CASE REPORT

Hodgkin’s Disease Preceded by Unique Neurological Symptoms

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Abstract

This is the first case report of Hodgkin’s disease (HD) which showed both remission and exacerbation of neurological signs before a confirmed diagnosis of HD. The episodes occurred three times and multiple lesions were involved. Immunoabsorption plasmapheresis and double filtration plasmapheresis were effective for the first episode, whereas, corticosteroids partly improved the second and third episodes. Fever and lymph node swelling were apparent afterward and she was diagnosed as having HD from a supraclavicular lymph node biopsy. The remaining neurological deficits responded to chemotherapy and radiotherapy. The neurological symptoms were considered as a paraneoplastic syndrome of HD.

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Key words: paraneoplastic syndrome, plasmapheresis, corticosteroid, chemotherapy, radiation therapy

Introduction

Some paraneoplastic neurological complications of Hodgkin’s disease (HD) have been reported. They include peripheral neuropathy, stiff-mann syndrome, anti-Hu syndrome, encephalomyelitis, cerebellar degeneration, myelopathy, and radiculomyelitis (1–7). In two cases, neurological deficits were improved by intrathecal dexamethasone (2, 3). Another responded to intravenous administration of high-dose methylprednisolone and MOPP-ABV chemotherapy (4). Benefits from plasmapheresis have also been reported (5), but other reports state no benefit (6, 7). We report here a case of probable paraneoplastic syndrome of HD that showed unusual reversible neurological deficits.

Case Report

A previously healthy 21-year-old woman was admitted to Nagoya Daini Red Cross hospital in November 1997 with itching, dysphagia, dysarthria, fever, and rigidity of the upper arm which had progressed over one month. She had no history of weight loss or night sweats. Physical examination showed itchy eruptions in breast and arms. Neurological findings revealed lead-pipe rigidity of neck and arms, bilateral hypesthesia and hyperalgesia of level C2–4, and bilateral paresthesia of level Th 4–12. All deep tendon reflexes, including masseter, biceps, triceps, brachioradialis, ulnar, patellar tendon, and achilles tendon reflex, showed hyperreflexia without Babinski or Chaddock signs. The white blood cell count was 12×10³/l with other laboratory data being normal. Cerebrospinal fluid (CSF) study showed normal opening pressure, a mild increase of cell count (29 WBC/mm³, 97% mononuclear cells, 3% polymonuclear cells), and normal levels of protein (18 mg/dl) and glucose (79 mg/dl). Chest X-ray and MRI of head, neck, and thorax, including gadolium enhancement, revealed no abnormalities. A nerve conduction study in upper and lower extremities and electromyogram in biceps and quadriceps were normal. Serum autoantibody activities against glutamic acid decarboxylase (GAD), GQ1b, and GM1 were also normal. Aseptic meningoencephalitis, acute disseminated encephalomyelitis (ADEM), and multiple sclerosis (MS) were suspected. She was treated with methylprednisolone (1,000 mg qd iv) for 3 days, 500 mg qd iv for 3 days, 100 mg qd iv for 7 days, and 50 mg/day qd iv for 19 days. With that treatment, dysphagia and dysarthria developed gradually and generalized seizure was apparent. She was admitted to the intensive care unit to be intubated. External ophthalmoplegia in all directions, ankle and patellar clonus, and spasticity in the legs developed. Her consciousness level was normal, although an EEG study showed diffuse slow waves. On the 26th day, she was treated with immunoabsorption plasmapheresis (IAPP). Double filtration plasmapheresis (DFPP) was then done five times every two days. External ophthalmoplegia, rigidity, spasticity, and paresthesia improved and CSF...
occurred. Recurrence of neurological signs has not size, and all neurological deficits, except for the left Chaddock irradiation. The enlarged lymph node was shrunk to normal were started on 1 May 1999, followed by mantle-veld (55Gy) Classification). Three courses of chemotherapy (C-MOPP) noused as having clinical stage IIB HD (Modified Ann Arbor and ultrasound examinations were normal, and she was diag- gram showed high uptakes at supraclavicular and mediastinal X-p revealed enlarged mediastinum. MRI of the head, cervical showed: WBC 21x10^9/l, LDH 541 IU/l (normal values <450 IU/l), and CRP 4.3 mg/dl. CSF examination was normal. Chest depicted the hospital again and was then admitted to Kumamoto City Hospital. Neurological examination demonstrated spastic gait, bilateral hyperreflexia in all deep tendon reflexes, Babinski and Chaddock signs, bilateral hyperesthesia, and hyperalgesia of level Th5–10. Laboratory data including anti-HTLV-1 antibody was normal. CSF examination including oligoclonal band and myelin basic protein was also normal. Chest X-p, EEG, CT brain scan, and MRI of the spinal cord with gadolinium enhancement were all within normal limits. Since she had had two attacks and more than two clinical lesions without paraclic- nical evidence, she was diagnosed as clinically definite (A1) MS by Poser’s criteria (8). She was treated with high-dose methylprednisolone (1,000 mg qd IV) for three days and prednisolone (60 mg qd po) was continued. Her general condition became better but bilateral hyperesthesia and hyperalgesia of level Th7-8 remained.

