EPILEPSY AND MITRAL STENOSIS

BY

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It has been recognized for a long time that epileptic convulsions may occur at the onset of or following cerebral infarction (Gowers, 1885; Hughlings Jackson, 1876; and Savill, 1909). It has been pointed out also that the incidence of epilepsy is higher in those suffering from rheumatic heart disease than in the general population. Chadbourne in 1903 while working in the Ohio Hospital for Epileptics noted that 5 per cent of the patients had rheumatic heart disease, and more recently Foster (1942) and Bruetch (1942) have made similar observations.

The ætiology of the epileptic seizures with rheumatic heart disease is not so clearly understood. Most writers state that seizures may occur in those with cardiac arrhythmia when momentary failure of cardiac output leads to cerebral anoxia (Symonds *et al.*, 1950). Others have claimed that the epilepsy is secondary to rheumatic obliterative arteritis affecting the cerebral vessels, and Bruetch (1942) describes three cases in which epilepsy occurred in patients who had rheumatic heart disease and evidence of multiple cerebral infarctions at autopsy, with histological changes that he interpreted as due to rheumatic arteritis. It has not been appreciated how frequently epilepsy in association with rheumatic heart disease could be due to emboli from the left atrium. Such emboli may cause infarction in vital areas of the brain, sometimes ushered in by a seizure and subsequently giving rise to epileptic attacks, associated with evidence of permanent cerebral damage; some, however, could cause infarction in "silent" areas of the brain and give rise to no immediate symptoms other than perhaps a momentary faint feeling, but could later develop into foci of epileptic activity.

A series of cases is presented in which emboli were thought to be the cause of the epileptic seizures. Since 1950, when a preliminary report of the success of operative treatment for mitral stenosis was made (Baker *et al.*, 1950) a large number of patients with this disease has been seen at Guy's Hospital. The occurrence of epilepsy with mitral stenosis was noted in some of the earlier patients and it was thought that this was a causal rather than a chance association of two common conditions. Since then, 22 patients have been seen where these two conditions were present and it is this group we are here reporting. Although some patients may have been missed, particularly in the large number who came in the earlier years when mitral valvotomy was not widely practised, we have not excluded any patient where epilepsy and mitral valve disease were both present. It is estimated that these 22 patients were collected from a total of about 600 who were seen with mitral valve disease. This large number was in itself a selected group as regards severity, for the great majority was referred with operative treatment in view.

Analysis of the Cases

The essential details are set out in the Table. There were 15 women and 7 men and the ages when first seen ranged from 19 to 47 with an average of 34 years. The sex and age incidence are in keeping with the large group of patients with mitral disease from which they were selected. Although it must be admitted that the family history was not studied in great detail there is only one patient (Case 20) with a family history of epilepsy. The age of onset of fits ranged from 19 to 47,

TABLE

PATIENTS WITH EPILEPSY AND MITRAL STENOSIS

No. and sex	Age at onset of fits	Age at onset of cardiac disability	Rhythm at onset of fits	Systemic embolism	Degree of mitral valve disease	Operative findings			Type of epy.	E.E.G.
						Size in cm.	Ca.	Age		
1F	47	47	Sinus	Hemi-plegia	Severe MS	1×0·5	—	48	Focal	Focal
2F	19*	17	Sinus	—	Severe MS and MI	1×0·3	Yes	19	Major	Abnormal
3M	41	39	Sinus	—	Severe MS (MI)	1·0	Yes	42	Major	Normal
4F	36	20	A.F.	—	Severe MS (TI)	0·8×0·4	—	43	Major	Abnormal
5F	34	23	Sinus	—	Severe MS	Refused valvotomy			Major and minor	Focal
6F	39	24	A.F.	1 Cerebral 1 Leg	Severe MS	0·5×0·3‡	—	39	Minor and focal	Abnormal
7F	41	27	A.F.	1 Mesen-teric 1 Arm	Severe MS	0·75×0·25	Yes	42	Major	Abnormal
8M	34	26	A.F.	Hemi-plegia	Severe MS and MI	Op. not advised Died aged 39			Minor focal	Normal
9F	29	None at 43	Sinus	—	Mild MS	Op. not advised			Major	Abnormal
10M	33*	24	A.F.	—	Severe MS (TI)	1·4×2·0	Yes	32	Minor focal	—
11M	32	27	A.F.	1 Cerebral	Severe MS	1·2×0·8	Yes	32	Minor focal	Focal
12F	20	29	Sinus	—	Moderate MS (AI)	Op. not advised			Major	Abnormal
13F	33	26	Sinus †	—	Severe MS (AI)	1·5×1·0	Yes	36	Major	Normal
14M	33	20	A.F.	Hemi-plegia 2 Renal	Severe MS (AI)	0·3×0·7	—	30	Major and minor focal	—
15F	33	24	A.F.	Hemi-plegia	Severe MS	0·5×0·4‡	—	34	Minor focal	Abnormal
16F	18	22	Sinus	—	Moderate MS (AI)	Op. not advised			Major focal	Focal
17M	28	28	A.F.	Hemi-plegia	Severe MS	"Small"	Yes	32	Minor focal	Normal
18F	30*	23	Sinus	—	Severe MS	1·0	—	29	Minor focal	Abnormal

