Short communications

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Peripheral neuropathy with predominantly motor manifestations in a patient with carcinoma of the uterus

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Summary. An autopsy case of a 56-year-old woman who had carcinoma of the corpus uteri and peripheral neuropathy with predominantly motor manifestations is described. The neurological abnormalities included subacute weakness of the limbs and loss of deep reflexes, which improved after the surgical removal of the uterine carcinoma. Neuropathologically, peripheral nerves mainly presented features of axonal degeneration with a mild loss of myelinated fibres. Anterior horns of the spinal cord showed central chromatolysis of the motor nerve cells and many spheroids without neuronal loss. Axonopathy of peripheral nerves was considered to be the main pathological process in this paraneoplastic syndrome.

Key words: Motor-dominant neuropathy – Carcinoma of the uterus – Paraneoplastic syndrome

Introduction

In paraneoplastic neuropathies due to remote effects of neoplasms [4, 7, 9], sensory or sensorimotor polyneuropathy is commonly found associated with neoplasms of the lung, breast and other organs, including the uterus. Cases presenting predominantly motor manifestations are uncommon.

We report such a case with carcinoma of the corpus uteri.

Case report

A 56-year-old Japanese woman developed weakness in both hands in early November 1985. Weakness subacutely extended and involved the entire upper and lower extremities. She showed a recent weight loss of 6 kg. She could not walk without support when admitted to the hospital on 28 November.

On neurological examination, she was found to have moderate muscle atrophy in all limbs. Muscle power was evaluated to be 3/5 in muscle strength in the entire upper and lower extremities. Muscle tone of the limbs was decreased. No fasciculation was found. Deep reflexes were absent in the upper extremities and diminished in the lower extremities. Babinski's sign was negative bilaterally. Sensation was intact in all modalities. Routine laboratory studies showed elevated serum LDH (lactate dehydrogenase) activity (639 U/l; normal, 125–220). Cerebrospinal fluid (CSF) showed a mild increase of protein (60 mg/dl) without pleocytosis. CSF cytology was negative for malignancy. Motor and sensory nerve conduction studies were performed in median, ulnar, peroneal, tibial, and sural nerves. The motor nerve conduction velocities were within or at the lower end of normal limits. Muscle action potentials were reduced in amplitude. Sensory nerve conduction studies were normal. In a needle electromyogram (EMG), a decrease in quantity of discharge and polyphasic potentials were diffusely found, and high-amplitude potentials were observed in the triceps brachii and thenar muscles. After admission, muscle weakness progressively worsened and the patient became bedridden and all of the deep reflexes disappeared. Sensory disturbances showing a slight decrease of light touch and pinprick sensations distal to the middle part of both legs and forearms appeared on 10 December and disappeared on 17 December. Abdominal echography and CT demonstrated swelling of the corpus uteri. Cytology of the endometrium indicated class V changes.

The patient underwent an extensive hysterectomy on 30 January 1986. During the operation, 3000 ml blood was transfused. The histopathological diagnosis of the surgically resected material was poorly differentiated adenocarcinoma of the corpus uteri. The neurological abnormalities improved after the operation. The muscle weakness improved, and she could walk with support. Deep reflexes again appeared in both upper and lower extremities. However, in early March, the muscle weakness became worse and all the deep reflexes absent. The patient again became bedridden and emaciated with generalized, severe muscular atrophy. Later, the patient developed atrophy of the right side of the tongue and paresis of the right side of the palate. Swelling of systemic lymph nodes appeared, which was considered to be metastases of the uterine carcinoma. Neither chemotherapy nor irradiation was performed because she was in a poor general condition. The patient developed sepsis, and atelectasis of the left lung and anuria, and died on 22 April 1986.

An autopsy was performed 3 h post mortem. The uterine carcinoma showed multiple metastases mainly in the systemic lymph nodes with no recurrence in the primary site. Metastatic infiltration of the nervous system was confined to only two sites; one was a small-finger-tip-sized metastasis in the dura covering the right ventral portion of the medulla oblongata, which involved the radicular fibres of the right hypoglossal nerves resulting in denervation atrophy of the right side of the tongue; the other was partial invasion of the left L1 and L2 spinal nerves by metastatic carcinoma in the paraaortic lymph node. There was no evidence of meningeal carcinomatosis.

