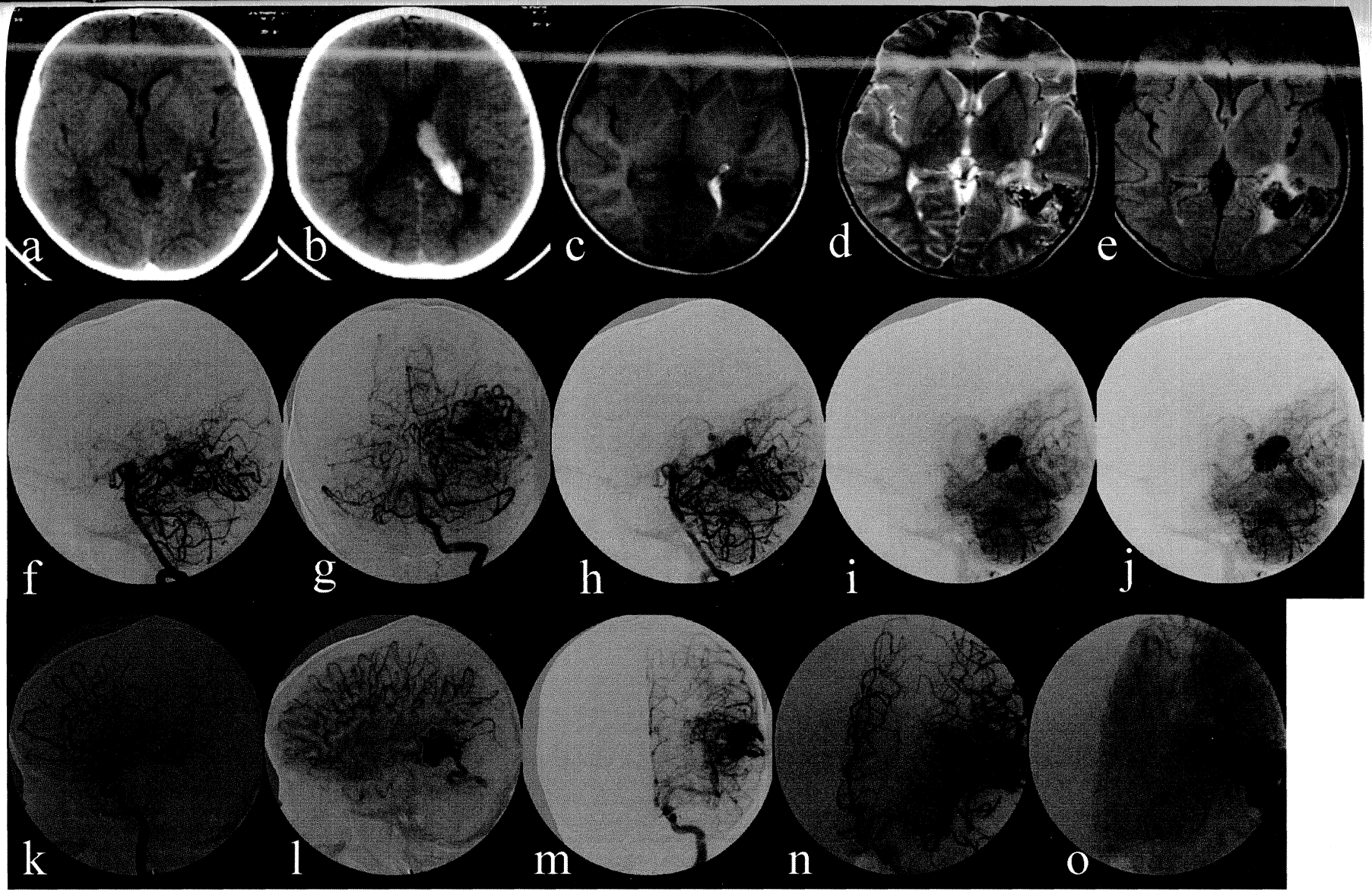

Figure 4: 7 year old child presented with sudden fall followed by holocranial headache and vomiting. CT (a, b)and MRI (c-e) revealed left tempero-parieto-occipital gliosis with prominent draining vein and intraventricular hemorrhage. DSA (f- o) showed a moderate sized AVM fed by Left MCA and PCA draining into a large venous sac and straight sinus. Suspicious small intranidal/perinidal aneurysm noted.

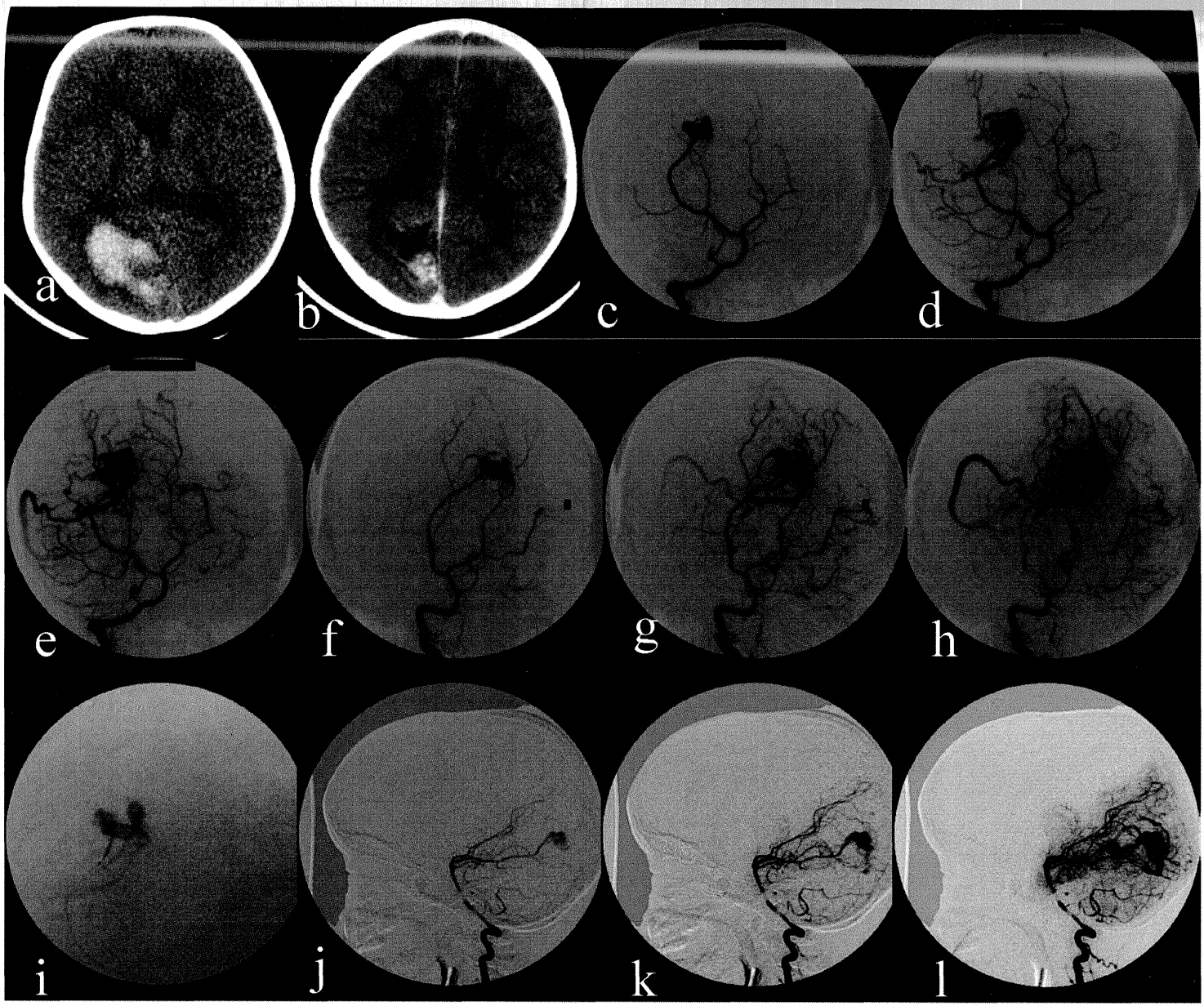

Figure 5: 4 year old female presented with sudden onset headache, vomiting, loss of consciousness and left hemiparesis. Plain and CECT head (a, b) revealed a right parieto-occipital hematoma with enhancing tortuous vessels seen along the midline. DSA (c – l) revealed a small AVM fed by parieto-occipital branch of right PCA draining into the SSS and right transverse-sigmoid junction. On super selective feeding artery injection (i), there was e/o arterio-venous shunting noted.

