AN AUTOPSIED CASE OF SUBACUTE MYELONEUROPATHY WITH PRECEDING ABDOMINAL SYMPTOMS, A SYNDROME RECENTLY RECOGNIZED IN JAPAN

HISATOSHI TAKEDATSU, HIROAKI SATO, MUNEATSU MATSUFUJI AND KUNIO OKUDA

Second Department of Medicine, Kurume University School of Medicine, Kurume, Japan

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The clinical picture of myeloneuropathy following abdominal symptoms has already been reported in details by us and others. Neurological manifestations that follow such abdominal complaints as pain, diarrhea, nausea, constipation or meteorism of varying duration, in most instances, suggest involvement of the spinal cord and peripheral nerve. The optic nerve is affected in certain proportion of the patients. This syndrome is seen sporadically as well as in epidemics.

There are several reports on the histopathological findings of the nervous system in autopsied materials. They have been identified with none of the established diseases.

The following is an account of the clinical picture of a patient who developed the symptoms during the treatment for pulmonary tuberculosis and of the histopathological findings of the nervous system.

CASE REPORT

A 54 year old male was referred to us from the Surgical Department because of numbness of the lower extremities. He had pulmonary tuberculosis for which he was receiving various antituberculous drugs for about 4 years. He was admitted to the Surgical Ward on June 6, 1964 for thoracoplasty. He had resection of the right upper lung with thoracoplasty in Oct. 1964, following which he was placed on PAS and isoniazid, but productive cough with sputum persisted with positive tuberculosis bacilli.

Physical findings on admission to Surgery: A well-developed but poorly nourished man without apparent illness. The pulse 80/min., regular and blood pressure 120/70. Palpebral conjunctiva was slightly anemic. Pupils normally reacted to light and accommodation. Ocular movements were normal. The tongue, throat and tonsils were all normal. Cardiac dulness was within normal limits. Heart sounds were clear, and moist rales were audible in the right lower lung.
The abdomen was soft and nontender. The knee jerks and Achilles jerks were normal.

_Course:_ On July 16, 1967 he started having diarrhea about six times daily, but the stool did not contain any blood or mucus. Diarrhea gradually ceased within one week. On August 16, he suddenly had dull pain over the entire abdomen without nausea, and there were slight fever and full sensation of the stomach. Two days later, he noted numbness of the distal portion of the lower extremities.

Constipation and abdominal pain persisted. There was no nausea, fever or disturbance of walking at that time. First neurological examination was made then, and hyperalgesia below the knee level with normal reflexes was elicited. Treatment with Vitamin B1, B6 and B12 was begun. Numbness of the lower limbs developed and ascended to the level of the umbilicus in four days. Occasionally there was epigastric dull pain, but it responded to antacids. Anti-tuberculous drugs were suspended. On August 26, abdominal pain and abnormal sensation of the legs recurred with lumbago. X-ray films on Sept. 8 of the lumbar vertebrae showed no abnormalities. He soon became unable to walk. Two days later, he began to note blurred vision while reading newspaper. The second neurological examinations showed atrophied disc in the fundi bilaterally, but there were no other cranial nerve involvements. Nuchal rigidity was negative. Muscular strength of the lower extremities was markedly diminished, but that of the upper extremities was normal. Both abdominal and cremasteric reflexes were absent. Knee jerks were markedly hyperactive but Achilles jerks were absent. Sensory examination disclosed hypesthesia and hyperalgesia, as well as marked diminution of vibratory and position senses below the level of Th10. There was muscular tenderness over the calves. Spastic paralysis of the lower legs still present.

Thereafter, visual disturbance gradually became worse, and soon urinary incontinence and speech disturbance occurred.

Lumbar puncture was performed on Oct. 20, and it revealed an initial pressure of 125 mm of water and an end pressure of 60 mm of water after the removal of 7 ml. The Queckenstedt test was negative. The cerebrospinal fluid was clear and the cell count 3/3, protein 53 mg and sugar 60 mg per 100 ml. On Oct. 23, he started having hiccups frequently and could not move his body. On the next day, his state of consciousness became deteriorated and suddenly died of cardiac arrest at 9.00 P.M.

Laboratory findings on August 19: Serum vitamin B12 level 0.76 m¿/ml., CCF (+), TTT 3.3 units, Kunkel 18.4 units, Total cholesterol 234 mg%, Total protein 8.0 g%, A/G ratio 1.06, Albumin 51.5 %, x1 4.3 %, x2 5.2%, f 11.1 %, y 27.9 %, Alkaline-phosphatase 11.7 Bodanski units, Amylase 43 Russel units, GOT 54 Karmen units, GPT 15 units, LDH 140 units, CRP (—), RBC 380×10⁴, Hb 68 %, WBC 3900, Ht 28.5 %, Urinarysis was negative.
Postmortem findings:
Autopsy was performed six hours after death. The body measured 158 cm. in length and weighed 42 kg. There were scattered bleedings in the left lung.

