PROGRESSIVE EXTERNAL OPHTHALMOPLEGIA*

BY

F. D. MCAULEY

London

THIS condition, in which the movements of the eyeballs tend progressively to diminish in amplitude, is usually accompanied by ptosis, and has an hereditary trait; it has been variously described as "Chronic Progressive Nuclear Ophthalmoplegia", "Chronic Dystrophy of the External Ocular Muscles", "Ocular Myopathy", "Familial Ocular Myopathy and External Ophthalmoplegia", "Progressive Muscular Dystrophy involving the Extra-ocular Muscles", and so on.

Kiloh and Nevin (1951) reviewed the literature on the subject giving an index of the 99 cases reported up to 1948, with a description of five further patients. Since then seventeen more cases have been described.

Recent histological examinations have shown almost conclusively that the condition is of the nature of a muscular dystrophy (Kiloh and Nevin, 1951; Beckett and Netsky, 1953; Schwarz and Liu, 1954); this is opposed to the conception that the symptomatology results from degeneration of the oculomotor nuclei (Möbius, 1900; Wilbrand and Saenger, 1900, 1921; Langdon and Cadwalader, 1928a, b; Jedlowski, 1943).

The following is a description of four cases. Histological examination of skeletal muscle biopsies from two of these patients would suggest that at least some, if not all, cases of progressive external ophthalmoplegia are in fact examples of a generalized muscular dystrophy, the clinical manifestations of which are usually confined to the extra-ocular muscles.

Case Reports

Case 1, a female aged 40, attended in March, 1955, complaining of increasing ptosis during the previous 12 months. She stated that her mother (Case 2) had worn ptosis-props for years and that her maternal grandfather and great-grandfather had had similar drooping of the lids as well as a maternal uncle who had had an operation on his eyes some years previously.

Examination.—She was found to have a moderate degree of ptosis, the orbicularis muscles being of normal strength. The eyes were in visual alignment, but there was an absence of elevation of the eyeballs, and downward and lateral gaze was restricted to about half of the normal amplitude; diplopia had never been a symptom. Intramuscular injection of prostigmine had no effect on the eye movements. The pupil reactions were normal and the eyes were otherwise healthy (Fig. 1, opposite).

Visual acuity varied but could never be improved beyond 6/18 in either eye and the

* Received for publication August 24, 1956.

FIG. 1.—Case 1, eyes in primary position.

fields were concentrically contracted; this contraction altered from time to time, suggesting the possibility of a functional element.

No abnormality was found in the central nervous system. The Wassermann reaction was negative. X-rays of chest, skull, and optic foramina showed no abnormality.

Her previous history disclosed that she had had a "nervous breakdown" 10 years previously, several Bartholin's abscesses, and a fistula-in-ano had had attention in 1949. In 1952 she complained of infertility and difficulty with intercourse and at that time she was awaiting admission to another hospital for an operation to the cartilage of her left knee. No abnormality was found on pelvic examination, nor was any local cause found for alleged urinary incontinence of which she complained in 1953. Ligation of the saphenous veins was performed in June, 1955, and at the same time the opportunity was taken to excise portions of the pectineus and inferior oblique muscles for biopsy. The history suggests a mental instability which would explain the apparently lowered visual acuity and field constriction.

Histological Report:

"Section 16313 (left inferior oblique muscle) shows muscle tissues with variation in size of the fibres. Many have lost their striation, are swollen, irregular, and stain a homogeneous pink or pale blue, and show proliferation of sarcolemmar nuclei, but healthy fibres are present. Fat and fibrous tissue separate many of the fibres. Special staining for nerve fibres shows no abnormalities; in these sections there is a marked granularity in the degenerate muscle fibres.

Section 16314 (pectineus muscle) shows less extensive changes, but some of the fibres are undergoing hyaline degeneration with loss of striations.

The histological picture favours *progressive ophthalmoplegia* as a form of muscular dystrophy."