In March 1999, she was again admitted to our hospital because of a fever and spastic gait. Neurological examinations revealed bilateral hyperesthesia and hyperalgesia of level Th6-10, hyperreflexia, Babinski signs, spastic gait, unsteady tandem gait, polissauria, and constipation. A laboratory study showed: WBC 21x10^9/l, LDH 541 IU/l (normal values <450 IU/l), and CRP 4.3 mg/dl. CSF examination was normal. Chest X-p revealed enlarged mediasitum. MRI of the head, cervical and thoracic spinal cord showed no abnormalities. The diagnosis of an unknown infectious disease and recurrence of MS was made. High-dose methylprednisolone (1,000 mg qd iv) for three days followed by prednisolone (60 mg qd po) with antibiotics were administered. The fever and symptoms, ex- cept for hyperesthesia and hyperalgesia, were improved, but the abnormalities of the laboratory data remained unchanged. One month later, her fever emerged again. Neurological sympto- mptoms were not changed. The laboratory study showed: WBC 24x10^9/l, LDH 809 IU/l, CRP 23.2 mg/dl, β2-microglobulin 1.9 mg/ml, and soluble IL-2 receptor antibody 1,486 U/ml. Serum anti-Hu antibody was negative. Chest X-p and computed tomo- graphy (CT) revealed a mediastinal mass. Gallium scinti- gram showed high uptakes at supraclavicular and mediastinal lymph nodes. A right supraclavicular lymph node biopsy was done under informed consent. The histological specimen revealed evidence of nodular sclerosing type HD. Abdominal CT and ultrasound examinations were normal, and she was diag- nosed as having clinical stage IIB HD (Modified Ann Arbor Classification). Three courses of chemotherapy (C-MOPP) were started on 11 May 1999, followed by mantle-veld (55Gy) irradiation. The enlarged lymph node was shrunk to normal size, and all neurological deficits, except for the left Chaddock sign, disappeared. Recurrence of neurological signs has not occurred since then.

Discussion

We report a case of clinical stage IIB HD presenting three episodes and multiple lesions of the central nervous system (CNS) before the diagnosis of HD could be confirmed. In this case, the neurological findings suggested the involvement of multiple lesions of the nervous system: external opthalmoplegia, dysarthria, and dysphagia suggested the involvement of the brainstem; rigidity, the extrapyramidal tract; spasticity and hyperreflexia, the pyramidal tract; sensory disturbance, the spinal cord and/or dorsal root; convolution, the cerebral cortex. Though the paraclinical findings, such as MRI of the head and CSF study showed no evidence, MS was suspected based on that clinical course, before the diagnosis of HD was confirmed. One case of MS developing after successful treatment of HD was reported previously (9). In that report, the MRI study with gadolinium enhancement demonstrated multiple lesions, which differed from the present case.

Neurological symptoms were improved by plasmapheresis and corticosteroid before a diagnosis of HD and this clinical feature might suggest that neurological signs were associated with the autoimmune mechanism. Although there was no di- rect evidence of serum antibodies, such as anti-Hu antibody, anti-Tr antibodies, anti-amphymphysin antibody, or antibodies to the metabotropic glutamate receptor subunit protein, the clinical feature was difficult to explain except for possible paraneo- plastic syndrome associated with HD. Some types of paraneo- plastic syndrome of HD have been reported previously (1–7), however no case has shown both remission and exacerbation of neurological signs without any evidence of MRI findings.

The efficacy of treatments for paraneoplastic syndrome of HD has differed among previous cases. In two cases of myelopathy, neurological deficit was improved by intrathecal dexamethasone (2, 3), and in a case of radiculomyelitis, intrave- nous administration of a high dose of methylprednisolone and MOPP-ABV chemotherapy were effective (4). In one case of paraneo- plastic syndrome of HD have been reported previously (1–7), but in others it was not (6). Plasmapheresis for paraneoplastic neuropathy was also not effective in one case (7). In the present case, partial neurological improvement was observed after plasmapheresis and corticosteroids, but complete recovery was achieved with C-MOPP chemotherapy and irradiation.

We conclude that the neurological symptoms in this case were a unique paraneoplastic syndrome of HD rather than MS. When a patient has symptoms like atypical MS, it is necessary to investigate a systemic disease such as HD.

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References

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