Table—*continued*

No. and sex	Age at onset of fits	Age at onset of cardiac disability	Rhythm at onset of fits	Systemic embolism	Degree of mitral valve disease	Operative findings			Type of epy.	E.E.G.
						Size in cm.	Ca.	Age		
19F	25	25	A.F.	Hemiplegia 1 Leg	Severe MS (MI)	1·5‡	Yes	27 —	Major	Borderline
20F	28	28	A.F.	—	Severe MS	0·75‡	—	30	Major and focal	Focal
21F	36	36	A.F.	Hemiplegia	Moderate MS (AS)	Op. not advised			Major and focal	Focal
22M	34	35	Sinus	—	Severe MS	0·5	Yes	45	Major and minor	—

No patient had a family history of epilepsy except Case 20.
* In these three, the fits started after mitral valvotomy, after 4 months in Case 2, after 5 months in Case 10, and after 6 months in Case 18.
† This patient had paroxysms of auricular fibrillation.
‡ There was an old thrombus in the left atrium at operation in these four patients.

with an average of 32 years, which is a late onset for idiopathic epilepsy. In all but 4 patients the onset of fits occurred after the onset of symptoms from mitral disease. In two of these (Cases 9 and 12) where epilepsy preceded disability from mitral disease, which in neither case was severe, the clinical evidence pointed to a diagnosis of idiopathic and post-concussional epilepsy respectively. In the remaining 18 patients the fits occurred when the heart disease was already advanced and in only two (Cases 16 and 21) was the disability other than severe. The absence of a family history of epilepsy except in one, the late onset, and the fact that they followed disability from mitral disease, all suggest that the fits are a direct consequence of that condition. When we first noted this association we considered that the epilepsy was due to or followed a cerebral embolism, and an analysis of the 20 patients, excluding Cases 9 and 12 where idiopathic and post-traumatic epilepsy were diagnosed, supports this explanation.

Embolism from mitral disease is most likely to occur in three circumstances: with the onset of atrial fibrillation which favours the formation of clot in the left atrium and atrial appendage; secondly, with mitral valvotomy where clots may be detached at operation or soon after; and thirdly, with tight mitral stenosis and high atrial pressures—particularly if there is extreme rigidity or calcification of the valve—where clots may form and be detached even when the rhythm is regular, and when there is no operative interference. These three points can be considered with reference to the data in the Table.

Twelve of the twenty patients were fibrillating when fits started; in six of these the fits followed within a few months of the onset of fibrillation and in a further four they followed within a year of a hemiplegia due to a cerebral embolism, occurring shortly after fibrillation. Of the eight in sinus rhythm, one (Case 13) had paroxysmal attacks that were probably atrial fibrillation for the arrhythmia was established three years later. Systemic embolism is not uncommon in mitral stenosis with sinus rhythm; in a series of 150 patients followed up at Guy's after mitral valvotomy there were 31 with a history of previous embolism and 8 of these were in sinus rhythm at the time.

Three patients developed fits after mitral valvotomy. One of these (Case 10) developed fibrillation as the result of operation, the other two (Cases 2 and 18) were in sinus rhythm when fits started, though both developed fibrillation later in the fourth year after mitral valvotomy.

Eighteen of the twenty patients had severe mitral disease and sixteen of these were treated surgically; one refused operation and one with significant mitral incompetence as well as stenosis was not advised to have an operation and died with heart failure. The other two patients both had moderate disability, were not deteriorating, and surgical treatment is being held in reserve. It is interesting that neither of the two patients where epilepsy was not thought to be secondary to embolism had severe mitral valve disease. The state of the mitral valve in the sixteen patients treated by valvotomy is shown in the Table. All but four had mitral stenosis without regurgitation. One (Case 2) had significant mitral incompetence found at operation, two (Cases 3 and 22) had an insignificant regurgitant jet through a calcified valve, and the fourth who was thought to have mitral incompetence (Case 8) was not advised to have an operation and subsequently died. Nine of the sixteen patients had calcified valves, which is a higher proportion than was found in the series followed up at Guy's (29 out of 150). In only one (Case 10) was the valve not tightly stenosed and this patient developed Jacksonian epilepsy after valvotomy.