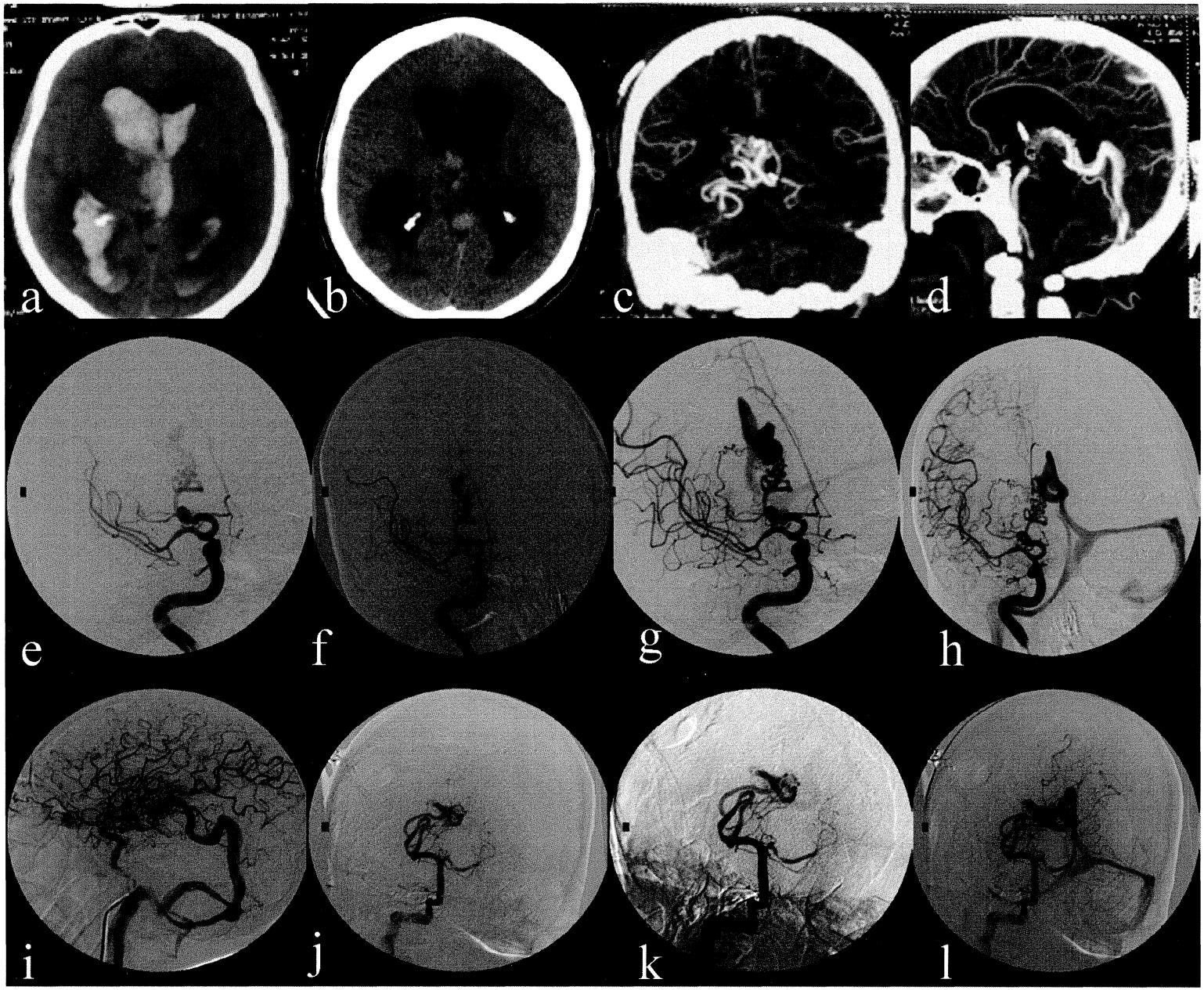

Figure 6: 42 year old gentleman presented with sudden onset of headache, vomiting and loss of consciousness, CT (a, b) revealed IVH, CTA (c, d) and DSA (e – l) revealed a small compact choroidal AVM fed by anterior choroidal, medial and lateral posterior choroidal with deep venous drainage (falcine sinus). Note the venous aneurysm at the origin of the draining vein and its subsequent ectatic course.

