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~~LIST OF PROCEDURES DONE~~

PROJECT REPORT

TITLE OF THE PROJECT:

PULMONARY VASCULAR CHANGES IN ENDOMYOCARDIAL FIBROSIS:

NAME.....R. KRISHNAN.....

PROGRAMME:.....D.M. CARDIOLOGY.....

MONTH & YEAR
OF SUBMISSION:.....NOVEMBER 1985.....

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM 695011

Name	
Page	of
Date	

CERTIFICATE

I, Dr. R. Krishnan hereby declare that I have actually performed all the procedures listed/carried out the project under report.

Signature R. Krishnan

Place: TRIVANDRUM

Name in R. KRISHNAN
capital letters

Date: NOVEMBER 15, 1985

Forwarded

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PULMONARY VASCULAR CHANGES IN ENDOMYOCARDIAL FIBROSIS

INTRODUCTION:

Endomyocardial Fibrosis is a disease of unknown etiology occurring in residents of tropical and subtropical Africa, Bragil, Srilanka and Columbia.[1,2] In India it is commonly found in the southern state of Kerala.[3,4] The pathological changes in the heart in this disorder have been extensively described.[5,6] There are reports of changes in other organs also.[7] So far we have not come across any report regarding the pulmonary vascular pathology in this disease. In this report our observations regarding pulmonary vascular changes in fifteen patients with endomyocardial fibrosis (EMF) is presented.

MATERIALS AND METHODS:

Fifteen consecutive patients with endomyocardial fibrosis where the diagnosis was confirmed at autopsy constitute the material for this study. All these patients had complete clinical workup which included haemodynamic and angiographic data. Eleven patients had surgery [TRICUSPID OR MITRAL VALVE REPLACEMENT with endocardiectomy] and died in the immediate post operative period. One patient had ventricular fibrillation 24 hrs after cardiac catheterisation and could not be resuscitated. The remaining three had progressive congestive failure and death was terminal event in them. They did not have surgical intervention. Partial autopsy was done in all and the pathological specimen were analysed.

TABLE 1. CLINICAL FEATURES IN PREDOMINANT RVEMF. (No of Patients 7)

Symptoms: NYHA class:

All in Class IV.

Signs:

Paffiness of face, Lower limb edema, Elevated JVP, Cardiomegaly, Hepatomegaly, RVS_3 } in all seven

Cyanosis 1/7
LPSH 0/7
Accentuated P_2 ... 1/7
Tricuspid regurgitation murmur } ... 3/7
No murmur 4/7
Ascites 4/7
Splenomegaly 1/7

EKG:

Sinus Rhythm 2/7
Atrial fibrillation 5/7
Right Atrial Abnormality 7/7
LAE, LVH, RVH, Conduction disturbance } 0/7

SKIAGRAM:

Cardiomegaly with Enlarged Right atrium } 7/7
Prominant RV outflow 7/7
Left Atrial Enlargement, Evidence of PVH, PAH } 0/7.

TABLE 2. Haemodynamic data in Predominant RVEMF.

	1	2	3	4	5	6	7
RA	a_{30} V_{28} $\overline{24}$	V_{20} $\overline{16}$	V 19 $\overline{17}$	V_{28} $\overline{25}$	V 19.5 $\overline{16}$	V_{38} $\overline{27}$	V_{36} $\overline{26}$
RV	30/20	21/15	25/19 , 21	28/18 , 20	NA	33/18 , 26	35/20 , 26
PA	28/20 $\overline{24}$	20/14	24/19 $\overline{18}$	28/21 $\overline{22}$	NA	33/20 $\overline{25}$	34/27 $\overline{28}$
PAW	$a_{17.5}$ V_{19} $\overline{15}$	NA	NA	NA	NA	NA	NA
LV	108/0 , 13.5	98/0 , 11	105/0 , 10	120/0 , 14	120/0 , 8	130/0 , 22	115/0 , 26
AO	108/62 $\overline{80}$	91/54 $\overline{60}$	95/65 $\overline{75}$	100/65 $\overline{75}$	110/82 $\overline{87}$	125/80 $\overline{110}$	115/65 $\overline{88}$
CO.	2.8	3.1	3.7	3.2.	3.0	2.0.	2.6.
ANGIO:	Grade III[19] RVEMF Grade III TR LV Normal	Grade II RVEMF RA injection TR not commentable No LVEMF No MR	Grade II RVEMF No LVEMF	Grade III RVEMF. Grade III TR Normal LV Ectopic ind MR.	Grade III. RVEMF Grade III TR ? Early LV disease Grade I MR	Grade III RVEMF Grade III TR ? Early LV involv Grade I MR	Grade III RVEMF Grade III TR LV - Normal.