A clot was found in the left atrium at operation in only four of the sixteen patients who had mitral valvotomy, although three had had previous cerebral embolism. This is in keeping with the experience in the Guy's series of 150 patients already referred to, where clot was found at operation in only 13 who gave a history of previous systemic embolism, while clot was found in 17 where there was no history of embolism. It is in fact the clot that does not remain attached in the left atrium that causes systemic embolism.

On the basis of the three factors of atrial fibrillation, mitral valvotomy, and severe distortion of the mitral valve, it will be seen that the circumstantial evidence suggesting that cerebral embolism is the cause of the epilepsy is strong.

There is further evidence pointing to this explanation. Nine of the twenty patients had clear clinical evidence of a cerebral embolism and seven of them had a hemiplegia, though only two (Cases 1 and 15) were left with any permanent disability after this. Four of these patients had clinical evidence of systemic embolism other than cerebral. The fits in thirteen of the twenty patients had focal features and in six of these the electroencephalogram showed evidence of a focal lesion. The electroencephalogram was normal in four patients (Cases 3, 8, 13, and 17), and was not done in Case 10; two of these had focal and two major epileptic attacks.

Reviewing all the evidence in these twenty-two patients there are two (Cases 9 and 12) where we think that the epilepsy is respectively idiopathic and post-concussional in origin. In the remaining twenty there are three where the epilepsy could be independent of the mitral valve disease, Case 4 where there is a history of meningitis in childhood and Cases 13 and 22 where it might be idiopathic. We think, however, that in these three patients the epilepsy was due to cerebral embolism and would add them to the remaining seventeen where the evidence is convincing.

Practical Considerations

The recognition that fits may occur as the result of cerebral embolism, whether clinically obvious or not, has practical advantages. Several of our patients were suspected of having multiple attacks of embolism when in fact the repeated attacks were epileptic and due to a previous cerebral embolism. Repeated systemic embolism would be a reason for advising valvotomy and although in most cases this may be necessary on account of the cardiac state alone, it may not be so, as in our Cases 16 and 21.

Of more practical importance to the patients was the fact that the fits had all been considered to be "heart attacks" due directly to their mitral disease and not one of them had been given sedative treatment to control their epilepsy. When this diagnosis was made and the appropriate treatment was given, there were no further fits except in four patients (Cases 1, 3, 6, and 15), and in two of these four a fit occurred only in the post-operative period when the sedative treatment had been temporarily discontinued. The practical advantage of making the diagnosis of epilepsy due to a previous cerebral embolism is well illustrated in Case 21.

Case 21. The patient, a woman of 46, was referred for an opinion as to the necessity for mitral valvotomy. She had been fibrillating for 15 years and 10 years before had had a left-sided hemiparesis from which she recovered fully. Since then she had had at least twenty attacks of sudden loss of consciousness, which had been diagnosed as repeated cerebral emboli. The doctor wrote "The only people who are not frightened by these occurrences now are the patient, who is unconscious, and myself who have seen so many of them". In the month before coming to hospital two attacks had been associated with abdominal pain before consciousness was lost, and the possibility of mesenteric embolism had been raised. When she attended as an out-patient, she was found to be mentally clouded, although her last attack had been seven days before, and as it was thought inadvisable for her to make the train journey home she was admitted as an emergency under the care of Dr. W. N. Mann, who diagnosed epilepsy following a previous cerebral embolism. It was several days before she made a complete recovery of mental function and for the first few days there was weakness and inco-ordination of the left side. In addition to her mitral stenosis there were signs of aortic stenosis, but as her cardiac reserve was adequate and there was no evidence of cardiac deterioration operation was not advised. On epanutin and phenobarbitone she had had no further attacks when seen four months later.

SUMMARY

The association between epilepsy and rheumatic heart disease is noted and the possible ætiology of the epilepsy is briefly discussed.

Twenty-two cases are reported where epilepsy occurred in association with mitral stenosis. The cases are analysed and it is concluded that in twenty of them the epilepsy was due to previous cerebral emboli.

The importance of recognizing the true nature of these attacks is emphasized and the response to anticonvulsant drugs was found to be very satisfactory.

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