Short report

Cerebrovascular disease in north-west India: a study of necropsy material

A K BANERJEE, M VARMA, R K VASISTA, J S CHOPRA

From the Departments of Pathology and Neurology, Postgraduate Institute of Medical Education and Research, Chandigarh

SUMMARY   The pattern of cerebrovascular disease in North-West India has been studied in a necropsy series of 362 cases over a 14 year period. One hundred and thirty eight cases of intracranial haemorrhage were found, 89 of cerebral embolism, 101 of cerebral arterial thrombosis and 34 of cerebral venous thrombosis. Nearly 37% of the affected patients were below 40 years of age. Cerebral embolism and cerebrovenous thrombosis were important causes of stroke in the young. Rheumatic heart disease and infective endocarditis formed the major causes of cerebral embolism. Cerebral venous thrombosis associated with pregnancy and puerperium was relatively more common in our series than has been reported in the West.

There is ample evidence to suggest that the incidence and aetio-pathogenesis of cerebrovascular disease (CVD) in the developing countries differ from those in the westernised nations in many important aspects. In the latter CVD is a disease of the elderly and rarely occurs below 40 years of age.[1] In contrast, CVD contributes very significantly to the morbidity and mortality in the younger age groups in Afro-Asian countries.[2,3] Cerebral embolism has been said to be more common in India than in the developed countries.[4,5] Yet, very little data are available on CVD in India. Most of the studies from this country have been clinical and there is no report on the pattern of CVD based on a large necropsy series. A report based on 200 consecutive brain necropsies over a period of 18 months had been published by one of us.[5] In this communication, an analysis of the pattern of CVD in consecutive necropsies over a period of 14 years is presented.

Material and methods

Necropsies were performed on 4753 subjects above one year of age during the 14 year period 1971 to 1984 in the

Address for reprint requests: Professor A K Banerjee, Department of Pathology, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India.

Department of Pathology. All the patients died in the hospital attached to this Institute. This hospital provides general as well as special medical care and is the largest referral centre in the region. Seriously ill patients with short hospital stay constitute a large proportion of the necropsy material. The brain was examined in 2023 only, in whom the clinical diagnosis had indicated involvement of the central nervous system (CNS) and an informed consent for examination of the intracranial contents could be obtained.

After exclusion of cerebrovascular lesions of traumatic origin or complicating tumours and infections of the CNS, 362 cases in which CVD was a major lesion, but not necessarily the cause of death, were analysed. Each brain was fixed by suspension in formalin for a minimum period of 10 days. One centimeter thick coronal slices were examined macroscopically. Paraffin sections of relevant portions of brain and blood vessels were examined microscopically. Extracranial organs were available in 293 of the 362 cases. The heart, the aortic arch including the origin of the great vessels, the kidneys and other organs were examined for evidence of hypertension, source of emboli, embolic lesions, vascular occlusion and other abnormalities. The carotid and vertebral arteries in the neck were available in only a very small number of cases and the data are not included in this analysis. Evidence of systemic hypertension was also obtained from the clinical protocol, such as history of pre-existing hypertension, clinical and electrocardiographic evidence of left ventricular hypertrophy, retinal changes and renal disease. Blood pressure recordings made immediately following stroke without additional clinical or pathological evidence were not considered for classifying the case as hypertensive. Cases of arterial cerebral infarction in which the source of embolus could be established and/or where

embolic lesions were found in other organs, have been classified as embolic and the rest as thrombotic. Microscopic examination of the occluded artery, whenever found, was also considered to distinguish thrombotic and embolic occlusion.

Observations

The 362 cases constituted 7·61% of all necropsies. The analysis of the different groups with age and sex distribution is shown in table 1. Cerebral infarction was more commonly encountered than intracranial haemorrhage. Embolic and thrombotic infarctions were found in comparable numbers. Venous infarction was much lower than the other subgroups. The mean age at death was 43·3 years and 36·8% of the cases were below 40 years of age. The average age of the venous thrombosis cases, both pregnancy related and unrelated, was lower than the other groups. The mean age of the cases of embolic infarction was slightly higher than that of haemorrhage but lower than the cases of thrombotic infarction.

