

## Brief Communication

### Motor neuron disease and its association with non-Hodgkin's lymphoma

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**M**otor neuron disease (MND) is a neurodegenerative disorder characterized by muscle atrophy, brisk reflexes, spasticity, fasciculation, and atrophy. The onset of the disease is generally insidious. The pathological process may involve the motor cortex, the spinal cord, and the brainstem.<sup>1</sup> Only upper or only lower motor neurons may be affected. The disease may or may not be seen with neoplasms, however, there have been cases of amyotrophic lateral sclerosis associated with paraneoplastic diseases. This clinical picture occurs with Hodgkin's disease (HD), non-Hodgkin's lymphoma (NHL), and leukemia. The clinical findings frequently start at the lower limbs and become generalized. In this report, we present a patient with NHL and MND to draw attention to this association and to emphasize that these patients should be observed for this condition.

A 70-year-old man was admitted to the clinic with weakness in the right foot. He did not have a family history. Results of a physical examination were normal. The results of a neurologic examination revealed 4/5 monoparesis and atrophy of the right foot (4/5), and fasciculation, prominent in the upper and lower proximal muscle groups. Results of standard laboratory analyses for total blood count, routine biochemical tests, protein electrophoresis, Bence Jones protein, and CSF protein level were normal. Results of abdomen-pelvic ultrasonography and spinal MRI did not show any pathological findings. Electromyography of 4 limbs demonstrated motor unit action potentials of long durations with fasciculation. Fibrillation was observed in the rectus femoris, tibialis anterior, and gastrocnemius of the right lower limb. The patient was diagnosed as having MND. Riluzole (100 mg/day) and vitamin E (600 mg/day) were begun. One year later, the patient presented with fever, night sweating, and fatigue. A physical examination revealed a 2 × 2 cm lymph adenomegaly in the right axilla. On neurologic examination, dysarthria, diminished gag reflex, atrophy, and fasciculation of the tongue muscle, and tetraparesis were detected. Deep tendon reflexes were hypoactive, the response to Babinski's sign was negative bilaterally, and the response to Hoffmann's sign was positive bilaterally. Atrophy was present in the thenar, hypothenar, and interosseal muscles of the hand, and the intrinsic foot muscles. Foot drop was present on the right side. The patient required assistance to walk. Results of an abdominal-pelvic ultrasonography were normal. Thoracic CT revealed diffuse lymph adenomegaly in the right axilla and mediastinum. The lymph adenomegaly

in the right axilla was excised. Immunohistochemical analyses demonstrated CD20 tumor cells, and NHL was diagnosed.

Lymphomas are divided into 2 major categories: NHL and HD. The NHL is a hematopoietic neoplasm constituting 4% of all cancer diagnoses. The NHL (graded as low, intermediate, and high) originates most frequently from B lymphocytes (approximately 85% of the time). The clinical findings of NHL vary according to geographical factors.<sup>2</sup> The NHL is seen more frequently in men than in women. The rate of NHL increases exponentially between the ages of 20 and 79 years. The HD is most common in young adults (aged 15-40 years) and in older people (aged ≥ 55 years). Several factors, including environmental and genetic factors, infections such as human T-lymphotrophic virus type 1, Epstein-Barr virus, *Helicobacter pylori*, human immunodeficiency virus, malaria, hepatitis B virus, and hepatitis C virus, and chemical factors, like benzene, have been linked to an increased risk of developing NHL.<sup>2</sup> Painless swelling of the lymph nodes in the neck, underarm, or groin are seen in these patients. Other symptoms may include unexplained fever, night sweating, extreme fatigue, unexplained weight loss, itchy skin, and reddened patches on the skin. In our patient, the clinical findings were fever, night sweating, weakness, swelling in the neck, and weight loss.

Motor neuron disease (MND) is one of the most common neurodegenerative diseases in adults. Its causes are progressive injury, and death of lower motor neuron cells in the spinal cord and brain stem, and of upper motor neurons in the motor cortex. More than one cause usually comprises the etiology, however, the exact cause of the disease is not known. Genetic factors, oxidative stress, excitotoxicity, paraproteinemia, infections, and paraneoplastic conditions have been proposed.<sup>1</sup> The importance of immunological abnormality and its role in the pathogenesis of MND remains controversial. Compared with the general population, monoclonal paraproteinemia seems to be more frequent in patients with MND.<sup>3</sup> Plasma cell neoplasias are not frequently associated with MND. Upper motor neuron signs are present in more than half of all patients with lymphoma and MND, and corticospinal tract degeneration has been shown in the half of all autopsies.<sup>4</sup> No population or case control studies have been performed that show the frequency of lymphoproliferative diseases in MND.<sup>1</sup> In one autopsy series, the range was 2.5-5%.<sup>5</sup>

There have been 3 studies regarding the association of MND with lymphoproliferative diseases or plasma cell neoplasias in 9, 2, and 3 patients.<sup>6</sup> Younger et al<sup>4</sup> studied 9 patients with MND and lymphoma and proposed that motor neuron syndromes are associated with either HD or NHL. The syndromes were not restricted

to lower motor neuron disorders, and 8 of 9 patients had definite or probable upper motor neuron signs as well, qualifying for the diagnosis of amyotrophic lateral sclerosis. The combination of MND and lymphoma was often accompanied by paraproteinemia (in 3 of 7 patients studied), increased CSF protein content (in 6 of 9 patients), and CSF oligoclonal bands (in 3 of 9 patients). The cause of this syndrome is not known. Both lymphoma and MND may have a common cause, possibly a retroviral infection. The frequency of paraproteinemia suggests that an immunological disorder may play a role in the pathogenesis of the neurologic disorder.<sup>6</sup>

Fifty-six patients with MND and lymphoproliferative diseases have been reported.<sup>3</sup> Two thirds of these patients were males, and in one third of these, the initial symptoms had begun before the patients were 50 years old. In 49 of them, HD and NHL were found, in the others, myeloma or Waldenström's macroglobulinemia was found. The initial symptoms may be a component of MND or lymphoproliferative disease.<sup>4</sup>

Our patient developed signs of NHL during follow-up of MND. We wish to emphasize that MND and NHL may be encountered together, coincidentally, as in the present case, and during the course of MND. While observing patients with MND, clinicians also must be

alert to the coincidental existence of lymphomas with a paraneoplastic syndrome as a potential etiology.

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## References

1. Koc F, Paydas S, Yerdelen D, Demirkiran M. Motor neuron disease associated with multiple myeloma. *Int J Neurosci* 2008; 118: 337-341.
2. Swerdlow AJ. Epidemiology of Hodgkin's disease and non-Hodgkin's lymphoma. *Eur J Nucl Med Mol Imaging* 2003; 30 Suppl 1: S3-S12.
3. Gordon PH, Rowland LP, Younger DS, Sherman WH, Hays AP, Louis ED, et al. Lymphoproliferative disorders and motor neuron disease: an update. *Neurology* 1997; 48: 1671-1678.
4. Younger DS, Rowland LP, Latov N, Sherman W, Pesce M, Lange DJ, et al. Motor neuron disease and amyotrophic lateral sclerosis: relation of high CSF protein content to paraproteinemia and clinical syndromes. *Neurology* 1990; 40: 595-599.
5. Rowland LP, Sherman WL, Hays AP, Lange DJ, Latov N, Trojaborg W, et al. Autopsy-proven amyotrophic lateral sclerosis, Waldenström's macroglobulinemia, and antibodies to sulfated glucuronic acid paralogoside. *Neurology* 1995; 45: 827-829.

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