Essential (familial, hereditary) tremor: a case report

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Familial tremor, or essential tremor, or hereditary familial tremor, has been recognized clinically for more than a century and was described as a morbid entity by Dana (1887), Gowers (1888), and Charcot (1888) among others.

Good descriptions of the symptoms and inheritance were published by Pelnár (1913), Minor (1922), Kehrér (1930), Pintus (1932), and in recent times by Critchley (1949) and Larsson and Sjögren (1960). Marshall (1962) was the first to point out that the tremor in this condition is similar to but an exaggeration of normal tremor.

Essential tremor has a dominant inheritance. It is usually not a serious disease. The major symptom is a rhythmic bilaterally symmetrical tremor (4 to 10 c/s), usually commencing in the fingers and often spreading to the hands, less often to the head, sometimes to the legs. Sometimes there is also a slight degree of ataxia in the finger-nose test. However, the important points in diagnosis are that the patient becomes ill in youth or in middle age, that the disease progresses very slowly, and that characteristics of Parkinson's disease, like rigidity and akinesia, do not develop. Also, these patients do not develop nystagmus or truncal ataxia. Apart from the tremor and slight final ataxia, neurological examination fails to reveal any other abnormality.

The pathological changes underlying this condition are not yet certain and there are few published cases which include post mortem findings. For this reason, the present case was thought to be of interest, although the structural abnormalities which were found were slight and not noticeably different from those sometimes seen in patients without tremor.

PREVIOUS CASES WITH POST MORTEM FINDINGS

CASE 1 (Hassler, 1939) was an alcoholic who, at the age of 45 years, developed gross tremor of his head, hands, and legs, worse on movement. He died aged 71 from heart failure. His brother had the same type of tremor. The essential post mortem finding in the brain was a re-

duction in the number of the small nerve cells in the striatum.

CASE 2 (Hassler, 1939) was a man who had severe oscillating tremor in his hands. He had choreiform and athetoid movements in his feet. The tremor was made worse by emotion and cold. He died at the age of 80 years. His father and his brother had the same tremor. Post mortem findings in his brain were severe advanced and diffuse arteriosclerosis, reduction of the small nerve cells in the striatum, small softenings in the dorsal two thirds of the putamen and caudate nucleus, and rarefaction of Purkinje cells, with laminar atrophy.

CASE 3 (Mylle and van Bogaert, 1940) was a man with a strong family history of psychopathies and two siblings with tremor. The tremor began when the patient was in his 40s. It was mostly in his head and arms, worse during voluntary movement, and improved at rest. He was an inmate in a psychiatric hospital and four and a half weeks before his death, at 61 years, he developed a stroke, together with cessation of the tremor in the homolateral side. Post mortem examination of his brain showed small softenings (lacunae) in the superior internal part of the right internal capsule, the pallidum not being affected by this softening. There was fibrillar gliosis of the superior cerebellar peduncles; of the cerebellar white matter and pallidum; increased cellular gliosis of the dentate nuclei and the roof nuclei; loss of Purkinje cells; loss of large nerve cells from striatum and pallidum with increased lipidic uptake.

CASE 4 (Mylle and van Bogaert, 1948) was a case of non-familial tremor in a woman. When she was 16 years old, tremor commenced in head and hands. In her 50s she developed a psychiatric condition and was confined to a mental hospital. Neurological examination showed a gross, very fast tremor in the head and hands. No definite clinical evidence of cerebellar abnormality was discovered nor extrapyramidal rigidity. The patient died at 72 years from an infectious disease, probably with myocarditis. Post mortem examination of the brain revealed small softenings in the nucleus caudatus and putamen, atrophy in the external segment of pallidum and bulbar olives; discrete rarefaction of the layer of Purkinje cells. The pallidum showed moderate and diffuse cellular and fibrillar gliosis.

PRESENT CASE

M.K., a male, when aged 46 years, had been admitted in 1935 to Hammersmith Hospital, London, where a gastrectomy was performed for (?) peptic ulcer. It was noted at the time that he had suffered from a cough in the winter and tremor for some years. In 1955, when he was 66 years old, he was re-admitted as an emergency to Hammersmith Hospital under the care of Dr. Sheila Sherlock (Hosp. no. 169253) because of an attack of unconsciousness of about 10 minutes' duration. Among other investigations, Wassermann's reaction on blood and CSF were negative, plain radiograph of the skull negative, CSF showed normal values, EEG revealed generalized chronic changes either of a degenerative or vascular origin. He was discharged after 12 days to Neurological Out-patients (Dr. J. Purdon Martin) without further attacks of unconsciousness and without a definite cause being found. Further attacks of unconsciousness occurred one, two, and 15 months later. Then, 18 months later, he was brought in dead without a terminal history. At necropsy myocardial infarction was found.

The tremor which commenced in his early 40s started in the right hand from which it spread to the left hand. It progressed extremely slowly. Sometimes his speech was tremulous. When he was admitted at the age of 66 years old there was slight tremor of the lower chin and tongue, gross tremor of the hands, aggravated by movement, minimal at rest, with no rigidity and normal reflexes. Its frequency was about 4 c/s in each hand. One of his parents suffered from a similar tremor but no definite family history of tremor could be traced. In his discharge notes the diagnosis of heredo-familial type of tremor with no evidence of Parkinsonism was made.

POST MORTEM EXAMINATION This was carried out by Dr. A. G. E. Pearse (PM no. 7805) with the following results.