Case 2, a female aged 64, mother of Case 1, gave a history of increasing ptosis for 14 to 16 years. She had had an operation for the correction of the left ptosis some years ago, but had been in excellent health otherwise.

Examination in April, 1955, showed well-developed ptosis, more marked on the right side where the pupil was practically obscured. Her eyes were in alignment for distance and, although converging power was absent, she experienced no diplopia. There was no elevation of the eyeballs, and depression and lateral movements were very restricted. The pupils were moderately sluggish. There was some calcareous change in the left cornea, resulting from an injury by a pillow-slip some years earlier, which reduced vision in this eye to 6/36. Visual acuity in the right eye (corrected) was 6/6. The eyes were otherwise healthy.

General physical examination did not disclose any other muscular or neurological abnormality. The patient was estimated to be of normal intelligence.

There were no notes available about this patient's brother, father, and grandfather who were evidently similarly affected, but her son, aged 24 (brother of Case 1), was examined and showed no ocular abnormality.

Case 3, a female aged 64, stated that her eyelids had drooped since childhood and that her mother had been similarly affected.

Examination in August, 1955, showed that the ptosis did not interfere markedly with her vision, the eyelid margins clearing the visual line by about 2 mm. The eyes were in alignment, but movements in all directions were defective, with no power of elevation above the horizontal (Fig. 2a-f).

Fig. 2a.—Case 3, eyes in primary position.
FIG. 2b.—Eyes in primary position (close-up).
FIG. 2c.—Eyes deviating to the left.

FIG. 2d.—Eyes deviating to the right.
FIG. 2e.—Attempted elevation.
FIG. 2f.—Attempted depression.

There was no diplopia. Intramuscular injection of prostigmine failed to influence the ocular movements. The visual acuity and pupils were normal, and there was no other apparent ocular disease apart from some retinal arteriosclerosis. The patient was quite fit for her age and general physical examination revealed no abnormality. Her intelligence was within normal limits.

Two daughters, aged 40 and 17, and a son, aged 31, showed no evidence of ptosis or ophthalmoplegia.

Case 4, a male aged 42, gave a history of drooping eyelids for 4 or 5 years, though he was not very certain about the time of onset.

Examination:—On June 15, 1956, he had bilateral ptosis, the lid margins half obscuring the pupils of each eye. The ocular movements were restricted to approximately one-sixth of the full amplitude, elevation being the most markedly affected. There were fine oscillating movements of the eyes in the primary position, and the patient was conscious of diplopia "only when he stared at an object for a considerable length of time". The pupil reaction was somewhat sluggish to light stimulation the left pupil reacting less briskly than the right. Visual acuity was 6/18 in each eye, with correction for myopia, the reduced vision being due presumably to the fine oscillations. General physical examination did not disclose defective action of any other muscles.

His intelligence appeared to be below average although he was capable of carrying out satisfactorily his work as a porter.

Histological Examination:—The left deltoid muscle was reported as showing “a few healthy fibres, but many of the fibres are swollen and separated by clear spaces, the cross striations of the myofibrillae are only faintly visible and stain a homogeneous pink except for a few irregular pale blue areas. Some of the fibres show proliferation of the sarcolemmar nuclei. No nerve tissue is apparent in the plane of the sections examined. The histological picture is suggestive of a muscular dystrophy and closely resembles the histological picture of an ocular muscle biopsy from another case of progressive ophthalmoplegia.”

A further biopsy of the overlying skin and subcutaneous tissues showed extensive hyalinization and fibrosis of the sub-epithelial tissues.

Discussion

Kiloh and Nevin (1951) state that, in one-quarter of the recorded cases, various other muscles have been shown on physical examination to be involved, and that with very few exceptions these have always included the orbicularis oculi. Histological examination of a biopsy from the vastus lateralis of their Case 1 showed no gross abnormality, but there was definite proliferation of the sarcolemmar nuclei and in places these were arranged in short chains. This patient had some weakness and wasting of the muscles of the upper limbs and the upper part of the trunk, but there was no evident clinical abnormality of the remaining trunk and lower limb muscles.