Patients with predominant involvement of one ventricular chamber with minimal lesions in the other ventricle, at autopsy, were categorised as having disease in the chamber with predominant involvement.

eg. Hearts with extensive involvement of right ventricle with a very small lesion in the left ventricle were considered as having predominant right ventricular endomyocardial fibrosis (RVEMF) and vice versa.. Hearts with equally severe involvement of both the ventricles were considered as having biventricular endomyocardial fibrosis. [BVEMF].

PULMONARY VASCULAR CHANGES:

Tissues for histopathologic studies were obtained from all the lobes of both the lungs in all the fifteen patients. Tissues were fixed in 10% buffered formalin and processed for paraffin embedding. 5-8 micron sections were stained with haematoxylin and eosin and Verhoeff's elastic tissue stain.

Blood vessels including elastic and muscular branches of pulmonary artery, arterioles, capillaries and veins were examined with reference to medial thickness and intimal proliferation. The arterial vessels were classified by Brennet's criteria[8] and using a micrometer eye piece the diameters were measured by the technique of Wagenvoort et al.[9] Medial thickness of arteries was measured from the external to internal elastic lamina along diameters at right angles to each other and the average of this was expressed as a percentage of the external diameter. The upper limit of normal medial thickness of muscular branches of pulmonary arteries was taken as 7%.[10]

TABLE 3. CLINICAL FEATURES IN PREDOMINANT LVEMF. (No of Patients 3)

Symptoms: NYHA class:
All in class IV

Signs:
Elevated JVP
Cardiomegaly
Parasternal heave
Accentuated Pa
murmur of MR
LVS3, RVS3
Hepatomegaly
Bibasal Rales
} in all 3 pts.

EKG:
Sinus Rhythm 2/3
Atrial fibrillation - 1/3
Left Atrial Enlargement 0
Right Atrial Enlargement 0
Ventricular hypertrophy 0
Incomp RBBB 1/3
QRS Axis + 105 2/3

Skiagram:
Right Atrial Enlarg .. 1
Left Atrial Enlarg - 2.
Pulm. Venous hypertension ... 3
Evidence of PAH 3

TABLE 4. HAEMODYNAMIC DATA IN PREDOMINANT LVEMF.

	1.	2.	3.
RA	a_{10} V_6 $\bar{6}$	$\bar{11}$	a_{20} $\bar{15}$
RV	$95/_0$, 2	$96/_0$, 12	$78/_0$, 23
PA	$70/_{30}$ $\bar{37}$	$97/_{38}$ $\bar{54}$	$75/_{38}$ $\bar{52}$
PAW	a_{27} V_{22} $\bar{22}$	—	—
LV	$120/_0$, 25	$118/_0$, 18	$120/_4$, 28
AO	$120/_{78}$ $\bar{88}$	$145/_{90}$ $\bar{100}$	$120/_{76}$ $\bar{94}$
C.O.	2.06	2.8	2.1.
ANGIO:	Grade I LVEMF No MR. ~~Normal~~	RV - Normal Grade III LVEMF grade II MR	Grade I LVEMF Grade 2 MR Grade I RVEMF No TR.