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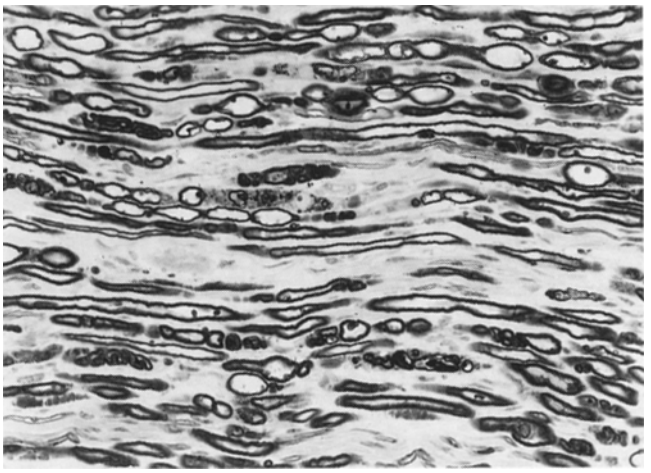

Fig. 1. Longitudinal section of the femoral nerve. There is mild loss of myelinated fibres, as well as swelling and breakdowns of myelin sheaths with formations of myelin ovoids. Epon-embedded semithin section, toluidine-blue, × 210

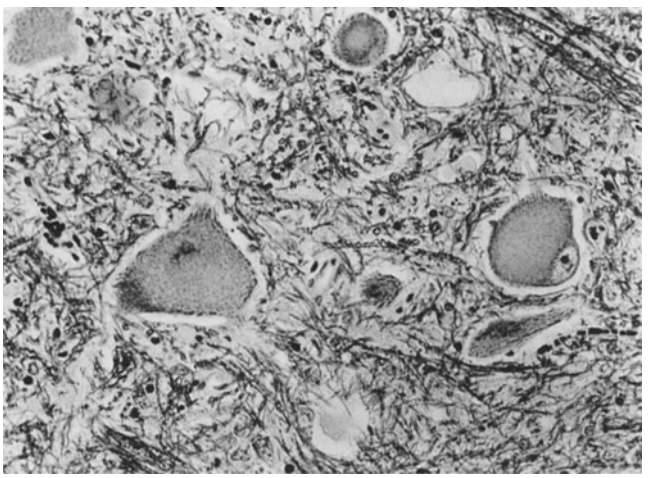

Fig. 2. Anterior horn of the spinal cord at the level of L4. The anterior horn cells show central chromatolysis. Klüver-Barrera, × 260

Peripheral nerves were systemically investigated including sciatic, femoral, and sural nerves, brachial plexus, and spinal nerve roots. Loss of myelinated nerve fibres was generally mild. In morphometric studies of the myelinated fibres (MFs), densities in the femoral and sural nerves were 7100 MFs/mm^2 (8370 in control case) and 5267 MFs/mm^2 (normal 7710 ± 1210 [1]), respectively. Both large and small MFs were decreased to a mild degree. The changes of the nerve fibres were scattered showing atrophy, swelling, and disintegration of axons and swelling, splitting, and breakdowns of myelin sheaths with the formation of ovoids (Fig. 1). On teased-fibre analysis of the femoral nerves, 20% of MFs showed linear rows of myelin ovoids and 8% showed segmental demyelination and remyelination. Although loss of MFs in the spinal nerve roots was slight, ventral roots were more affected than dorsal roots. Electron microscopic studies were performed on the femoral and sural nerves. MFs showed atrophy and swelling of axons with cleft and infolding of myelin sheaths. Schwann cell cytoplasm with abnormal MFs sometimes contained myelin debris. Unmyelinated fibres (UMFs) were 32800 UMF/mm^2 in density (33400 in control [1]) with normal distribution in morphometry of the electron micrograph of the sural nerve. Formations of collagen pockets were occasionally found. In the spinal dorsal root ganglia (DRG), ganglion cells were rather well preserved. Residual nodules were rarely found in DRG. In the spinal cord, anterior horns (Fig. 2) showed central chromatolysis of the motor nerve cells with appearances of many spheroids in the cervical and lumbosacral levels. A hyaline inclusion was found in cytoplasm of the anterior horn cell at the C7 level. There was no neuronal loss, inflammation, microglia activation, or gliosis in anterior horns. No degeneration was found in corticospinal tracts or in posterior columns. Skeletal muscles of the upper and lower extremities showed marked neurogenic atrophy. Small intramuscular nerves presented with a mild loss of MFs. There was no lesion in the brain.