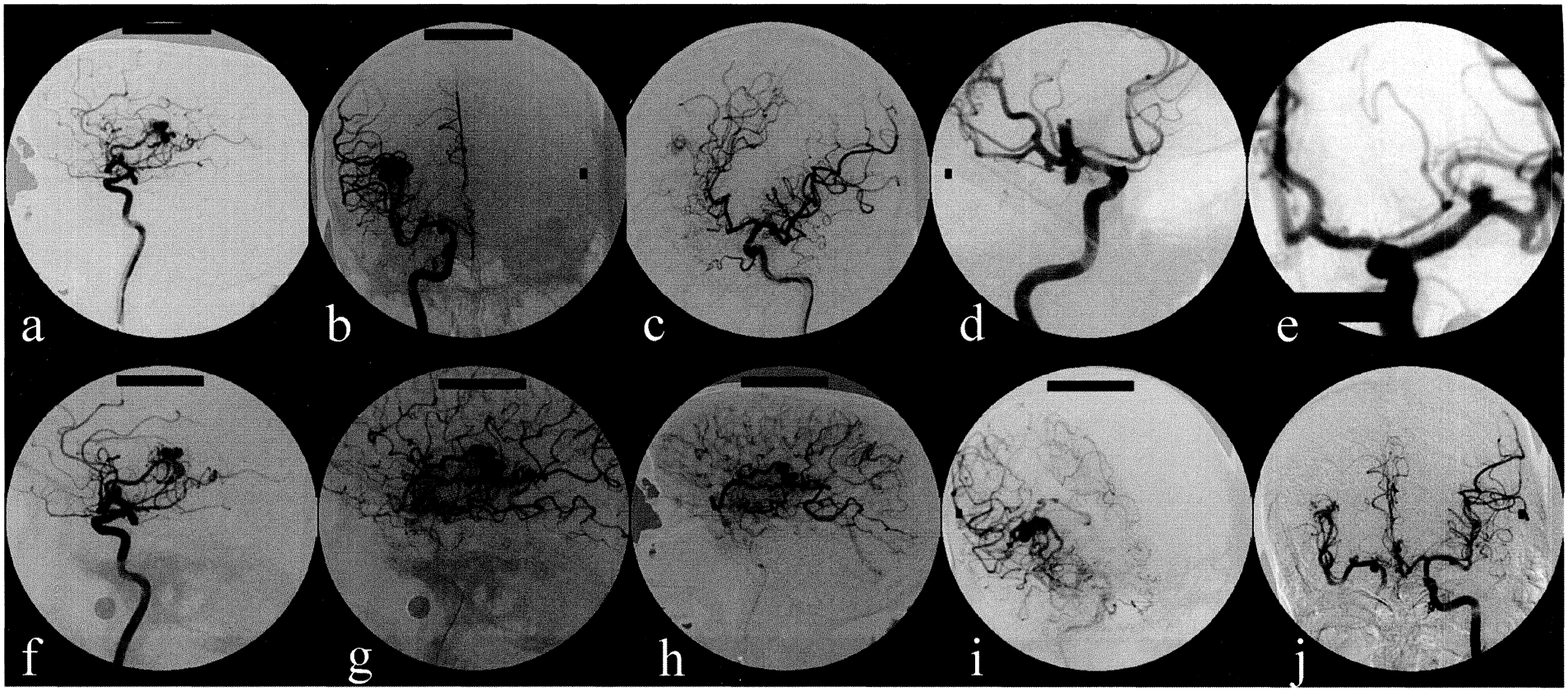

Figure 7: 53 year old gentleman, presented with h/o holocranial headache lasting for 12 hours. CT showed IVH. DSA (a – j) revealed a right insular AVM, with multiple unruptured intracranial aneurysm- 1. distal M1 segment of MCA projecting super-laterally (a,b), 2. Right ParaPcom aneurysm measuring 6.4x4.3 mm, projecting postero-superiorly (a, b, d), 3. Lt MCA bifurcation measuring 3.7x 3.6 mm, projecting antero-superiorly (e). The AVM was fed from right MCA, mid post frontal branch and callosomarginal branch of right ACA, with venous ectasia and deep vein drainage into Basal vein of Rosenthal and ICV (f-i).

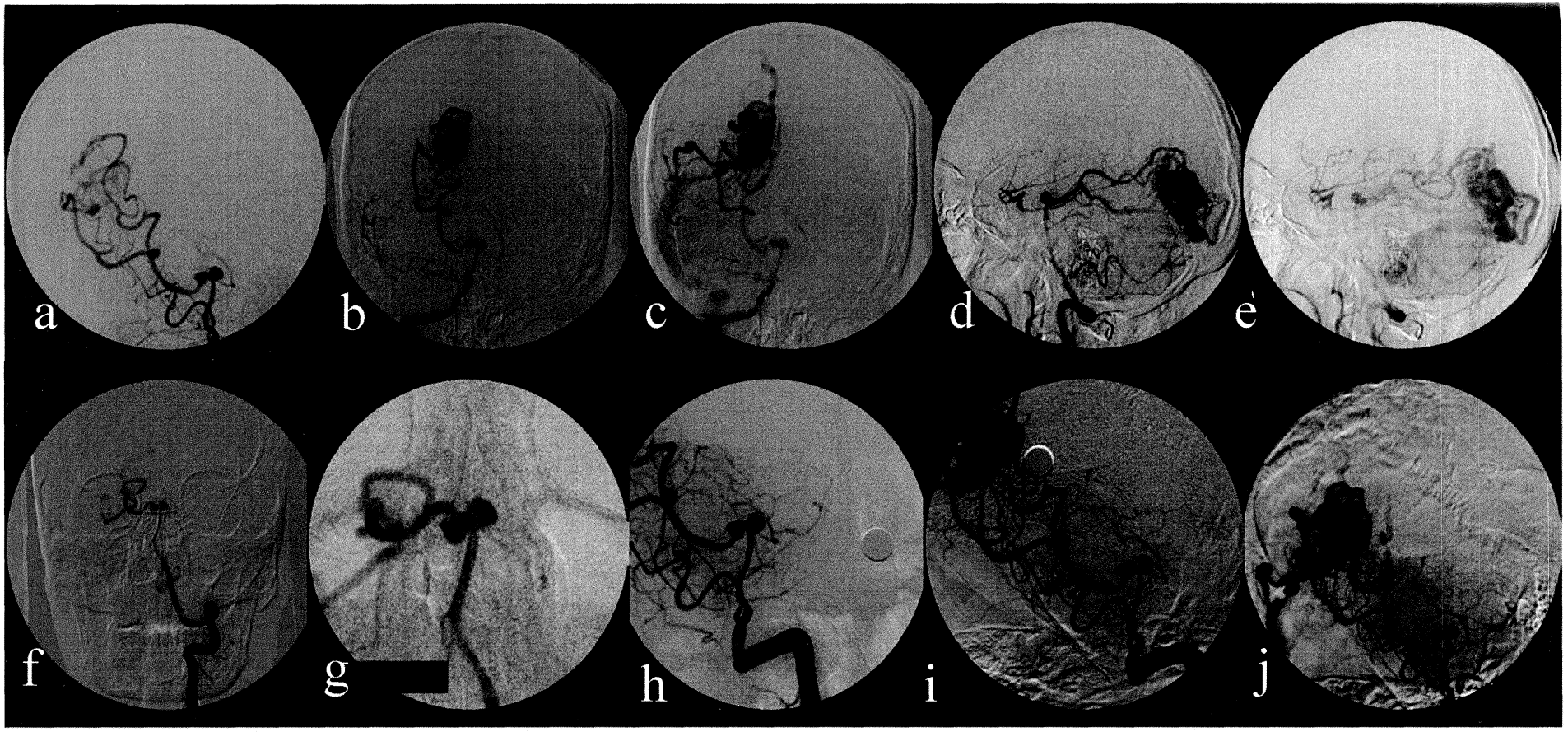

Figure 8: 53 year old lady with sudden onset of headache, loss of consciousness and urinary incontinence. CT revealed SAH with right occipital lobe AVM. DSA (a –j) showed a compact nidus (b) in right occipital region measuring 26 x 18 mm with feeders from parieto-occipital and calcarine branches of right PCA (a,d) draining into right transverse sinus and SSS (c,d). There was a basilar quadrification bilobed, saccular aneurysm, projecting superiorly at basilar top measuring 4.6x5.9 mm; with the other aneurysm measuring 5.4x4.7 mm projecting antero-inferiorly (f-j).