Pulmonary veins were analysed for the presence of medial hypertrophy, arterialisation and intimal fibrosis. Alveolar changes such as interalveolar septal thickening haemosidderosis, alveolar epithelialisation and calcification were routinely sought.

Eccentric intimal fibrosis, when present in the arteries were considered to be due to old thrombo embolism and the extent of it was also noted.

The vascular and parenchymal changes in the lungs were correlated with the haemodynamic data.

RESULTS:

The patients were subdivided into three subgroups depending on the degree of involvement of the ventricles by the disease process as

a. Predominant right ventricular endomyocardial fibrosis (predominant RVEMF)

b. Predominant left ventricular endomyocardial fibrosis (predominant LVEMF)

c. Biventricular endomyocardial fibrosis. (BVEMF)

PREDOMINANT RVEMF:

There were seven patients in this category with age ranging from 7 to 23 years. There were 5 males and two females. The salient clinical, radiological

TABLE 5. CLINICAL FEATURES IN BIVENTRICULAR EMF. (No. of Patients 5)

Symptoms: NYHA class.
Class IV ... 2.
class III .... 3.

Signs:
Cyanosis ... 0
Puffiness of face ... 3
Edema feet ... 3
Elevated JVP ... 5
Cardiomegaly ... 5
Parasternal heave ... 1
Accentuated P_2 ... 1
Mitral Regurgitation ... 2
Trichspid regurgitation ... 2
Both MR and TR ... 2.
No murmur ... 0

LVS_3 1
RVS_3 ... 3
Hepatomegaly 5
Asuites ... 3
L. Crepitations ... 3

EKG:
Sinus Rhythm 2.
Atrial fibrillation 3
Left Atrial Enlargement 1
Right Atrial Enlargement 3
Chamber hypertrophy (RV & LV) ... 0
Conduction disturbance ... 0

Skiagram:
Right Atrial Enlargement 3
Left Atrial Enlargement 2
Enlarged RV outflow 3
Pulmonary Venous hypertension 2
Pulmonary Arterial Hypertension 0.

TABLE 6. Haemodynamic data in BIVENTRICULAR EMF:

	1.	2.	3.	4.	5.
R.A.	a_{28} V_{26} $\overline{24}$	a_{12} $\overline{8}$	V_{24} $\overline{18}$	V_{25} $\overline{19}$	a_{23} V_{23} $\overline{19}$
R.V.	$30/20$	$65/0$, 12	$26/10$, 18	$42/10$	$25/10$, 22
P.A	$30/20$ $\overline{24}$	$61/36$ $\overline{42}$	$24/16$ $\overline{18}$	$42/23$ $\overline{27}$	$24/14$ $\overline{19}$
PAW	a_{18} V_{20} $\overline{15}$	$\overline{30}$	—	$\overline{10}$	—
LV	$110/0$, 13.5	$125/0$, 30	$100/80$, 15	$116/80$, 10	$100/5$, 10
AO	$110/60$ $\overline{78}$	$119/71$ $\overline{93}$	$100/60$ $\overline{70}$	$116/80$ $\overline{90}$	$100/60$ $\overline{75}$
CO:	2.8	3.1	4.7	3.6	3.3
ANGIO:	Grade III RVEMF Grade III TR No LVEMF No MR	Grade II RVEMF Grade I TR Grade III LVEMF Grade 3 MR	Grade I LVEMF Grade III RVEMF grade II TR	Grade II RVEMF Grade III TR Huge clot in RA Grade II LVEMF Grade I MR	Grade III RVEMF Grade II TR Grade I LVEMF grade I MR

and electrocardiographic features are given in Table 1. All had features of severe systemic venous hypertension. Haemodynamic data and angiographic features are given in Table 2. All had severe elevation of right heart filling pressures with normal pulmonary arterial pressures. Two patients had elevated left ventricular filling pressure for no apparent reason.

