On Fisher's Syndrome

—Report of Two Cases—

Kazuo OTSU, Tatsuro SASAKI*,
Koichi KASHIWAMURA*, Taku SHIGEMOTO*,
Tamio OTA* and Michio YAMADA*

Yamaguchi Rosai Hospital, Neurological Clinic, Onoda
**Department of Neuropsychiatry, Yamaguchi University School of Medicine, Ube*

INTRODUCTION

Several cases of acute idiopathic polyneuritis with ophthalmoplegia, ataxia and areflexia were reported by Fisher (1956)[1]. Smith and Walsh (1957)[2] reported two similar cases. This disease has since been called Fisher's syndrome. However, whether it is different from Guillain-Barré syndrome still remains the subject of debate. With reports on the variant type theory appearing one after another, arguments denying the independence of this syndrome are also being heard[3].

Recently, we encountered two cases which were considered to belong to Fisher's syndrome as judged by the old standard for diagnosis, the details of which are reported here.

CASE REPORT

Case 1: Male, 14 years old.
Past history: Not remarkable.
Family history: Not contributory.
Present illness: In March at age 14, he had cold-like symptoms and started receiving medical treatment. From the second day of treatment he suddenly developed a diminution of vision in the right eye, with diplopia and slight blepharoptosis on both eyes. On the fifth day he felt weak in the lower limbs and was prone to fall. On the sixth day, he was hospitalized because he was no longer able to stand up and also because the disturbance of ocular movements became intensified.
Findings on admission: Consciousness was clear. Intelligence and mental state were normal. He spoke clearly, though with a little nasal tone. The olfactory sense was normal; vision (1.0 on both right and left), the visual field, and fundus showed no abnormal findings. The pupils were equal and regular and medium in size; the eyeballs were fixed on the

median line and movements in all directions were limited. Reaction to light and reaction to accommodation were quick and maintained well. Blepharoptosis was found with both eyelids, particularly with the left, and this condition showed no change even on the vagostigmine test. Corneal reflexes were normal. Both the sense of taste and hearing were normal. The pendulous palate and soft palate were normal. Difficulty in swallowing was not observed. The movements of the tongue were normal. The muscles of the limbs were relaxed and markedly weak. Tendon reflexes were slightly depressed in the upper limbs and were absent in the lower limbs. But abdominal reflexes were maintained well and no pathological refexes were noted. Motor disturbances consisted of the inability to stand up and walk in addition to a slight disorder of coordination. Sensory disturbances, meningeal irritating symptoms and cystorectal disturbances were not observed. Chest X-ray examinations were normal.

Laboratory findings: Examination of the peripheral blood showed RBC, 460×10^4; WBC, 9800; Hb, 15.0g/dl; Ht, 42.8%. Tests on the function of the liver and kidneys revealed CCFT, 0; A/G ratio, 0.86; serum protein, 7.8g/dl; cholinesterase, 0.82 ×pH; alkaline phosphatase, 47 u; GOT, 7 u; GPT, 5 u; cholesterol, 156mg/dl; NPN, 27mg/dl; Urea N, 10mg/dl. Serum electrolytes: Na, 137 mEq/1; K, 4.9mEq/1; Ca, 5.2 mEq/1; Cl, 102mEq/1; P, 5.2mEq/1. CPK, 33 u. ASLO, CRP and RA tests were all negative. Urinalysis was normal. Serologic test for syphilis was negative.

EEG on the day of admission showed 6-7 c/s theta wave with 50-100 μV cropping up dominantly in the frontal area and also high voltage 3-4 c/s delta waves appearing occasionally. Continual theta waves were also observed from other areas. EEG recorded on five occasions on a time-course basis showed findings of theta waves cropping up prominetly.

A lumber puncture immediately after admission revealed watery clear fluid under an opening pressure equivalent to 220mmH_2O and a closing pressure equivalent to 150 mmH_2O after removal of 5 ml of liquor. The fluid contained total protein 30 mg/dl, sugar 70 mg/dl, cell count 0/3 and gave a negative Pandy test, a negative Nonne-Apelt test and a negative tryptophane test.