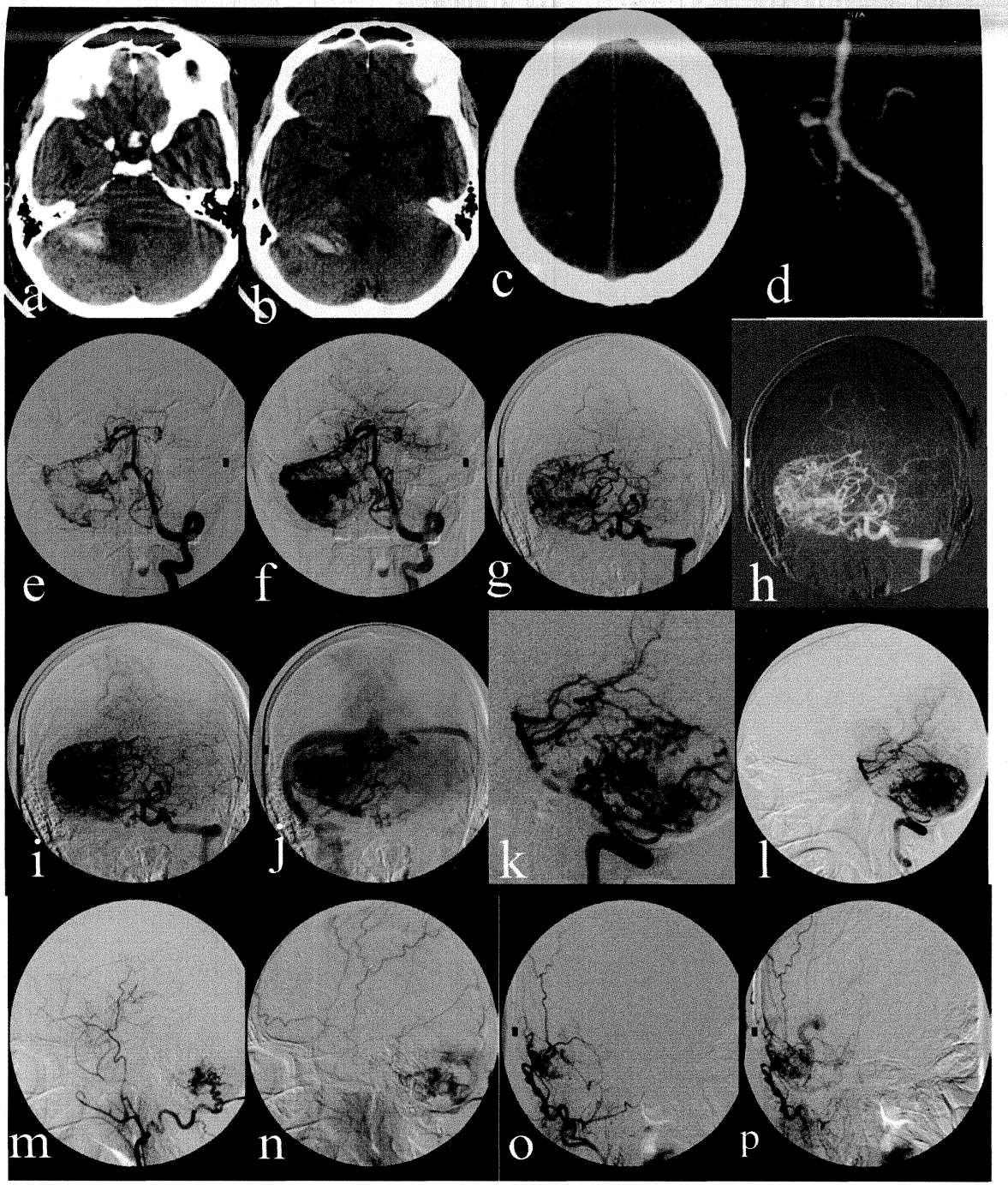

Figure 9: 45 year old presented with sudden onset headache, giddiness, vomiting and LOC for 10 minutes. CT revealed Right cerebellar hematoma (a, b) and SAH (c). CTA was s/o right cerebellar AVM with a nidus measuring 2.2 x 1.8 cm with multiple aneurysmal sacs seen within. Flow related saccular aneurysm seen arising from the basilar artery proximal to the right AICA origin (d). DSA (e-p) showed a diffuse right cerebellar mixed pial-dural AVM with right AICA feeding artery aneurysm. The feeders were from SCA, AICA (e-h), right occipital artery(m-p); predominantly from AICA and draining into vein of Galen and deep veins and torcula (i-l). Right AICA is supplying the ipsilateral PICA territory (e).

Discussion

We conducted this study to assess the angiographic profile of patients with underlying cerebral arteriovenous malformation who presented with hemorrhage. A total of 112 patients were recruited in the present study of native hemorrhage with underlying brain arteriovenous malformations.

The minimum age group of patients recruited is 4 years and the maximum being 58 years with a mean age being 29 years. Brown and his team conducted a population-based study of intracranial vascular malformations in Olmsted County, Minnesota. As compared to the mean age of presentation of 29 years in our study, the mean age of patients at first ICH was 38.7 years, which was slightly younger than the mean age at detection for all intravascular malformations (IVMS) (mean 44.2 years, range 3 to 81 years). The peak occurrence of hemorrhage was during the fifth decade of life, and 75% of hemorrhages occurred before the patient reached 50 years of age (14).

We found that out of the 112 patients, 55 (49.1%) were young adults, 32 (28.6%) were pediatric and adolescents while 25 (22.3%) were middle aged. Stapf describes brain AVMs as a neurovascular disorder that comes to clinical attention mainly in young adults in their mid-thirties (15). In our study, males accounted for 64.3% (n=72), the remaining being females. Out of the 72 male patients, 36 were young adults, 16 were children and 20 were middle aged. Of the 40 female patients, 19 (47.5%) of females were young adults, 16 (40%) were pediatric or adolescents while only 5 (12.5%) were middle aged. Thus, in confirmation with the findings of Stapf it can be said

that the disease predominantly affects young individuals, especially males. However, gender predilection was not found in the pediatric age group in our study, as male and female children were found to be equally affected.

Although AVMs are more common above the tentorium, in children the ratio of supra to infratentorial AVM is reduced to approximately 3:1 (17). In contrast, children in our study did not show this decrease and the ratio of supra- to infratentorial AVM was the same as adults. The importance of infratentorial AVM, particularly cerebellar AVM, in children is that there is still a very high mortality rate (17).

Majority of the patients 70 (62.5%) presented in the chronic time frame and 16 patients presented after 1 year of ictus.

In spite of the late presentation, 94 (83.9%) of the patients had a favorable GCS (13-15), 5 (4.5%) were in the borderline (7-12) while 6 (5.4%) were in the critical group (4-7). This is comparable with the population-based studies of Van Beijnum et al, who found that the patients with AVM related cerebral bleed were younger, had lower pre-stroke and admission blood pressure, had a favorable GCS, and were more likely to have a lobar location as compared to the patients with spontaneous bleed. They also reported that the patients in the AVM subgroup had reported a better outcome. However, they admitted that this may be partially due to the under diagnosis of AVM in routine clinical practice (16).

Hartmann et al studied the morbidity of intracranial hemorrhage in patients with cerebral arteriovenous malformation. They found that 47% had no neurological deficit, 37% were functionally independent and only 16%

were moderately or severely disabled following hemorrhage (18). Perret and Nishoika in their cooperative study of intracranial aneurysms and subarachnoid hemorrhage found an incidence neurological deficit to be 58% (13) However in our study, headache was the predominant presenting complaint in 92 (82.1%) patients, followed by vomiting in 74 (66.1%), loss of consciousness in 49 (43.8%), altered sensorium in 42 (37.5%), paresis in 40 (35.7%), with the incidence of seizures being 26(23.6 %). This is comparable with the findings of Graf et al, who studied the natural history of cerebral AVMS that bleed, found that the incidence of neurological deficit was 81% (8). In children the incidence of seizures was only 15.6%. Seizures when present, are more common in the younger patients (57.7%), and are associated with headache in 65.4%, vomiting, and loss of consciousness in 57.7% and weakness in nearly half of the patients presenting with the same.

Langer et al have predicted hypertension as one of the risk factors to be associated with the risk of hemorrhagic presentation of cerebral arteriovenous malformation (38). In contradiction, Szabo et al did not find hypertension to be a risk factor for spontaneous intracranial hemorrhage (39). In corroboration with Szabo et al, a mere 1.8% of patients had hypertension as the underlying risk factor in our study. The low incidence of hypertension in our study could be due to the fact that most of our patients belonged to the younger age group, where the incidence of hypertension is low. Investigations did not reveal anything significant, except leucocytosis in 25 and raised ESR in 24 patients, respectively.

Literature states that ninety percent of these malformations are found in the supratentorial compartment, near the watershed areas, the remaining being infratentorial. Our study corroborates this fact, as out of the 112

patients studied, 100 (89.3%) were in the supratentorial compartment, while 12 (10.7%) were in the infratentorial compartment.

Out of the 112 patients, 95 (84.8%) were parenchymal, 13 (11.6%) were periventricular and only 4 (3.6%) were intraventricular. Of the 100 supratentorial AVM's, 84 (84%) were parenchymal, 13 (13%) were periventricular and 3 (3%) were intraventricular. In the infratentorial compartment, 11 (91.7%) were parenchymal, and only one (8.3%) was intraventricular. It can be seen that the overall incidence of parenchymal lesion in both the supratentorial as well as infratentorial compartment was 95 (84.8%).

Small nidus size (20,21,38,41,42,46) and deep seated location of AVM (36,43,47); pathomorphological changes viz presence of arterial aneurysms (32,36,47); venous drainage (single draining vein) (41,42,45) and impaired venous drainage (41,43,48) are proven angiographic predisposing factors for hemorrhage.