PREDOMINANT LVEMF:

There were three females age ranging from 26 to 55 in this group. Their relevent symptoms, physical signs electrocardiographic and radiological features are given in Table 3. Haemodynamic data and angiographic features are given in Table 4.

BIVENTRICULAR ENDOMYOCARDIAL FIBROSIS:

There were five patients in this group, 4 males and a female, ages ranging from 11–38 years. Their symptoms, physical signs, electrocardiographic and radiological features are given in Table 5. Haemodynamic data and angiographic features are given in Table 6.

[P.T.O]

		PREDOMINANT RVEMF							PREDOMI. LVEMF			BVEMF				
		1	2	3	4	5	6	7	1	2	3	1	2	3	4	5
MUSCULAR PULMONARY ARTERIES	MEDIAL HYPERTROPHY	0	0	0	0	0	0	0	++	++	+	0	+	0	0	0
	INTIMAL FIBROSIS — CONCENTRIC	0	0	0	0	0	0	0	++	++	0	0	++	0	0	0
	INTIMAL FIBROSIS — ECCENTRIC	+	0	0	+	0	+	0	0	0	0	+	+	0	0	+
	Cellular intimal Proliferation	0	0	0	0	0	0	0	+	+	0	0	+	0	0	0
	Dilatation and Plexiform lesions	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Arteritis.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ARTERIOLES	MUSCULARISATION	0	0	0	0	0	0	0	++	++	+	0	+	+	0	0
PULM. VEINS.	Medial Hypertrophy	0	0	0	0	0	0	0	+	+	+	0	+	+	0	+
	Intimal fibrosis	0	0	0	0	0	0	0	+	+	0	0	+	0	0	0
	Muscularisation	0	0	0	0	0	0	0	++	++	+	0	+	0	0	0
ALVEOLAR CHANGES	Interalveolar Septal thickening	0	+	0	0	0	0	0	++	+++	++	0	++	+	0	0
	Haemosiderosis	0	0	0	0	0	0	0	++	+++	0	0	+	0	0	0
	Epithelialisation	0	0	0	0	0	0	0	+	+	0	0	+	0	0	0
	calcification / Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	* GRADE	TE	0	0	TE	0	TE	0	Severe	Severe	Moderate	TE	Severe + TE	Mild	0	TE

+ MILD ++ MODERATE +++ MARKED 0 ABSENT. TE - Thrombo Embolism.

PULMONARY VASCULAR CHANGES:

Of the fifteen patients significant changes in the pulmonary vascular tree were found in five. - three with LVEMF and two with BVEMF-. Pulmonary arterioles were muscularised in all the five. Alveolar changes suggestive of pulmonary venous hypertension [inter alveolar septal thickening, epithelialisation] were found in four of them. None of the lungs showed dilatation and plexiform lesions and arteritic changes. Eccentric intimal fibrosis in the muscular pulmonary arteries due to probable thrombo embolism was found in 6 patients, three each in predominant RVEMF and Biventricular EMF categories. None of the seven patients with predominant RVEMF showed significant pulmonary vascular changes and the changes were seen only in patients with significant left ventricular disease, either predominant LVEMF or Biventricular EMF.

The profile of pulmonary histologic lesions in the 15 patients is given in Table 7.

Grading of Histological changes:

Mild: Evidence of pulmonary venous hypertension with muscularisation of arterioles.

Moderate: In addition to the above medial hypertrophy of the muscular arteries.

Severe: Presence of intimal changes in addition to the above.

[P.T.O].