Serous sacs 400 ml. of dark straw-coloured fluid was found in the pericardial sac.

Cardiovascular system The heart (610 g weight) showed hypertrophy and dilatation of the left ventricle, which measured 22 mm at its widest point. Right ventricle and auricles were normal, as were the pulmonary, tricuspid, and mitral valves. There was calcification at the base of the aortic cusps. The left circumflex coronary artery was completely blocked by old atheroma and the vessel was calcified up to its origin. In the left descending coronary artery there was also extensive atheroma and, at a point about 2 cm from its origin, there was a recent thrombus adherent to a plaque of atheroma. The aorta was severely atheromatous.

Respiratory, reticulo-endothelial, genito-urinary, and endocrine systems No significant abnormality was observed macroscopically.

Alimentary system The old gastro-jejunostomy was seen to be healthy.

Central nervous system The brain weighed 1,640 g. The cerebral vessels were atheromatous. On section, the ventricles were dilated. Through the courtesy of Dr. A. G. E. Pearse and Dr. Edwin Clarke, the sliced brain was sent to the Department of Neuropathology, The National Hospital, Queen Square. Further examination of the

basal vessels showed moderate atheroma of the basilar artery. There was an old softening in the right occipital cortex.

Sections were taken for microscopical examination of the right frontal, parietal, and occipital regions, the corpus striatum, basal ganglia, midbrain, pons, medulla, and cerebellum, embedded in celloidin and stained with HvG, PTAH, Loyez and Gross-Nissl stains. It was decided that, with the extensive bilateral clinical abnormality, it was sufficient to restrict the microscopical examination of the cerebral and cerebellar hemispheres to one side. The pons and medulla were examined bilaterally.

On examination, there was generalized arteriolosclerosis such as that found in hypertension.

Cortex No significant abnormality was found apart from old ischaemic scarring of the right occipital region.

Putamen There were numerous old small haemorrhagic softenings in the putamen, more posteriorly than anteriorly, with haemosiderin in phagocytes. Between the softenings both large and small nerve cells were numerous.

Pallidum Large nerve cells were numerous. Significant abnormality was not found.

Caudate nucleus Significant loss of large or small nerve cells was not seen.

Corpus Luysii Significant abnormality was not found.

Red nucleus Significant abnormality was not found.

Substantia nigra Significant abnormality was not found.

Cerebellar hemisphere Significant abnormality was not found. There was occasional loss of Purkinje cells, but not relevant in view of his age.

Nucleus dentatus Significant abnormality was not found.

Pons Significant abnormality was not found.

Medulla Significant abnormality was not found. No significant abnormality was found in the bulbar olives.

In summary, in this case, there was old ischaemic scarring in the right occipital region (with no clinical correlation), a few old softenings in the putamen, and some degree of atheroma and of arteriolosclerosis.

DISCUSSION

This paper adds a further case to the two described by Hassler and the two by Mylle and van Bogaert. The essential pathological findings in the five cases are summarized in Table I. All occurred in people who died at an advanced age. The changes found in the present case were not noticeably different from those seen in patients with hypertensive cerebrovascular disease and without tremor. It is difficult not to agree with the implication of Mylle and van Bogaert (1948) that, up to now, no definite structural lesions have been found to which the clinical disorder can indisputably be attributed. They, however, considered it important that all cases of essential tremor with pathological examination should be published.

The clinical findings suggest a disorder of the extra-pyramidal and/or cerebello-olivary systems and

TABLE I
ABSTRACT OF PATHOLOGICAL FINDINGS

	Striatum	Subst. nigra	Red nucleus	Cerebellum	Dentate	Others
Case 1 Hassler (1939)	Numerical reduction of small cells in caudate and putamen	NRA ¹	NRA	NRA	NRA	NRA
Case 2 Hassler (1939)	Reduction of small cells. Small softening in caudate and putamen	NRA	NRA	Diffuse Purkinje cell loss	NRA	Arteriosclerosis
Case 3 Mylle and van Bogaert (1940)	Fibrillar gliosis in pallidum	NRA	NRA	Loss of Purkinje cells. Fibrillar gliosis in superior cerebellar peduncles and central white matter	Abnormal cellular gliosis also n. fastigii	Increase lipidic uptake in large nerve cell of pallidum
Case 4 Mylle and van Bogaert (1948)	Atrophy of putamen and caudate—état criblé, small softening and gliosis. Pallidum—cellular rarefactions	NRA	NRA	NRA	NRA	NRA
Case 5 Present case	Putamen—small softening	NSA	NSA	NSA	NSA	Moderate atheroma in vessels, arterio-sclerosis

¹Case 1 to 4. NRA = No reported abnormality. Case 5. NRA = No significant abnormality.

attention is usually focused on these regions. That this is not necessarily correct is suggested, for instance, by cases of hemiballismus with no discoverable lesion, using routine methods, in the subthalamic nucleus at necropsy (Martin, 1957).

Experience since 1956 has shown that structural changes in the fibre pathways, not revealed by routine stained celloidin sections, may be revealed by Marchi preparations. This technique was not employed. Enzyme histochemical methods were not used. In future cases these methods should be considered.

SUMMARY

A clinicopathological study of a patient with essential tremor is presented. The brain showed ischaemic lesions secondary to atherosclerotic hypertensive vascular disease of a non-specific distribution. The situation of these lesions is not considered to be responsible for the tremor. Suggestions are made for the histological investigation of the brains of future cases.

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