The nervous system was grossly normal except for whitish color in the posterior column of the spinal cord. The cerebrospinal fluid was clear. The brain weighed 1440 gm. There was no congestion or turbidity in the pia mater. The nerve tissue was studied microscopically by Hematoxylin-Eosin, Luxol-Fast-Blue, Sugamo's myelin sheath, Nissle and Fat stains.

Brain: not remarkable
Brain stem, cerebellum and medulla oblongata were normal.

Optic nerve: Diffuse demyelination was observed inside the chiasm, but there was no perivascular cell infiltration (Fig. 1).

Spinal cord: In the posterior column, diffuse degeneration was noted between the cervical and the lumbar level. Fasciculus gracilis were marked

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**Fig. 1** Optic nerve (−Demyelinated area) (Sugamo's myelin sheath stain)

**Fig. 2** Lower thoracic cord (Sugamo's myelin sheath stain)

**Fig. 3** Degenerated area of the posterior column in lower thoracic cord (Sugamo's myelin sheath stain)

**Fig. 4** Patchy degeneration in cervical cord (Sugamo's myelin sheath stain)
degenerated bilaterally, particularly in the lower thoracic level, but the involvement of faciculus cuneatus was minimal (Fig. 2). Free fat macrophages and slight gliosis were observed in the degenerated area of the posterior column (Fig. 3). In the lateral column, degeneration was observed in the thoracic cord, but the involvement of both tracts was asymmetric. Furthermore, degeneration of the right anterior column was noted in the middle and lower thoracic cord, and several sites of patchy degeneration were seen in the lateral column of cervical cord (Fig. 4).

In the nerves of cauda equina, there were marked destructions and many vacuoles of the myelin sheath (Fig. 5).

The changes of spinal cord are given schematically in Fig. 6.

Main pathological findings of this case were secondary degeneration of the posterolateral column and demyelination of the optic nerve and peripheral nerves.

Fig. 5 Peripheral nerve (Luxol-Fast-Blue stain)

Fig. 6 Illustrative drawings of the histologic alterations of the spinal cord
DISCUSSION

The clinical picture and postmortem findings of this case closely resembled combined system disease which is a common complication of pernicious anemia. However, the blood pictures, Vitamin B\textsubscript{12} measurement and other laboratory findings readily excluded pernicious anemia.

In his history, a long episode of taking isoniazid suggested a possible neurotoxicity of this drug as cause. It has been known that isoniazid induces polyneuropathy, and accelerates excretion of Vitamin B\textsubscript{6} into the urine. However, there have been no case reports of degeneration of posterolateral column in patients receiving isoniazid in the literature. The lack of response to a large dose of vitamin B\textsubscript{6} will also rule out such possibility.

So far, there have been 19 autopsied case of this syndrome which is generally called “Subacute myelo-optico-neuropathy” with preceding abdominal signs in this country. Tsubaki, Toyokura and Tsukagoshi\textsuperscript{5)} reported the histological changes of the nervous system in six similar cases, demonstrating degeneration of the posterolateral column, demyelination of the optic nerve and patchy and/or plaque demyelination in the peripheral nerves and dorsal ganglia. Perivascular infiltration was minimal or absent in the spinal cord. They introduced the term “Symmetrical pseudo-system degeneration”, and concluded that the main pathological picture was compatible neither with combined system disease of pernicious anemia nor primary demyelinating disease and allied disease, because of the lack of changes in perivascular area. Maekawa\textsuperscript{6)} also noted similar degeneration in the posterolateral column, the optic nerve and peripheral nerves, but he attached importance to perivascular infiltration of lymphocytes in the spinal cord and the optic nerve. In sympathetic ganglia, similar degeneration and slight perivascular infiltration were reported by Nakao\textsuperscript{7}). Examination of sympathetic ganglia and dorsal ganglia in our case was not done, but changes of the spinal cord, the optic and peripheral nerve were very close to those described in these reports.

SUMMARY

An autopsied case of myeloneuropathy with preceding abdominal symptoms developing during the treatment of pulmonary tuberculosis is reported. Histologically, degeneration in the posterolateral column and peripheral nerves and demyelination of the optic nerve were observed without demonstrable inflammatory changes. The clinical and pathological changes are compatible with none of the established demyelinating or systemic degenerative diseases of the nervous system.
REFERENCES