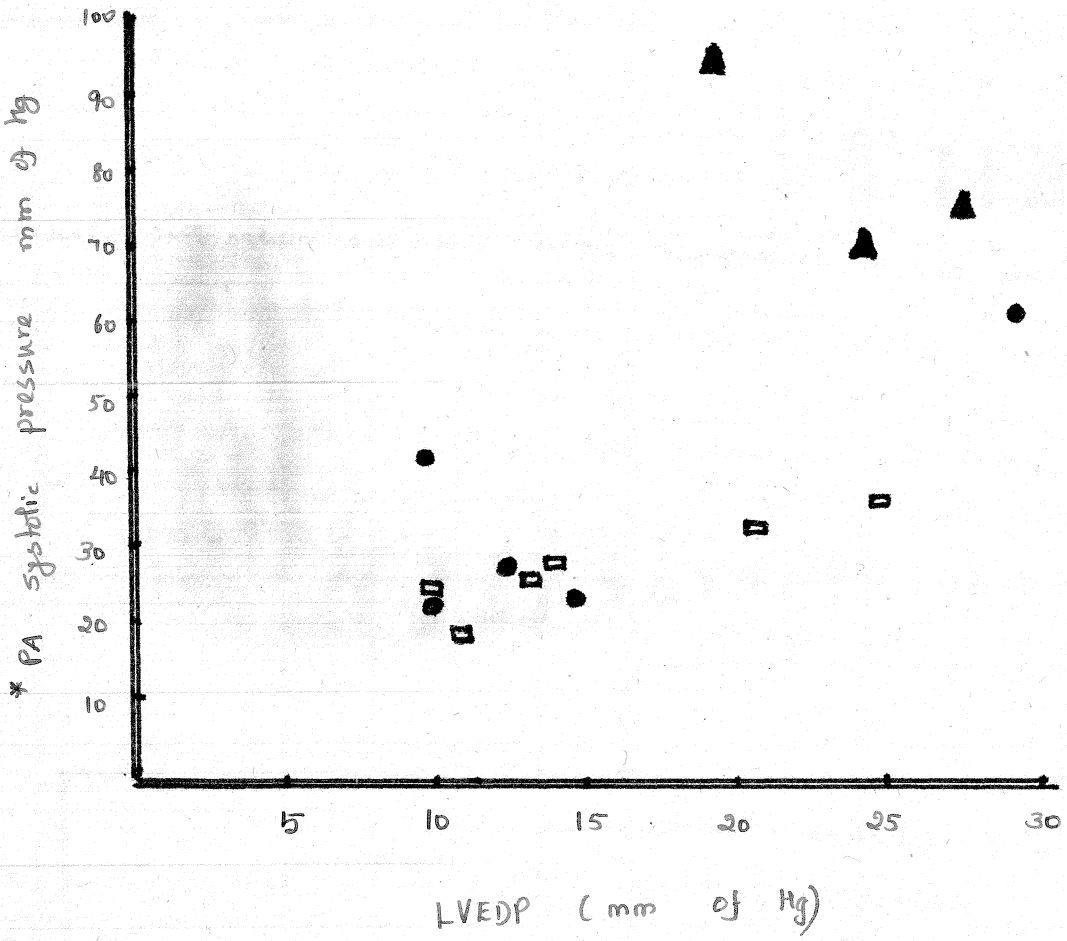

Figure 1.

▭ Predominant RVEMF.

▲ Predominant LVEMF.

● Biventricular EMF.

* Not available in one patient with predominant RVEMF.

HAEMODYNAMIC CORRELATION.

Figure 1 is the scattergram of the Pulmonary Artery peak systolic pressures and the LVEDP in 14 patients. (Pulmonary artery was not entered in one patient with predominant RVEMF due to severe tricuspid regurgitation) It can be seen that in none of the predominant RVEMF patients Pulmonary artery peak systolic pressure is more than 35 and barring two patients all had LVEDP less than 15 mm of Hg. The two patients who had elevated LVEDP (cases 6 and 7) did not show elevation in Pulmonary arterial pressures. There was no significant pulmonary vascular changes in these cases. Similarly out of the 5 patients with BVEMF 4 had pulmonary artery peak systolic pressures less than 40 and LVEDP less than 15 mm of Hg. One patient (No.2) in this group had elevated LVEDP and the Pulmonary artery peak systolic pressure was 50 mm of Hg in him. This patient also had changes in the pulmonary vascular tree suggestive of pulmonary venous hypertension.