In Cases 1 and 4 above there was no clinical evidence of abnormality of the skeletal muscles, nor of the orbiculares oculi, and yet biopsy specimens from the pectineus of Case 1 and from the deltoid of Case 4 showed changes closely resembling those found in the eye muscles of patients with progressive external ophthalmoplegia. It was not possible to obtain biopsies from Cases 2 and 3, but, as Case 2 showed the same clinical picture as her daughter Case 1, it may be presumed that a similar histological picture might be found on examination.

These findings suggest that while the clinical signs may point to a disease restricted to the ocular muscles, progressive external ophthalmoplegia is in fact due to a generalized muscular dystrophy manifested to a greater or lesser extent in the external muscles of the eye. It is suggested that in further cases of this disease histological examinations should be made of skeletal muscle biopsies to determine whether these show changes of a dystrophic nature. It may also be significant that Cases 1 and 4 in whom the visual acuity could not be improved beyond 6/18 in either eye, were both adjudged to have subnormal intelligence.

Summary

Four cases of progressive external ophthalmoplegia are described. Histological evidence suggests that the dystrophic changes are not confined to the extra-ocular muscles, despite the lack of clinical confirmation. It is suggested that biopsies of the skeletal muscles of cases presenting with this affection should be performed, in order that further light may be thrown upon it.

I wish to record my thanks to Mr. E. F. King, under whose care two of the patients were admitted to Westminster Hospital for investigation, to Mr. A. G. Leigh for access to the case notes at Moorfields Eye Hospital of Case 4, and to Dr. C. J. M. Clarke who referred Case 3.

I am also indebted to Dr. N. Ashton and Dr. P. B. Schofield of the Department of Pathology, Institute of Ophthalmology, London, for the histological reports, and to Dr. P. Hansell of the Department of Clinical Photography, Westminster Hospital, for the photographs.

REFERENCES

- BECKETT, R. S., and NETSKY, M. G. (1953). *Arch. Neurol. Psychiat.*, **69**, 64.
 JEDLOWSKI, P. (1943). *Riv. Oto-neurol-oftal.*, **20**, 203.
 KILOH, L. G., and NEVIN, S. (1951). *Brain*, **74**, 115.
 LANGDON, H. M., and CADWALADER, W. B. (1928a). *Ibid.*, **51**, 321.
 ———, ——— (1928b). *Trans. Amer. ophthal. Soc.*, **26**, 247.
 MÖBIUS, P. J. (1900). *Quoted by Wilbrand and Saenger* (1900), p. 130.
 SCHWARZ, G. t., and LIU, C.-N. (1954). *Arch. Neurol. Psychiat.*, **71**, 31.
 WILBRAND, H., and SAENGER, A. (1900). "Die Neurologie des Auges", vol. 1. Bergmann, Wiesbaden.
 ———, ——— (1921). *Ibid.*, vol. 8. Bergmann, Wiesbaden.

ADDITIONAL BIBLIOGRAPHY

- HOLMES, W. J. (1956). *Amer. J. Ophthal.*, **41**, 615 (One case).
 HUSSAIN, K. K. (1949). *Brit. med. J.*, **2**, 1392 (One case).
 MORPURGO, F. (1949). *Atti 37 Congr. Soc. oftal. ital.*, 1948, **10**, 397 (One case).
 ÖRGEN, CAHID (1953). *British Journal of Ophthalmology*, **37**, 365 (One case).
 SCHARF, J. (1950). *Klin. Mbl. Augenheilk.*, **116**, 654 (One case).
 THIEL, J. H. (1954). *Folia psychiat. (Amst.)*, **57**, 554 (Eight cases).