Site of the AVM also is a determining factor for hemorrhages. Deep seated cerebral arteriovenous malformations as well as certain sites in the neuroparenchyma like cerebellum, brain stem, temporal lobe, insular, callosal and periventricular regions are susceptible for hemorrhage as studied by Stephani MA et al in their study of angioarchitectural factors in brain arteriovenous malformations (45). Turjman et al in a series of 100 patients with AVMs treated between 1987 and 1990 found that the basal ganglia was the only significant location associated with hemorrhagic presentation. The team also found that midline locations were significantly related to hemorrhage (23). We found that deep grey matter is less

frequently involved in children. The right versus left preponderance was almost equal and only 5.4% had midline presentation in our study. Of the total, 13 (11.6%) patients had lesions in deep grey matter, out of which only one pediatric patient had involvement of deep grey matter.

In our study, where all the 112 patients presented with hemorrhage, 91 had small malformations of less than 3 cm's size, 20 were medium sized and only one had a malformation of greater than 6 cm's, respectively. This is consistent with the studies which show that small cerebral arteriovenous malformations present more frequently with hemorrhage (8,44). In contrast, Stephani MA et al have found that large and deep brain AVMS are more prone to hemorrhage. They argued that small AVMS present with hemorrhage, as they do not tend produce alarming symptoms of seizures or bruits, in contrast to their larger counterparts (45). In corroboration, 81% of the patients who presented with seizures had a small size AVM.

Separate studies conducted by Kader and Spetzler et al show that larger AVMS mostly present with seizures (20,21). In our study 23.6 %(n=26), presented with seizures, however only one patient had a large sized AVM. Probably the low incidence of infratentorial involvement could be a contributing factor, as infratentorial AVMS are conceivably less likely to cause seizures as shown by Khaw et al in their study on the association of infratentorial brain AVMS with hemorrhage at initial presentation (22). Our study corroborates the findings of Khaw et al, as only 11.5 % of these patients who presented with seizures with hemorrhage harboring an AVM, had an infratentorial location, the rest being supratentorial. Another reason could be the brain damage due to the hemorrhage caused by some of the supratentorial AVMS could have contributed to seizures. Turjman et al in an

multivariate analysis of angioarchitectural characteristics in patients with epilepsy harboring AVM found 6 parameters to be predictors of epilepsy viz; cortical location of the AVM; feeding by the middle cerebral artery (MCA); cortical location of the feeder; absence of aneurysms; presence of varices in venous drainage; and finally the association of varix and absence of intranidal aneurysms (23).

Young et al tried to measure the pressure gradients across the nidus of an AVM to delineate any relationship with the deep venous pressures. In 21 patients there was positive correlation between feeding arterial pressures and draining venous pressures associated with the AVM, particularly when the head (as opposed to the heart) was the reference point. Despite this direct relationship the transnidal pressure gradient (feeding artery minus draining vein pressures) is lower in larger AVMS, supporting the notion that less stress is placed on the intranidal structures, thus exhibiting a lower hemorrhage rate. There was also evidence demonstrating that the AVM shunt is not merely a passive conduit transmitting feeding arterial pressure into the venous side. However, these authors noted that changes in the systemic mean arterial and central venous pressures affect the AVM arterialized draining veins more as venous structures than arterial (50).

Demographic as well as underlying angiographic profile may play a role in the incidence of cerebral arteriovenous malformations presenting as hemorrhage. Hence defining these factors might help in understanding the disease process better, as well as triaging patients for various modalities of treatment.

In our study, atrophy of the brain parenchyma was present in 22(19.6%) of all the patients, which was nearly the same as that in children

(22%). Hence, the atrophy could be attributed to compression by hematoma or mass effect, and unrelated to senile changes. We demonstrated that nearly 50.9% (n=57), patients had a large sized hemorrhage measuring more than 6 cm's. Edema surrounding the hematoma was present in 42(37.5%), post-hemorrhage hydrocephalus in 39(34.8%) and mass effect due to hematoma in 37(33%), respectively. As nearly half of our patients had a large sized hemorrhage, consequentially could have resulted in mass effect and hydrocephalus in approximately a third of the patients. The presence of arterial steal, mass effect and hydrocephalus could also be the factors responsible for the presence of paresis in 35.7% of our patients.

In majority of the cases (n=74), Digital Subtraction Angiography (DSA) was done after 30 days of ictus. Only in 14 patients was the DSA done within 0-7 days of presentation. Forty (35.7%) patients underwent DSA 100 days after the ictus.

Turjman et al have documented steal, gliosis of the brain after previous subclinical hemorrhage and secondary epileptogenesis in the site distant from the primary AVM as the possible reason for seizures (23). We hypothesized that the presence of steal, venous ectasia and compact nidus morphology, could be other contributing factors for the presence of seizures. This was substantiated by the incidence of steal (61.5%), venous ectasia (53.8%), and compact nidus (76.9%) demonstrated in patients with seizures in our study. The size of the hemorrhage is unlikely to be the causative factor for seizures, as 11 out of 26 had small size hemorrhage, and 12 out of 26 had large size hemorrhage respectively.

Angiographic abnormalities in all the three different components of a cerebral arteriovenous malformation have been implicated as risk factors towards the incidence of hemorrhage. Increased intra-arterial pressures within the feeding arteries, development of perinidal or intranidal arterial aneurysms and hindrance in the venous outflow are potential factors which lead to the adverse outcome of hemorrhage (21,35-37).

The absence of normal high resistance capillaries predisposes the feeding arterial compartment to a relatively high volume of blood. The nidal dysplastic, thin-walled vessels harboring focal dilatations may act as a low threshold points and thus succumb to the high volume of blood resulting in rupture and hemorrhage. Size and hemodynamics have been correlated to document large, high flow AVMS being fed by low-pressure arteries (21).

In 53.6% of our cases, the arteriovenous malformation was being fed from the anterior circulation or as in 29.5%, a combination of anterior and posterior circulation, the remaining being fed by the posterior circulation. 45.5% had a single feeding artery, 31.3% had double and the remaining had three or more feeding arteries, respectively.

Spetzler et al studied the relationship of perfusion pressure and size, to risk of hemorrhage from AVMS. They have found the feeding arterial pressures to be higher and almost double the systolic blood pressures in patients with cerebral arteriovenous malformations presenting with hemorrhage. Feeding arterial pressures were higher in small sized cerebral arteriovenous malformations irrespective of their presentation (21). When the feeding arterial pressures decreased in angiomatous transformation of the nidus, there was a decrease in incidence of hemorrhage. This might be due to

transcortical arterial collateralization from adjacent vascular territories (51,58).

Persistent primitive trigeminal artery (PPTA) is the most common anomaly of the carotid-basilar anastomosis and is usually an incidental finding with an incidence of 0.1-0.6%. However, the reported incidence of association of PPTA with cerebral AVM is 4.5% (56). In contrast, in our study, the incidence of PPTA was only 0.9%.

The middle cerebral artery (MCA), was variably recruited in different age groups, though overall, in isolation or with other arteries, it was the most commonly recruited in 62(55.3%) cases, followed by anterior cerebral artery (40.1%) and posterior cerebral artery (39.2%) respectively. In children, however, the MCA (25%) and anterior cerebral artery (22%) were recruited almost equally. Turjman F et al in their multivariate analysis of angioarchitectural characteristics of epilepsy patients associated with AVM have found that the MCA was recruited most commonly (23). However, we did not have a similar finding, as MCA was recruited only in 31% of the cases with seizures.

Perforating feeding vessels also lead to an increase in the incidence of hemorrhage as shown by Turjman et al when they correlated the angioarchitectural features of cerebral arteriovenous malformations with the clinical presentation of hemorrhage. These vessels supply deep AVMS, hence are more prone to bleed (54). In our study 73 out of 112 patients demonstrated to have cortical feeders, 12 had cortical and perforators, while 23 had perforators on angiography.