Clinical course after admission: The patient had a slight fever of around 37°C and a headache, which remained unchanged for three days after admission. On the fourth hospital day, the muscular power of the upper limbs started improving, and on the sixth hospital day the muscule strength of the lower limbs also began to improve gradually. On the

10th hospital day, the patient was able to stand up by himself. From the 14th day, he was able to perform ocular movements in the horizontal direction, slight as they were. From the fourth hospital week, administration of prednisolone was initiated, and ocular movement was markedly improved two weeks after the administration. With a slight decline in the muscular power of the limbs still remaining, the patient was discharged home in the 20th hospital week. Seven days later, however, he was readmitted because the occipital pain and diplopia recurred. With administration of prednisolone, he was doing well and discharged home two months later. One year after discharge, the patient showed no findings other than hypoactive tendon reflexes in the upper limbs and loss of tendon reflexes in the lower limbs.

Case 2: Female, 72 years old

Past history: Typhoid fever at age 19; hospitalized for 30 days due to Basedow's disease at age 65.

Family history: Not contributory.

Present illness: In April at age 71 she noticed diplopia on looking upward or downward, but it gradually improved by itself. In February at age 72, she had strong general fatigue with a slight rise in the body temperature; thinking it was a cold, she did not receive any treatment, but this condition persisted. At the end of April she suddenly developed a severe headache, light-headedness, ataxia in walking and diplopia, and was consequently hospitalized. Findings on admission: Consciousness was clear; intelligence and mental conditions were normal for her age. Speech was somewhat slow, but dysarthria was absent. The olfactory sense was normal. Vision and visual field showed no abnormalities. The artery of the fundus showed arteriosclerotic changes, but there was no crossphenomenon and the optic disc was normal. The eyeball was fixed on the median line; the upward movement was limited and the inward, outward, and downward movements were also limited, but not as severely. The reactions to light and accommodation were fast and well maintained. Hearing was about equal on both sides, with moderate sound-perceiving loss of hearing. The pendulous palate and soft palate were normal. The movements of the tongue were normal and difficulty in swallowing was not observed. The muscles of the limbs were relaxed and muscular power was also decreased. Tendon refexes were depressed in both upper and lower limbs. Abdominal reflexes were absent. As for ataxic symptoms, slight dysdiadochokinesis was noted. She was able to stand up but her upper body would shake so that she could hardly walk. This condition remained almost the same whether the eyes were open or closed. Pathological refelexes were negative. Sensory disturbance,

meningeal irritating symptoms, and cystorectal disturbances were not observed. Laboratory findings:

Laboratory findings: Examination of the peripheral blood showed RBC, $513\times10^4/mm^3$; WBC, $8400/mm^3$; Hb, 12.8g/dl; Ht, 44.3%. Tests on the functions of liver and kidneys revealed CCFT, O; A/G ratio, 0.94; serum protein 6.8g/dl; cholinesterase 1.29 ⊿pH; alkaline phosphatase, 43 u; GOT, 10 u; GPT, 11 u; cholesterol, 265 mg/dl; Urea N, 18 mg/dl. Serum electrolytes: Na, 142 mEq/1; K, 4.8 mEq/1; P, 2.3 mEq/1; Cl, 101 mEq/1. CRP (−), ASLO test, 99; RA test (−). Findings of urinalysis were normal. Serologic test for syphilis and TPHA test were questionable (±), and glass plate test 1+; the Wassermann test was performed on a dilution of 1:20 and the glass plate test on a dilution of 1:2.

Lumber puncture revealed watery clear fluid under an opening pressure equivalent to 150 mmH_2O and a closing pressure equivalent to 100 mmH_2O after removal of 5 ml of liquor. The fluid contained protein 35 mg/dl, sugar 92 mg/dl, cell count 4/3 and gave a negative tryptophane test and negative serological test for syphilis. Lumbar puncture performed one month after admission gave results almost similar to those in the first lumbar puncture, except that the cell count was 1/3.

