Medical Memoranda

Familial Myasthenia Gravis

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Myasthenia gravis is described in textbooks of medicine and neurology as a disease of the third and fourth decades of life. Its occurrence in infancy and childhood is rare. During 1900–65 only 54 cases in 22 families have been reported. To find the disease in more than one generation in the same family is rarer still, only four such instances so far having been recorded. Myasthenic symptoms persisting from the time of birth (congenital myasthenia) is also rare. The following four cases of myasthenia gravis in a brother, sister, and two children of an unaffected sister are of interest from these various aspects of the disease.

Case Reports

Case 1.—A man aged 28 attended the Medical College Hospital, Calicut, for drooping of the upper lids, difficulty in focusing near objects, and blurring of vision of two years' duration. On direct questioning he admitted that he had had slight drooping of the eyelids for at least 12 years. He denied any weakness in the limbs or difficulty in swallowing. The history of his past illness showed nothing contributory. One of his sisters, aged 17 (Case 2), had had the same complaints since the age of about 5 years, as also had two nephews (Cases 3 and 4).

General physical examination showed nothing contributory. Bilateral ptosis was present. The ocular movements were almost completely absent in all directions in both eyes. He could not look to one side or the other without turning his head. The pupils were normal. There was no other abnormality in the central nervous system. Examination of the other systems did not reveal any abnormality. Laboratory investigations were negative. The *x*-ray picture of the chest was normal. About 20 minutes after he was given neostigmine subcutaneously (2.5 mg. mixed with 0.5 mg. of atropine) he could lift his eyelids normally and the ocular movements were restored to complete range. The effect lasted for about three hours. He was put on neostigmine bromide 10 mg. thrice daily and ephedrine 30 mg. twice daily. He has since remained significantly improved.

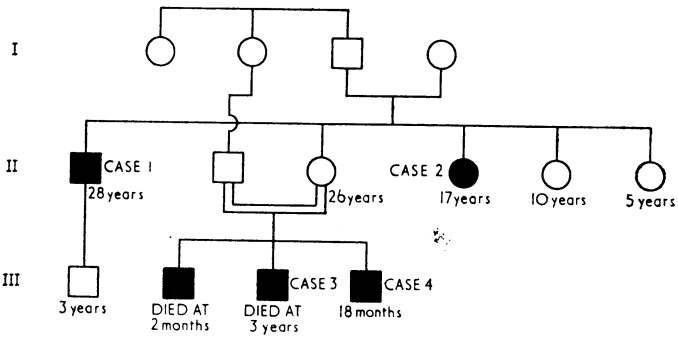
Case 2.—A 17-year-old unmarried girl, sister of Case 1, had had ptosis and restricted movements of the eyeballs from the age of 12 years. The disability was worse towards the evening. From the age of 15 tiredness and weakness of both upper limbs were also noticed. General examination did not reveal any abnormality. Ptosis was present on both sides. Movements of the eyeballs were very restricted in all directions. The pupils were normal. The muscles of the upper limbs showed diminution in motor power not limited to any specific muscle groups. There was no wasting. The deep reflexes were sluggish. Physical examination did not reveal any other abnormality in the central nervous system or any other system. *X*-ray examination of the chest showed widening of the superior mediastinum consistent with a thymic shadow. Other investigations were negative. As in Case 1, there was prompt relief of symptoms and restoration of ocular movements and disappearance of ptosis after neostigmine injection. The patient improved from the regular administration of neostigmine bromide 10 mg. thrice daily.

Case 3.—A 2-year-old boy, son of a normal sister of Cases 1 and 2, was noticed to have ptosis from birth. The parents found that he could not look to one side or the other without turning his head. The extremities were floppy. He was not yet steady in his walk and tended to fall. Physical examination showed bilateral ptosis, restriction of ocular movements in all directions, and hypotonia of the limb muscles. The deep reflexes were sluggish. No other abnormality was detected. The *x*-ray picture of the chest was normal. The ocular movements and the strength of the muscles improved and the ptosis disappeared after the injection of 1.25 mg. of neostigmine. The parents were advised to give the child 5 mg. of neostigmine bromide twice daily. He was doing well, but 11 months after the first admission he had an attack of pneumonia and died.

Case 4.—An 18-month-old boy, younger brother of Case 3, was brought to us immediately after that brother had died of bronchopneumonia. The cases, as stated by the parents, were similar. The boy was found to be weak and slow in his movements and to have had bilateral ptosis since birth. The weakness became more pronounced towards the evening, when the ptosis was also more prominent. Physical examination showed hypotonia of muscles, ptosis, external ophthalmoplegia, and sluggish deep reflexes. An *x*-ray picture of the chest was normal. There was prompt response to a subcutaneous injection of 1.25 mg. of neostigmine, with disappearance of ptosis and external ophthalmoplegia.

Family Tree

The family tree is shown in the Chart. The affected members are shown in black. The members of generation I were examined and all were found to be normal. In this generation there were no marriages between relations. The history did not suggest the presence of similar illness in the previous generation. The disease presumably made its first appearance in generation II, to which Cases 1 and 2 belong. The other members of generation II were examined and found to be normal. The unaffected sister of Cases 1 and 2 and her husband are first cousins. They had three male children in generation III. All were affected by the disease. Their first child died at the age of 2 months. We did not see the child, therefore the case is not reported here. Case 3 died at the age of 3 years. Case 4 is still alive and is being followed up. The 3-year-old son of Case 1 is normal.



Follow-up

Cases 1, 2, and 3 came under our observation in August 1963 and Case 4 in September 1964. Case 3 died in July 1964. Cases 1, 2, and 4 are still being followed up. They are on maintenance treatment with neostigmine and ephedrine. Case 2 married recently, and it will be of interest to observe the children of the marriage.