Nineteen (17%) of patients in our study had associated underlying aneurysms. Out of these, majority, 12 had feeding artery aneurysm and 6 had intranidal aneurysm. This corroborates with existing literature (20, 24-27).

The feeding arteries were the favored site of aneurysm in the study by Brown at al, and this is consistent with our study, where almost two thirds of the aneurysms were feeding artery ones (35), and comprised all the patients in the middle aged group. However, children in our study showed almost equal finding of feeding artery (2 out of 32) versus intranidal aneurysms (3 out of 32). We could not draw any conclusion from this finding as the sample size of children is small. We could not document a single intranidal aneurysm in the middle aged subgroup.

Over a 5 year period, risk of hemorrhage in patients with saccular aneurysm and unruptured AVM was 7% per year compared to only 1.7% when associated with arteriovenous malformations alone. Risk of re-rupture was seen in aneurysms arising from the midportion of the feeding artery termed pedicle aneurysms (30).

The presence of intranidal aneurysms does contribute to risk of hemorrhage in cerebral AVMS (51). Flow related (41%) and intranidal (63%) aneurysms were seen in patients presenting with cerebral AVMS and hemorrhage (32). Marks et al have shown that intranidal aneurysms which are thin walled structures, are exposed to arterial pressure and hence at a potential site for hemorrhage. However, they can be effectively treated with embolization (36). Hence diagnosing them on angiography is important from therapy point of view.

In spite of the studies that show an association of aneurysms with AVMS, only 5 aneurysms were detected in association with cerebral AVMS in 154 patients in the statistical analysis on the location of aneurysms associated with intracranial AVM by Okamoto et al (28). While 0.8% of unrelated vessels revealed aneurysms in patients with cerebral arteriovenous malformation (32), no association was seen between presentation as initial hemorrhage in patients with cerebral arteriovenous malformation and aneurysm(45,52).

Various innovative and risk stratifying methods have been employed to explore the other possible underlying causes leading to hemorrhage, of which hemodynamic risk factors like feeding arterial pressures are foremost (20,21,38,40-42).

It is a known fact that vascular pressure is directly proportional to flow velocity and inversely proportional to mean transit time. Young et al studied direct pressure measurements in the feeding arteries or draining veins of an arteriovenous malformation (50). As seen earlier, Nornes and Grip have demonstrated that there is high flow velocity (70cm/sec) in large arteries, however highest velocities for smaller arteries was found in several patients (29). This high velocity gives rise to shear stress in the vessels, causing weakening of the vessel wall. Not surprisingly, in our patients who presented with hemorrhage, 63.4% of the arteriovenous malformations were characterized as high flow, thus indicating to having a high pressure.

The venous drainage compartment of an AVM plays a role in hemorrhagic incidence of a cerebral arteriovenous malformation. Over time the draining veins too change in their in-situ pressures and become arterialized. These arterialized veins are susceptible to changes in the

systemic mean arterial and central venous. Thus, a sudden rise in systolic arterial pressure may increase the in-situ venous pressures beyond result factors contributing towards venous hypertension have also been implicated in the hemorrhagic incidence in patients with cerebral AVM. Thus, it is no surprise that deep venous pressures are inversely related to the number of draining veins and size of the arteriovenous malformation (37). Turjman et al did not find lone venous drainage to be a factor responsible for hemorrhage. They felt that the discrepancy could be due to selection bias in recruitment of the patients (54). However, in our study, 46.4% had single draining vein, 17% had two and 36.6% had three or more draining veins, respectively. Hence, by extrapolation, the high venous pressures in patients with a lone draining vein might have contributed to hemorrhage in nearly half of the patients.

Deep venous drainage is a risk factor for bleed, as these veins drain deep structures, which itself is a risk factor for hemorrhage. Patients having deep venous drainage either alone or in combination with the superficial veins were 56.3%. As nearly half of the patients had a single draining vein and deep venous drainage, this could have given rise to a higher venous pressure, resulting in hemorrhage. In 59 patients, a single vein reached the sinus, while in 36 patients three or more veins reached the sinus.

Venous ectasia was defined as "a markedly ectatic vein" or as "pouches," usually associated with a stenotic draining vein. Reduction of 50% or more of the vein diameter defined venous stenosis (45,54).

Venous stenosis in high flow draining veins was suggested by Hademenos and Massoud as a risk factor for hemorrhage (48). In a study by

Willinsky et al, stenosis was seen in cerebral arteriovenous malformations presenting as hemorrhage in young adult females (47).

Turjman et al found no association between venous stenosis and initial bleeding, defining a venous stenosis as reduction of 50% or more of the vein diameter. In our analyses it did not present as a significant feature either, as only two patients had constriction or stenosis of the draining vein. Though some studies have found no association between venous ectasia and initial bleeding, in our study venous ectasia was found in 55 out of 112 patients and in 19 out of 25 middle aged patients (45;54). Children in contrast did not show a high incidence of venous ectasia as only 9 out of 32 patients (28.1%) had ectasia.

In our study, only one of the patients had a venous aneurysm, thus proving that venous aneurysms are not associated with hemorrhage. Thirty-eight had a periventricular location, in corroboration with other studies which have found the periventricular location to be associated with bleed (54).

The Spetzler and Martin grading system attempts to predict the risk of surgical morbidity and mortality by assigning points to an arteriovenous malformation on the basis of its size, the eloquence of the adjacent brain, and the pattern of venous drainage. The grade of a lesion is determined by summing the points given in each of the 3 categories. Surgical treatment of a grade I arteriovenous malformation, therefore, presents little risk of morbidity and mortality. By contrast, a grade V lesion is associated with significant risk (57).

Involvement of the eloquent cortex has got therapeutic implications, as it is one of the factors which determine grading of the AVM by Spetzler and Martin. 38(33.9%) of patients had involvement of underlying eloquent cortex, of which the sensorimotor followed by the basal ganglia was the most commonly involved. In children, however, eloquent cortex was involved only in 6 out of 32 cases (18.8%) and in 26 out of 32(81.3%) no eloquent area could be specifically defined. It is important to note that 47 of our patients had a Spetzler- Martin grading of 2, while 29 had a grading of 1, 31 had a grading of 3 and 4 had a grading of 4 respectively . Only one patient had a grading of 5.

Thus, a majority of our patients had a good prognosis, with a lower risk of morbidity and mortality and were amenable to treatment. Hence, angiographic assessment of these patients becomes of paramount importance, not only to study the demographic profile, the risk factors, the vascular supply, but also for prognosticating the treatment meted out to these patients, who belong to the productive age group and incur a considerable load on the health care system.

Conclusion

We conducted this study to assess the angiographic profile of patients with cerebral arteriovenous malformation presenting with hemorrhage. A total of 112 patients were recruited in the present study of native hemorrhage with underlying brain arteriovenous malformations.

From our study, we conclude that:

1. The disease predominantly affects young adults, especially males, and hence belonging to the productive age group. In children, males are equally affected as females. These patients usually present with headache and vomiting in the sub acute to chronic state, with a favorable Glasgow Coma Scale. Some of them may have loss of consciousness, altered sensorium, paresis and seizures. Hypertension is not a risk factor for hemorrhage with underlying brain AVM, even in the middle age group.

2. In the pediatric age group, there is no gender predominance, and the supratentorial region is involved to the same extent as adults. AVMS occur more commonly in frontal, followed by callosal and temporal lobes. The eloquent cortex is affected to a lesser extent, and it is not defined. MCA is recruited in only a quarter of children, as compared to nearly half in adults. The incidence of seizures is relatively less and so is venous ectasia.

3. Seizures when present in any age group are associated with vomiting, loss of consciousness and weakness in nearly half of the presenting group of patients. Compact nidus, supratentorial AVMS, small in size are associated with seizures. Steal and venous ectasia could also be contributing to seizures in these patients.