All the three patients with predominant LVEMF had significant elevation of LVEDP and PA pressures and had changes secondary to pulmonary venous hypertension, in the histological studies.

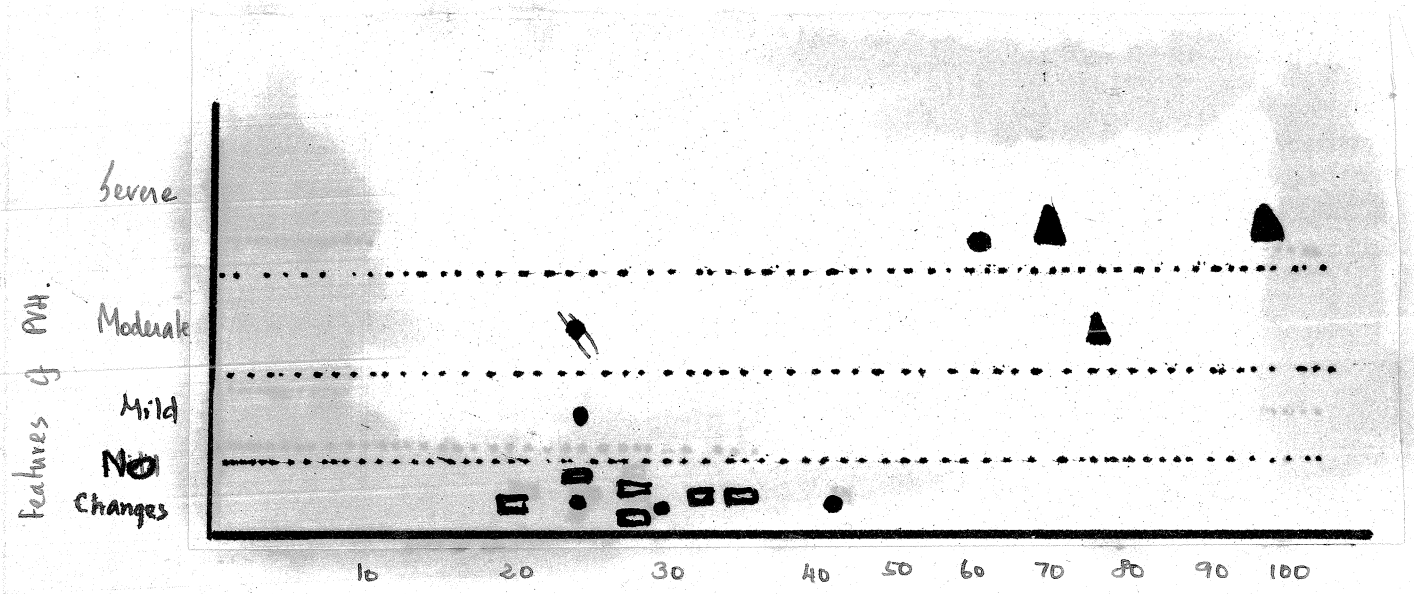

Figure 2.

- Predominant RVEMF.
- Predominant LVEMF.
- Biventricular EMF
- * Not available in one with RVEMF.

Figure 2 is a scattergram relating pulmonary artery peak systolic pressure to pulmonary vascular changes suggestive of pulmonary venous hypertension. It is obvious that all patients with predominant LVEMF have severe changes of pulmonary venous hypertension and severe elevation of pulmonary arterial pressures. In addition one patient with BVEMF also showed significant elevation in PA pressure with similar pulmonary changes. None of the patients with predominant RVEMF showed pulmonary vascular changes.