The various sources of emboli are shown in table 2. The vast majority (70·8%) originated in the heart. Infective endocarditis and rheumatic heart disease (RHD) accounted for most of the cases among younger patients while in older subjects the most common cause was myocardial infarction. In 24 cases classified as embolic infarction, no source of embolus could be identified, although in four cases the emboli were thought to have originated from the carotid arteries in the neck. In all these cases there was occlusion of the appropriate intracranial artery and these were interpreted as embolism on microscopic examination. One case of systemic lupus erythematosus with atypical verrucous endocarditis had multiple organ embolic infarctions. An unusual case of embolus into the middle cerebral artery from a thyroid carcinoma without intracranial metastasis, presented as stroke.[6] The embolic infarctions were multiple in 41·6% and bilateral in 34·8%. The carotid territory was involved in 84·3% while the vertebrobasilar territory was involved in 4·5% and both in the rest. The middle cerebral artery territory was the most

Table 2   *Source of emboli in embolic infarcts*

Source	Number	Per cent
Heart: Non infective	46	51·6
RHD	17	
RHD + AF	6	
MI	20	
Verrucous Endocarditis	2	
Aneurysm-sinus of valsalva	1	
Heart: Infective	17	19·10
RHD + IE	6	
CHD + IE	2	
Normal valve IE	9	
Other	26	29·21
Tumour	1	
Fat	1	
Unknown	24	

RHD: chronic rheumatic heart disease; AF: atrial fibrillation; MI: myocardial infarction; IE: infective endocarditis; CHD: congenital heart disease.

common site of embolism. Occlusion was demonstrated in the appropriate artery in 55·1%.

Infarctions due to thrombosis were slightly more common than embolism. Twenty nine point seven percent of the former were bilateral and the middle cerebral artery territory was most commonly affected. Occlusion noted in 27·8% was less than that in the embolic group. Evidence of systemic hypertension was found in 38·6%. Among these cases of thrombotic infarction, there was a 50 year old man with disseminated prostatic adenocarcinoma associated with cerebral infarction in the left middle cerebral artery territory. This artery was occluded by thrombus but no tumour metastasis was found.

Five instances of arterial cerebral infarction were associated with pregnancy or the puerperium. Three had had full term normal delivery, one was 6 months pregnant while another had an induced abortion at 6 weeks. Three of these were associated with sinovenous thrombosis (SVT). However, only one of these three cases showed venous infarction. In addition 21 cases of SVT associated with pregnancy or puerperium and 13 cases of pregnancy unrelated SVT were encountered.

Haemorrhagic lesions constituted 38·12% of CVD in this series. Ruptured aneurysms, arteriovenous malformations (AVM) and blood dyscrasias accounted for 55 cases. Ten cases classified as intracranial haemorrhage due to blood dyscrasia had generalised bleeding manifestations due to fulminant hepatitis in four, snake bite in two, disseminated intravascular coagulation with septicaemia in two and severe thrombocytopaenia in two cases. Among the rest 48 patients with intracerebral haemorrhage (ICH) were hypertensive. The pathogenesis of haemorrhage in 27 cases of ICH and eight cases of subarachnoid haemorrhage (SAH) could not be determined. The average age of patients with ICH was 44·7 years and 26·6% were under 40 years of age. The predominant

Table 1   *Age and sex distribution in a CVD group*

Disease	Number	Male/ Female	Mean age (yr)	% CVD
Haemorrhage	138	89/49	41·8	38·12
Ruptured Aneurysm	42	23/19	38·1	11·6
Ruptured AVM	3	3/0	46·3	0·8
Bleeding Dyscrasias	10	6/4	32·2	2·7
Spontaneous	83	57/26	44·7	22·9
Infarction: Arterial	190	132/58	45·1	52·4
Embolic	89	57/32	42·5	24·5
Thrombotic	101	75/26	47·4	27·9
Infarction: Venous	34	8/26	26·2	9·3
Pregnancy Related	21	0/21	25·1	5·8
Pregnancy Unrelated	13	8/5	26·2	3·5

location of ICH was the basal ganglia region. Cerebral white matter was affected in 10 cases, pons in six cases and cerebellum in three cases. All the patients of pontine haemorrhage and 70% of ganglionic haemorrhages in this group of 83 cases were hypertensive. Bilateral ganglionic haemorrhage was observed in two cases. Hypertensive was secondary to renal disease in six cases.

Out of the 42 cases of ruptured aneurysm nine were mycotic, secondary to infective endocarditis, and 33 saccular. The latter constituted 9·1% of CVD and 0·69% of necropsies in this series. Seven unruptured aneurysms including one giant aneurysm encountered during the study period are not included in the analysis. Mycotic aneurysms affected younger subjects compared to saccular aneurysms, the average age being 25·8 and 43·45 years respectively. In 16 cases the ruptured saccular aneurysms were located on the anterior communicating artery and in 14 of these ICH was the terminal event. Other locations were seven at the bifurcation of middle cerebral, six at the junction of posterior communicating and internal carotid arteries and four in the posterior circulation. Evidence of hypertension was detected in 15 cases. One case of ruptured AVM had interesting associated lesions of intact aneurysm of anterior communicating artery, polycystic kidneys and polycystic liver.[7]

Discussion

Necropsy studies are subject to considerable bias because of the nature of case selection and the kind of hospital population. Nevertheless valuable information can be derived particularly about the relative frequency of the different groups of CVD among fatal cases. Seriously ill patients with very short hospital stay constituted a large proportion of our necropsy material and this may have a bearing upon the relative frequency of various types of stroke in this series.