4. The most common site of the AVM is the supratentorial region, and in both the supratentorial as well as the infratentorial region, parenchyma is predominantly involved. Small malformations of less than 3 cm's size are common and a third of patients has involvement of underlying eloquent cortex, but is comparatively less in pediatric group. Nearly two-thirds of the patients have parenchymal bleed and in fifty percent of the total, the size of the hematoma measured is more than 6 cm's. A large sized hemorrhage can result in mass effect and hydrocephalus in approximately a third of the patients.

5. Increased intra-arterial pressures within the feeding arteries, development of perinidal or intranidal arterial aneurysms and hindrance in the venous outflow are potential factors which lead to the adverse outcome of hemorrhage. All these factors can be documented in our study. In our study, compact nidus on angiography, steal, venous ectasia, kinks in the draining vein occur commonly in association with hemorrhage. However, venous ectasia is not a common finding in children. All the aneurysms documented in the middle-aged group are those involving the feeding artery. The

presence of arterial steal, mass effect and hydrocephalus can contribute to neurological deficit.

6. The middle cerebral artery or its branches in isolation or with other arteries is the most commonly recruited, however in patients complaining with seizures, children and in the middle aged group, MCA is recruited to a lesser extent. Nearly half of the patients have a single draining vein and deep venous drainage, which can give rise to a higher venous pressure, resulting in hemorrhage. As a high flow has been associated with these AVMS, not surprisingly, in our patients who presented with hemorrhage, two-thirds arteriovenous malformations were characterized as high flow, thus indicating a high pressure.

7. Almost seventy-five percent of our patients had a Spetzler-Martin Grading of one and two and hence had a low risk of morbidity and mortality. Thus studying the demographics, risk factors and the angiographic profile of these patients, who belong to the productive age group, involve a considerable cost to health care system and have a good prognosis if detected early, is important for understanding the disease process better, as well as triaging patients for various modalities of treatment.

Reference List

(1) De BL, Di LF, Perna S, Spalloni A, Ferranti F, Lucani A, et al. Recurrent episodes of syncope in a patient with cerebral arteriovenous malformation. Clin Ter 2007 Mar;158(2):147-50.

(2) Mast H, Mohr JP, Osipov A, Pile-Spellman J, Marshall RS, Lazar RM, et al. 'Steal' is an unestablished mechanism for the clinical presentation of cerebral arteriovenous malformations. Stroke 1995 Jul;26(7):1215-20.

(3) Valavanis A. The role of angiography in the evaluation of cerebral vascular malformations. Neuroimaging Clin N Am 1996 Aug;6(3):679-704.

(4) Norris JS, Valiante TA, Wallace MC, Willinsky RA, Montanera WJ, terBrugge KG, et al. A simple relationship between radiological arteriovenous malformation hemodynamics and clinical presentation: a prospective, blinded analysis of 31 cases. J Neurosurg 1999 Apr;90(4):673-9.

(5) Brown RD, Jr., Wiebers DO, Forbes G, O'Fallon WM, Piepgras DG, Marsh WR, et al. The natural history of unruptured intracranial arteriovenous malformations. J Neurosurg 1988 Mar;68(3):352-7.

(6) Crawford PM, West CR, Chadwick DW, Shaw MD. Arteriovenous malformations of the brain: natural history in unoperated patients. J Neurol Neurosurg Psychiatry 1986 Jan;49(1):1-10.

(7) Ondra SL, Troupp H, George ED, Schwab K. The natural history of symptomatic arteriovenous malformations of the brain: a 24-year follow-up assessment. J Neurosurg 1990 Sep;73(3):387-91.

(8) Graf CJ, Perret GE, Torner JC. Bleeding from cerebral arteriovenous malformations as part of their natural history. J Neurosurg 1983 Mar;58(3):331-7.

(9) Miller CE, Quayyum Z, McNamee P, Al-Shahi SR. Economic burden of intracranial vascular malformations in adults: prospective population-based study. Stroke 2009 Jun;40(6):1973-9.

10) Jellinger K. Vascular malformations of the central nervous system: a morphological overview. Neurosurg Rev 1986;9(3):177-216.

(11) Mullan S, Mojtahedi S, Johnson DL, Macdonald RL. Embryological basis of some aspects of cerebral vascular fistulas and malformations. J Neurosurg 1996 Jul;85(1):1-8.

(12) Pile-Spellman JM, Baker KF, Liszczak TM, Sandrew BB, Oot RF, Debrun G, et al. High-flow angiopathy: cerebral blood vessel changes in experimental chronic arteriovenous fistula. AJNR Am J Neuroradiol 1986 Sep;7(5):811-5.

(13) Perret G, Nishioka H. Report on the cooperative study of intracranial aneurysms and subarachnoid hemorrhage. Section VI. Arteriovenous malformations. An analysis of 545 cases of cranio-cerebral arteriovenous malformations and fistulae reported to the cooperative study. J Neurosurg 1966 Oct;25(4):467-90.

(14) Brown RD, Jr., Wiebers DO, Torner JC, O'Fallon WM. Frequency of intracranial hemorrhage as a presenting symptom and subtype analysis: a population-based study of intracranial vascular malformations in Olmsted Country, Minnesota. J Neurosurg 1996 Jul;85(1):29-32.

(15) Stapf C. [The neurology of cerebral arteriovenous malformations]. Rev Neurol (Paris) 2006 Dec;162(12):1189-203.

(16) van BJ, Lovelock CE, Cordonnier C, Rothwell PM, Klijn CJ, Al-Shahi SR. Outcome after spontaneous and arteriovenous malformation-related intracerebral haemorrhage: population-based studies. Brain 2009 Feb;132(Pt 2):537-43.

(17) Griffiths PD, Blaser S, Armstrong D, Chuang S, Humphreys RP, Harwood-Nash D. Cerebellar arteriovenous malformations in children. Neuroradiology 1998 May;40(5):324-31.

(18) Hartmann A, Mast H, Mohr JP, Koennecke HC, Osipov A, Pile-Spellman J, et al. Morbidity of intracranial hemorrhage in patients with cerebral arteriovenous malformation. Stroke 1998 May;29(5):931-4.

(19) Locksley HB. Natural history of subarachnoid hemorrhage, intracranial aneurysms and arteriovenous malformations. Based on 6368 cases in the cooperative study. J Neurosurg 1966 Aug;25(2):219-39.

(20) Kader A, Young WL, Pile-Spellman J, Mast H, Sciacca RR, Mohr JP, et al. The influence of hemodynamic and anatomic factors on hemorrhage from cerebral arteriovenous malformations. Neurosurgery 1994 May;34(5):801-7.

(21) Spetzler RF, Hargraves RW, McCormick PW, Zabramski JM, Flom RA, Zimmerman RS. Relationship of perfusion pressure and size to risk of hemorrhage from arteriovenous malformations. J Neurosurg 1992 Jun;76(6):918-23.

22) Khaw AV, Mohr JP, Sciacca RR, Schumacher HC, Hartmann A, Pile-Spellman J, et al. Association of infratentorial brain arteriovenous malformations with hemorrhage at initial presentation. Stroke 2004 Mar;35(3):660-3.

(23) Turjman F, Massoud TF, Sayre JW, Vinuela F, Guglielmi G, Duckwiler G. Epilepsy associated with cerebral arteriovenous malformations: a multivariate analysis of angioarchitectural characteristics. AJNR Am J Neuroradiol 1995 Feb;16(2):345-50.

(24) Gibbons GH, Dzau VJ. The emerging concept of vascular remodeling. N Engl J Med 1994 May;%19;330(20):1431-8.

(25) Kondziolka D, Nixon BJ, Lasjaunias P, Tucker WS, TerBrugge K, Spiegel SM. Cerebral arteriovenous malformations with associated arterial aneurysms: hemodynamic and therapeutic considerations. Can J Neurol Sci 1988 May;15(2):130-4.