For the purpose of detecting anti-neural antibody in the patient's serum, indirect fluorescent antibody staining was performed. Cryostat sections of normal human sciatic nerve and spinal cord were reacted with the patient's serum, and later reacted with fluorescein-conjugated rabbit immunoglobulins to human immunoglobulins. No immunofluorescence was found in the nerve or spinal cord.

Discussion

This case was characterized by the association of uterine carcinoma and motor-dominant manifestations, which improved after the hysterectomy. Direct metastatic infiltration of the nerves was found to be minimal at autopsy and could not explain the symmetrical involvement of both upper and lower extremities and the improvement after the removal of the tumour. The condition should be considered to be a paraneoplastic syndrome. It was a problem to distinguish peripheral neuropathy with predominantly motor manifestations from motor neuron disease (MND). Pathologically, there were significantly high incidence of axonal degeneration, atrophy and other changes of axons in electron microscopic observations, and central chromatolysis of the motor nerve cells and formation of spheroids in the anterior horns of the spinal cord. The sural nerve, a pure sensory nerve, was also affected pathologically. The pathological process should be categorized as a peripheral nerve axonopathy. The condition was different from paraneoplastic MND [3, 7, 10, 12, 14] because there was no loss of the anterior horn cells. Several cases of paraneoplastic motor-dominant peripheral neuropathy have been reported in bronchial carcinoma [8, 13] and macroglobulinaemia [11], and demyelination has been suggested to be characteristic of the neuropathy [8, 11].

The pathogenesis of the neuropathy in our case remains unknown. The improvement after surgical removal of the uterine carcinoma and a large amount of blood transfusion might be suggestive of the presence of unknown causative factors in the serum related to the uterine carcinoma. The unknown factors may be anti-neural antibody or a toxic substance produced by the carcinoma. Although antibodies against nervous tissue have been reported in various paraneoplastic syndromes [2, 5, 6], we were unable to demonstrate the presence of the antibody against human peripheral nerve and spinal cord in the patient's serum by immunofluorescent studies.

References

1. Asbury AK, Johnson PC (1978) Pathology of peripheral nerve. Saunders, Philadelphia
2. Babikian VL, Stefansson K, Dieperink ME, Arnason BGW, Marton LS, Levy BE (1985) Paraneoplastic myelopathy: antibodies against protein in normal spinal cord and underlying neoplasm. Lancet II:9–50
3. Brain L, Croft PB, Wilkinson M (1965) Motor neurone disease as a manifestation of neoplasm. Brain 88:479–500
4. Bruyn GW (1979) Carcinomatous polyneuropathy. In: Vinken PJ, Bruyn GW (eds) Handbook of clinical neurology, vol 38. Elsevier, Amsterdam, pp 679–693
5. Graus F, Cordon-Cardo C, Posner JB (1985) Neuronal antinuclear antibody in sensory neuropathy from lung cancer. Neurology 35:538–543
6. Greenlee JE, Brashear HR (1983) Antibodies to cerebellar Purkinje cells in patients with paraneoplastic cerebellar degeneration and ovarian carcinoma. Ann Neurol 14:609–613
7. Henson RA, Urich H (1982) Cancer and the nervous system. Blackwell, Oxford
8. Lennox B, Prichard S (1950) The association of bronchial carcinoma and peripheral neuritis. Q J Med 19:97–110
9. McLeod JG (1984) Carcinomatous neuropathy. In: Dyck PJ, Thomas PK, Lambert EH, Bunge R (eds) Peripheral neuropathy, vol 2. Saunders, Philadelphia, pp 2180–2191
10. Norris FH (1979) Remote effects of cancer of the spinal cord. In: Vinken PJ, Bruyn GW (eds) Handbook of clinical neurology, vol 38. Elsevier, Amsterdam, pp 669–677
11. Rowland LP, Defendini R, Sherman W, Hirano A, Olarte MR, Latov N, Lovelace RE, Inoue K, Osserman EF (1982) Macroglobulinemia with peripheral neuropathy simulating motor neuron disease. Ann Neurol 11:532–536
12. Schold SC, CHo E-S, Somasundaram M, Posner JB (1979) Subacute motor neuronopathy: a remote effect of lymphoma. Ann Neurol 5:271–287
13. Stephens TW, Rousgas A, Ghose MK (1966) Pure motor neuropathy complicating carcinoma of bronchus recovered after surgery. Br J Dis Chest 60:107–109
14. Stoll DB, Lublin F, Brodovsky H, Laucius JF, Patchefsky A, Cooper H (1984) Association of subacute motor neuronopathy with thymoma. Cancer 54:770–772

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