Electroencephalograms were recorded three times on a timecourse basis. No abnormal findings were shown. CT scan showed no abnormal findings except for a slight enlargement of the encephalocoele.

Clinical course after admission: Up to one month after admission, the patient showed fluctuation in the extent of the limitation of ocular movement, particularly in the horizontal and downward movements, showing some improvement one day, but then returning to the same conditions as seen on admission the following day. Tendon reflexes showed a tendency to improve, slow as they were, particularly in the lower limbs. Oral administration of prednisolone 30 mg/day was initiated from the first month after admission. As the blood sugar level rose (fasting blood sugar 264 mg/dl) from the second week after administration of this preparation, the dosage was reduced first to 10 mg/day and then to 5 mg/day while an oral antidiabetic agent was administered jointly. Consequently, the blood sugar levels were brought under control. Improvement in the ocular movements was observed and upward movement was also improved considerably from the second week of administration of prednisolone. However, the degree of improvement in upward movement started falling off when the dosage of prednisolone was reduced to 5 mg/day. Administration of prednisolone was continued for

two months. With symptoms almost all improved except for the restricted upward movement, the patient was discharged home. At present, she is attending the out-patient clinic, with the condition stable.

DISCUSSION

Fisher (1956)[1] reported three cases with the syndrome of ophthalmoplegia, ataxia and areflexia. He thought of it as an unusual variant of acute idiopathic polyneuritis. And he himself regarded this acute idiopathic polyneuritis as Guillain-Barré syndrome. In 1957, Smith and Walsh[2] reported two cases that showed similar findings. With these two cases and the three reported by Fisher for a total of five cases, they classified the characteristics common to these cases into 14 items. Since the publication of a report by Hynes (1961)[4], these cases have come to be known as "Syndrome of Fisher" or "Fisher's Syndrome" (Goodwin et al., 1963)[5]. Yet, Hynes strictly regarded one of his cases as a variation of Guillain-Barré syndrome. Fisher himself maintained that acute idiopathic polyneuritis is synonymous with Guillain-Barré syndrome. Hirayama[3] is of the opinion that among the cases of Guillain-Barré syndrome, those presenting ophthalmoplegia, ataxia and areflexia are actually Fisher's syndrom.

As pointed out by Munsat and Barnes (1965)[6], even before many cases presenting ophthalmoplegia and ataxia were found among the cases which had been previously reported as Guillain-Barré syndrome, mainly in Europe. Guillain (1938)[7] himself had already classified Guillain-Barré syndrome into four groups. Of them, one classified as "la forme mésocephalique pare" refers to those who had paralysis of the central nervous system. Herein is one of the grounds for the argument that establishing the classification of Fisher's syndrome is not necessary. Certainly, many cases presenting ophthalmoplegia are to be found among the cases of Guillain-Barré syndrome (Marshall, 1963)[8].

For six cases of acute polyneuritis presenting ophthalmoplegia, Gibberd (1970)[9] divided them into four groups and made a detailed report. The four groups were 1: complete ophthalmoplegia, 2: copmlete external ophthalmoplegia and normal pupils, 3: partial external ophthalmoplegia and complete pupillary involvement and 4: partial external ophthalmoplegia and partial pupillary involvement. According to his classification, our two cases may be considered to belong to group 2, and as the theory of Guillain[7] is concerned, they may be classified as "la forme mésocephalique". The questionable point is that the albuminocytologic dissociation of cerebrospinal fluid was absent in our cases. Case

3 of Fisher[1] also lacks in this finding. Katayama et al. (1976)[10] reviewed the literature on 49 cases in Japan and also found no albuminocytologic dissociation in seven cases. Having found cerebrospinal fluid changes with concomitant with the stage of illness, this question cannot be discussed merely on the basis of the findings observed early in the onset of disease as in Case 1. It is also said that albuminocytologic dissociation is not a symptom common to all cases of Gullian-Barre syndrome.