(26) Lasjaunias P, Piske R, TerBrugge K, Willinsky R. Cerebral arteriovenous malformations (C. AVM) and associated arterial aneurysms (AA). Analysis of 101 C. AVM cases, with 37 AA in 23 patients. Acta Neurochir (Wien) 1988;91(1-2):29-36.

(27) Miyasaka K, Wolpert SM, Prager RJ. The association of cerebral aneurysms, infundibula, and intracranial arteriovenous malformations. Stroke 1982 Mar;13(2):196- 203.

(28) Okamoto S, Handa H, Hashimoto N. Location of intracranial aneurysms associated with cerebral arteriovenous malformation: statistical analysis. Surg Neurol 1984 Oct;22(4):335-40.

(29) Nornes H, Grip A. Hemodynamic aspects of cerebral arteriovenous malformations. J Neurosurg 1980 Oct;53(4):456-64.

(30) Perata HJ, Tomsick TA, Tew JM, Jr. Feeding artery pedicle aneurysms: association with parenchymal hemorrhage and arteriovenous malformation in the brain. J Neurosurg 1994 Apr;80(4):631-4.

(31) Suzuki J, Onuma T. Intracranial aneurysms associated with arteriovenous malformations. J Neurosurg 1979 Jun;50(6):742-6.

(32) Redekop G, TerBrugge K, Montanera W, Willinsky R. Arterial aneurysms associated with cerebral arteriovenous malformations: classification, incidence, and risk of hemorrhage. J Neurosurg 1998 Oct;89(4):539-46.

(33) Gao E, Young WL, Pile-Spellman J, Joshi S, Duong H, Stieg PE, et al. Cerebral arteriovenous malformation feeding artery aneurysms: a theoretical model of intravascular pressure changes after treatment. Neurosurgery 1997 Dec;41(6):1345-56.

(34) Rinkel GJ, Djibuti M, Algra A, van GJ. Prevalence and risk of rupture of intracranial aneurysms: a systematic review. Stroke 1998 Jan;29(1):251-6.

(35) Brown RD, Jr., Wiebers DO, Forbes GS. Unruptured intracranial aneurysms and arteriovenous malformations: frequency of intracranial hemorrhage and relationship of lesions. J Neurosurg 1990 Dec;73(6):859-63.

(36) Marks MP, Lane B, Steinberg GK, Chang PJ. Hemorrhage in intracerebral arteriovenous malformations: angiographic determinants. Radiology 1990 Sep;176(3):807-13.

(37) Miyasaka Y, Kurata A, Tokiwa K, Tanaka R, Yada K, Ohwada T. Draining vein pressure increases and hemorrhage in patients with arteriovenous malformation. Stroke 1994 Feb;25(2):504-7.

(38) Langer DJ, Lasner TM, Hurst RW, Flamm ES, Zager EL, King JT, Jr. Hypertension, small size, and deep venous drainage are associated with risk

of hemorrhagic presentation of cerebral arteriovenous malformations. Neurosurgery 1998 Mar;42(3):481-6.

(39) Szabo MD, Crosby G, Sundaram P, Dodson BA, Kjellberg RN. Hypertension does not cause spontaneous hemorrhage of intracranial arteriovenous malformations. Anesthesiology 1989 May;70(5):761-3.

(40) Duong DH, Young WL, Vang MC, Sciacca RR, Mast H, Koennecke HC, et al. Feeding artery pressure and venous drainage pattern are primary determinants of hemorrhage from cerebral arteriovenous malformations. Stroke 1998 Jun;29(6):1167-76.

(41) Miyasaka Y, Yada K, Ohwada T, Kitahara T, Kurata A, Irikura K. An analysis of the venous drainage system as a factor in hemorrhage from arteriovenous malformations. J Neurosurg 1992 Feb;76(2):239-43.

(42) Miyasaka Y, Kurata A, Irikura K, Tanaka R, Fujii K. The influence of vascular pressure and angiographic characteristics on haemorrhage from arteriovenous malformations. Acta Neurochir (Wien) 2000;142(1):39-43.

(43) Vinuela F, Nombela L, Roach MR, Fox AJ, Pelz DM. Stenotic and occlusive disease of the venous drainage system of deep brain AVM's. J Neurosurg 1985 Aug;63(2):180-4.

(44) Guidetti B, Delitala A. Intracranial arteriovenous malformations. Conservative and surgical treatment. J Neurosurg 1980 Aug;53(2):149-52.

(45) Stefani MA, Porter PJ, terBrugge KG, Montanera W, Willinsky RA, Wallace MC. Angioarchitectural factors present in brain arteriovenous malformations associated with hemorrhagic presentation. Stroke 2002 Apr;33(4):920-4.

(46) Stapf C, Mohr JP, Sciacca RR, Hartmann A, Aagaard BD, Pile-Spellman J, et al. Incident hemorrhage risk of brain arteriovenous malformations located in the arterial borderzones. Stroke 2000 Oct;31(10):2365-8.

(47) Willinsky R, Lasjaunias P, TerBrugge K, Pruvost P. Brain arteriovenous malformations: analysis of the angio-architecture in relationship to hemorrhage (based on 152 patients explored and/or treated at the hopital de Bicetre between 1981 and 1986). J Neuroradiol 1988;15(3):225-37.

(48) Hademenos GJ, Massoud TF. Risk of intracranial arteriovenous malformation rupture due to venous drainage impairment. A theoretical analysis. Stroke 1996 Jun;27(6):1072-83.

(49) Todaka T, Hamada J, Kai Y, Morioka M, Ushio Y. Analysis of mean transit time of contrast medium in ruptured and unruptured arteriovenous malformations: a digital subtraction angiographic study. Stroke 2003 Oct;34(10):2410-4.

(50) Young WL, Kader A, Pile-Spellman J, Ornstein E, Stein BM. Arteriovenous malformation draining vein physiology and determinants of transnidal pressure gradients. The Columbia University AVM Study Project. Neurosurgery 1994 Sep;35(3):389-95.

(51) Hirai S, Mine S, Yamakami I, Ono J, Yamaura A. Angioarchitecture related to hemorrhage in cerebral arteriovenous malformations. Neurol Med Chir (Tokyo) 1998;38 Suppl:165-70.:165-70.

(52) Pollock BE, Flickinger JC, Lunsford LD, Bissonette DJ, Kondziolka D. Factors that predict the bleeding risk of cerebral arteriovenous malformations. Stroke 1996 Jan;27(1):1-6.

(53) Turjman F, Massoud TF, Vinuela F, Sayre JW, Guglielmi G, Duckwiler G. Aneurysms related to cerebral arteriovenous malformations: superselective angiographic assessment in 58 patients. AJNR Am J Neuroradiol 1994 Oct;15(9):1601-5.

(54) Turjman F, Massoud TF, Vinuela F, Sayre JW, Guglielmi G, Duckwiler G. Correlation of the angioarchitectural features of cerebral arteriovenous malformations with clinical presentation of hemorrhage. Neurosurgery 1995 Nov;37(5):856-60.

(55) Nataf F, Meder JF, Roux FX, Blustajn J, Merienne L, Merland JJ, et al. Angioarchitecture associated with haemorrhage in cerebral arteriovenous malformations: a prognostic statistical model. Neuroradiology 1997 Jan;39(1):52-8.

(56) Uchino A, Matsunaga M, Ohno M. Arteriovenous malformation of the corpus callosum associated with persistent primitive trigeminal artery--case report. Neurol Med Chir (Tokyo) 1989 May;29(5):429-32.

(57) Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. J Neurosurg 1986 Oct;65(4):476-83.

(58) Norbash AM, Marks MP, Lane B. Correlation of pressure measurements with angiographic characteristics predisposing to hemorrhage and steal in cerebral arteriovenous malformations. AJNR Am J Neuroradiol 1994 May;15(5):809-13.