DISCUSSION

Raised pulmonary pressures secondary to elevated pulmonary venous pressure is well known. Restrictive heart diseases altering left ventricular compliance is an important cause of such pulmonary venous hypertension and secondary pulmonary arterial hypertension.[2,10] In such cases morphological changes in the pulmonary arterial and venous systems have been well described. These consist of medial hypertrophy and concentric intimal fibrosis in muscular pulmonary arteries and arterialisation of the pulmonary venous walls and medial hypertrophy in them.[10]

Interalveolar septal thickening and haemosidderosis constitute additional features noted. The morphological

features seen in this study in patients with pulmonary arterial hypertension are the same described by various workers[10,11] in conditions secondary to pulmonary venous hypertension. Their correlation with LVEDP and the absence of pulmonary arterial hypertension and morphological changes in predominant RVEMF adds further to such a conclusion. Such correlations with haemodynamic data and pulmonary vascular changes have been reported[12] in a number of studies of patients with mitral stenosis, the commonest cause of secondary pulmonary arterial hypertension.

Though isolated reports of necrotising pulmonary arteritis in pulmonary venous hypertension are available[13] such lesions are unusual in pulmonary venous hypertension.[10] Similarly dilatation lesions and plexiform lesions do not occur in chronic pulmonary venous hypertension.[10] There is only an isolated report[12] of dilatation lesions occurring in chronic pulmonary venous hypertension. None of the 15 patients in this report had arteritis, dilatation lesions or plexiform lesions.

Thrombo emboli lodged in the pulmonary arteries may be a cause of increased pulmonary arterial resistance and pressure. Embolic obstruction of small elastic or of muscular pulmonary arteries is of little consequence unless numerous arteries are involved. Chronic embolic pulmonary hypertension is not a common disease.[10,11] Organisation of such thrombi

in the pulmonary arterial wall leads to the development of cushion like patches of intimal fibrosis protruding into the lumen, are eccentric and lack the laminar onion skin arrangement as is seen in vasoconstrictive pulmonary hypertension. Such lesions were seen in 6 patients in this study. (Three with predominant RVEMF and three with BVEMF). These were rather occasional and not extensive. It is not unexpected, as most patients with RVEMF have dilated right atrium with sluggish blood flow and fresh as well as organised clots are frequently noted in right atrium at surgery or necropsy. Rather their not being extensive is surprising. None of these six patients had elevated pulmonary arterial pressures suggesting that it is not a contributing feature in these cases of pulmonary arterial hypertension.

Etiology of endomyocardial fibrosis is still obscure and the various theories that have been put forward relate to the processes in which vascular changes may be expected. This is true if EMF is considered as a form of rheumatic disease[14] or hypersensitivity disease[6] of the connective tissue. Other workers[15] believe that EMF is closely related to Loeffler's endomyocardial disease and suggest similar pathogenesis. They believe that the eosinophil granules and its cytotoxicity play a significant role in the pathogenesis of both

these entities. Pulmonary vascular changes in hypereosinophilic syndromes have been described.[16] Extensive and advanced lesions in the muscular pulmonary arteries and arterioles in the form of angiomatoid and plexiform lesions have also been observed.[17] Though occlusive coronary arterial lesions in EMF have been documented in the literature[18] we are yet to come across reports of arterial involvement in the pulmonary arterial tree. None of the patients in this study had pulmonary arterial lesions as described in hypereosinophilic syndrome.

CONCLUSION

From this study it may be concluded that morphological changes found in the pulmonary vascular tree in patients with EMF are secondary to disease of the left ventricle resulting in loss of compliance and secondary elevation of pulmonary venous pressure. Pulmonary vascular changes are not present with predominant RVEMF and there are no characteristic morphological changes in the lung attributable to this disease. Though thrombo embolism occurs in pulmonary vascular tree it is never a cause of pulmonary hypertension in these patients.

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