EEG abnormalities in Fisher's syndrome were reported by Darcourt et al. (1959)[11], Van Allen et al. (1964)[12], Munsat et al. (1965)[6], Shibasaki et al. (1972)[13], Katayama et al. (1976)[10]. This serves as a basis for the theory that disorder of the central nervous system is responsible for oculomotor paralysis. The abovementioned authors mentioned transient appearance of delta waves and beta waves as EEG abnormalities. When theta waves and delta waves appear in the frontal region in a bilateral synchronous monorhythmic manner, as in Case 1, it is thought to suggest the presence of deep subcortical lesion.

The two cases reported here had the 14 items noted by Smith et al.[2] as characteristics of Fisher's syndrome and the 10 items mentioned by Katayama et al[1].[10], except that albuminocytologic dissociation was not observed. However, whether or not these two cases may be classified as Fisher's syndrome simply for those reasons will require further studies.

SUMMARY

We have reported two cases of acute idiopathic polyneuritis which developed ophthalmoplegia, ataxia and areflexia. It was pointed out that this sort of disease is usually considered to belong to Fisher's syndrome, particularly in Japan, but can also be taken as "la forme mésocephalique" of Guillain-Barré syndrome. According to the classification of Gibberd, our two cases are thought to belong to the group of "complete external ophthalmoplegia and normal pupils."

REFERENCES

1) Fisher, M.: An unusual varient of acute idiopathic polyneuritis (syndrome of ophthalmoplegia, ataxia and areflexia). *New Eng. J. Med.*, 225 : 57-65, 1956.
2) Smith, J.L. and Walsh, F.B.: Syndrome of external ophthalmoplegia, ataxia and areflexia (Fisher), ocular manifestations in acute idiopathic polyneuritis (Guillian - Barré syndrome); report of two cases. *A.M.A. Arch. Ophthal.*, 58 : 108-114, 1957.
3) Hirayama, K.: Fisher's syndrome. *Brain & Nerv.*, 26 : 371, 1974. (in Jap).
4) Hynes, E.A.: Syndrome of Fisher, ophthalmoplegia, ataxia and areflexia. *Am. J. Ophthal.*,

51 : 701-704, 1961.
5) Goodwin, R.F. and Poser, C.M.: Ophthalmoplegia, ataxia and areflexia, Fisher's syndrome. *JAMA.*, 186 : 258-259, 1963.
6) Munsat, T.L. and Barnes, J.E.: Relation of multiple cranial nerve dysfunction to the Guillain - Barré syndrome. *J. Neurol. Neurosurg. Psychiat.*, 28 : 115-120, 1965.
7) Guillain, G.: Les polyradiculonervites avec dissociation alambinocytologique et a evolution favorable. (Syndrome de Guillain-Barré). *J. Belge Neurol. Psychiat.*, 38 : 323-329, 1938.
8) Marshall, J.: The Landry-Guillain-Barré syndrome. *Brain*, 86 : 55-66, 1963.
9) Gibberd, F.B.: Ophthalmoplegia in acute polyneuritis. *Arch. Neurol.*, 23 : 161-164, 1970.
10) Katayama, S., Abiko, S. and Aoki, H.: Fisher's syndrome-case report and review of literature-. *Yamaguchi Med J.*, 25 : 181-187, 1976. (in Japanese).
11) Darcourt, G. et Cossa, P.: Syndrome de Guillain-Barré avec ophthalmoplegie extrineseque bilaterale et ataxie aigue. *Rev. Oto-Neuro-Ophthal.*, 31 : 416-418, 1959.
12) Van Allen, M.W. and Macqueen, J.C.: Ophthalmoplegia and the syndrome Landry-Guillain-Barré; a report of four cases with comments on the ophthalmoplegia. *Trans. Amer. Neurol. Ass.*, 89 : 98-103, 1964.
13) Shibasaki, H., Igusu, H. and Kuroiwa, Y.: EEG abnormality in Fisher's syndrome. *Folia Psychiat. Neurol. Jap.*, 26 : 201-207, 1972.