Comment

The myasthenic syndrome has often been reported in neonates born of myasthenic mothers since Strickroot *et al.* (1942) reported the case of a mother with myasthenia gravis whose newborn child developed signs of generalized weakness on the third day of life and died on the seventh day from respiratory failure. Since in these cases the symptoms are transient and are probably due to a curare-like substance transferred through the placenta it is not correct to include these cases as familial myasthenia gravis. The first report of familial incidence of myasthenia gravis is that of Oppenheim (1900). Celesia (1965) reported the cases of a brother and sister suffering from

myasthenia, and reviewed all the cases of familial myasthenia gravis recorded in the literature up to that time, bringing the total number to 54, distributed among 22 families.

The four cases reported here bring the total so far to 58 cases in 23 families. Since in these cases the lesion is mostly confined to the ocular muscles the problem of differentiation from ocular myopathy (Kiloh and Nevin, 1951) arises. But the tendency of the disability to worsen towards evening and the favourable response to the administration of neostigmine favoured the diagnosis of myasthenia gravis.

Certain other observations may be made in these cases. They represent individuals of two generations. In only four of the 22 previously reported families were two generations affected. Peters (1906) reported the cases of two sisters, two brothers, and the father. Noyes (1930) reported cases of a brother, sister, and father; Eaton (cited by Levin, 1949) the cases of a father and son; and Foldes and McNall (1960) the cases of two sisters and their mother. The present report is the fifth instance of familial myasthenia gravis affecting more than one generation. Celesia (1965) observed that in instances where more than one generation is affected by the disease the onset is in adulthood. Our cases, however, prove otherwise, for Cases 3 and 4 showed myasthenic symptoms from birth.

The first case of congenital myasthenia was reported by Bowman (1948). Levin (1949) considered three types of myasthenia gravis in children. They are the transient neonatal myasthenia, the familial myasthenia occurring in siblings, and the ordinary or acquired myasthenia. Acquired non-familial myasthenia is rare in childhood; but among 41 cases of familial myasthenia limited to one generation, in 20 the onset of the disease was in infancy and in 12 in childhood or adolescence (Celesia, 1965). All our four cases had their onset before the age of 16 years, thus proving the early age of onset in familial myasthenia. This difference of the familial cases from the non-familial ones may be of importance from the genetic point of view.

Levin (1949) used the term "congenital myasthenia" to describe the form of myasthenia which begins at birth (or before), and is characterized by a mild onset, marked external ophthalmoplegia, partial ptosis, and symmetrical weakness of the involved muscle groups. In contrast to the usual myasthenia gravis it is not progressive and does not show remissions. There is a dramatic response to the administration of neostigmine. Though the basic defect is the same the disease may be different from the myasthenia gravis described by Erb (1879) and Goldflam (1893). Among the cases of familial myasthenia gravis reported there are only six patients in four families in whom the disease was present from birth and hence qualify as congenital myasthenia. These were reported by Levin (1949, two cases in a family), Osserman (1961, three cases in two families), and Walsh and Hoyt (1959, one case in a family with four affected members). In all these cases ptosis, ophthalmoplegia, and generalized weakness were the prominent symptoms. Our Cases 3 and 4 are the seventh and eighth cases of congenital myasthenia gravis among the familial myasthenics recorded to date. Though Levin thought it probable that these cases would show marked improvement in course of time, one of our patients died at the age of 3 years from an intercurrent respiratory infection.

So far there is only one report of thymus enlargement in familial myasthenia gravis. At necropsy Marinesco (1908) noticed persistence of the thymus, and the histopathological features suggested hyperplasia. In our Case 2 the *x*-ray picture of the chest showed widening of the superior mediastinum consistent with enlargement of the thymus.

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Self-inflicted Oleogranuloma of Breast

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While oleogranuloma of the breast is a well-recognized condition in the Orient, it must be unusual to encounter a case in Britain. The following case of bilateral granulomata of the breasts in an English woman is especially interesting, in that the condition was self-inflicted after she had read an article in the lay press which mentioned that Japanese women have had petroleum jelly injected into their bosoms to increase their size.

CASE REPORT

An unmarried woman aged 26, the mother of twins aged 6 years, was concerned about the flatness of her chest and consulted a plastic surgeon who, 10 years previously, had removed a tattoo from her arm. As she had recently been under psychiatric treatment, it was thought unwise to advise operation at that time. She therefore decided to treat herself by making multiple injections of warm, molten petroleum jelly into each breast, using a 20-ml. syringe and intramuscular needles which she had purchased for this purpose. Pain was not experienced at the time of the injection, but several days later she described tenderness and discomfort in both axillae. This was followed during the next few months by a severe reaction, more marked on the right side, and the breasts became nodular, painful, and inflamed, and finally sinuses formed exuding petroleum jelly (Fig. 1).

Mammograms showed extensive cystic changes in the breasts, presumably due to grease globules (Fig. 2). *Treatment:* Bilateral simple mastectomy was advised but rejected by the patient. It was therefore decided to try to evacuate the grease globules through several small incisions. Each breast was operated on separately, with an interval of three months between operations.

At operation some of the oleogranulomata were so well defined that they could be dissected free intact (Fig. 3). Other areas of the breast had diffuse fibrotic changes with infiltration of grease, and the best that could be done here was to extrude as much of the petroleum jelly as possible. The wounds were closed and a small corrugated rubber drain was inserted. Postoperative antibiotic therapy was given, though bacterial culture of the excised tissue was