CVD is not an uncommon diagnosis at necropsy. In this series it was found in 7·61% of necropsies in patients above 1 year of age. However such data can not be directly extrapolated to the general population. Since these cases often pose diagnostic difficulties during life, a relatively larger proportion are necropsied as compared with other diseases. On the other hand a significant number die at home and are not necropsied.

The mean age at death (43·3 years) in this study is lower than the mean age at presentation (56·6 years) observed by Dalal *et al* in a clinical series from India.[8] We found that 36·8% of our cases were below 40. This is similar to the experience of other workers in India[2 3] but is in sharp contrast to that in Western countries where less than 2% of all stroke cases occur in patients below 40 years of age.[1] This difference is due to the

higher incidence of SVT and embolic infarctions in this series. The latter in turn results from a higher incidence of RHD and infective endocarditis both of which affect a younger population of patients. The male predominance (1·7:1) of CVD in this study should be considered in the context of the general male predominance at necropsy. The male to female ratio is 1·6:1 in this hospital.

Cerebral infarctions were found almost twice as often as intracranial haemorrhage similar to the report of Johnson *et al*[9] but diametrically opposite to the findings of Brewer *et al*.[10] In this study almost half of the cases of cerebral infarction were embolic. Even this figure is probably an underestimation because in many cases only the brain was examined at necropsy and the infarction classified as "thrombotic" because our diagnostic criteria for embolism could not be fulfilled. This indicates that embolism is as important a cause of fatal cerebral infarction as thrombosis. This is in agreement with the observations of Blackwood *et al*.[11] Most of the embolic infarctions were secondary to heart disease particularly RHD. Many of the cases of RHD with cerebral embolism were complicated by either atrial fibrillation or infective endocarditis. However, 17 cases of embolic infarctions were associated with apparently uncomplicated RHD. The most important cause of cerebral embolism in the elderly found during this study was mural thrombi over myocardial infarction.

The middle cerebral artery was the most common site of lodgement of emboli as has been the experience of others.[12] Occlusion of a major cerebral artery was found in only 55% of cases of embolic infarction. In 24 cases the source of emboli was not detected and the diagnosis of embolism was made on the basis of microscopic examination of the occluded artery. Examination of single level sections may not be absolutely accurate for distinguishable embolism from thrombosis. Therefore, it is possible that some cases of this group were indeed thrombotic. The extracranial portion of the carotid arteries has been studied in only a few cases so the possibility of embolism from this level can not be ruled out.

In the thrombotic infarction group occlusion of the intracranial arteries were found less frequently than in the embolic cases. This observation may be consistent with the notion that occlusion in the former cases may occur more frequently in the extracranial arteries.[13] Prabhakar *et al* from this Institute (personal communication), however, did not observe significant disease in the neck arteries of 100 cases of stroke of all age groups by the Doppler technique.

In the present study there were five cases of arterial infarction associated with pregnancy. During this period, 21 cases of venous infarction associated with pregnancy were encountered. Hence, it may be con-

cluded that while SVT accounts for the majority of pregnancy and puerperial strokes, arterial infarction is also an important cause. This point is important as many of the latter are misdiagnosed as SVT clinically.

SVT forms a relatively large group of CVD in India. The occurrence of SVT in relation to pregnancy and puerperium has been more frequently reported in India than in the West.[14-16] In the present study in addition to the 21 cases of SVT related to pregnancy there were 13 cases unrelated to pregnancy. While 79% of the pregnancy related cases had been correctly diagnosed, SVT had been suspected antemortem in only 23% of the pregnancy unrelated cases. Awareness of other clinical settings may increase diagnostic accuracy and allow therapy.

Ruptured aneurysms accounted for 9·1% of CVD which appears to be significant and does not support the view that aneurysms are uncommon in India.[17] This is also supported by the collaborative study in which 37·7% of SAH were found to be due to ruptured aneurysms.[18] Mycotic aneurysms were found to be more frequent than those reported from the West.[19] This is another group which contributes to the higher number of stroke in the young and related to the higher incidence of RHD and infective endocarditis in this geographic area.[20]

Absence of adequate explanation regarding the cause of intracranial haemorrhage in 35 necropsies is unsatisfactory. This could have been due to failure on our part to detect sources like a small aneurysm or hypertension. Nevertheless the association of hypertension and ICH is not always possible to establish and therefore their casual relationship remains controversial.[21]

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