EDITORIAL COMMENTARY

Carcinoma associated paraneoplastic peripheral neuropathy

In patients with cancer, the development of a peripheral neuropathy usually represents a side effect of therapy, the infiltration of nerves or spinal roots by the tumour, or metabolic and nutritional deficits. A neuropathy is defined as paraneoplastic when none of the above causes are detected or when cancer related immunological mechanisms are involved. At least 15% of patients with cancer develop a paraneoplastic sensorimotor neuropathy, which is usually mild and develops during the terminal stage of the disease.¹ There is another group of paraneoplastic neuropathies that often precede the diagnosis of the tumour and can be more debilitating than the cancer itself. The diagnosis of these disorders is a challenge for the neurologist, and requires extensive investigations. On pp 7–14 of this issue, Antoine *et al*² review their experience with 26 patients whose neuropathy was considered to be paraneoplastic. Most of these patients had severe neuropathies that preceded the diagnosis of the tumour.

In seven patients, the detection of antineuronal antibodies helped to identify the neuropathy as paraneoplastic. Studies have shown that the anti-Hu antibody is a useful marker of paraneoplastic sensory neuronopathy, which often develops in association with encephalomyelitis or autonomic dysfunction.³ Although some patients may present with signs of a sensorimotor neuropathy with axonal and demyelinating features, as found in one of the patients of Antoine *et al*, the detection of the anti-Hu antibody in these patients indicates involvement of the dorsal root ganglia. Of note, some patients with a predominant sensory neuropathy and small cell lung cancer can be anti-Hu negative.^{2,3} Thus, the absence of this antibody does not rule out the possibility that a neuropathy is paraneoplastic or that the tumour is in the lung.

In the absence of the anti-Hu antibody, several clinical findings raise the suspicion of the paraneoplastic origin of a neuropathy, especially the development of subacute multifocal deficits, including CNS or autonomic dysfunction. In the study of Antoine *et al*, five of 14 patients with

neuropathies that developed up to 30 months before the tumour diagnosis had multifocal neurological deficits. Studies also show that 10% to 15% of patients with vasculitis of the nerve and muscle have an underlying neoplasm.^{2,4} Symptoms include progressive, asymmetric, proximal-distal, sometimes painful, sensorimotor neuropathy; the diagnosis is confirmed by nerve or muscle biopsy.

Loss of weight and cachexia may suggest the presence of a neoplasm, or be a cause of myopathy. For any patient, if paraneoplastic neuropathy is suspected, the priority is to demonstrate the presence of a tumour. Studies for tumour markers in the blood (CEA, CA-125), or the detection of a monoclonal gammopathy may assist in identifying the underlying neoplasm. Because lung cancer is the most common cause of paraneoplastic syndromes, all patients with peripheral neuropathy of unknown aetiology should have chest imaging, whether or not they are smokers, and regardless of their anti-Hu antibody status.

When antineuronal antibodies are negative, the diagnosis of a paraneoplastic neuropathy remains a challenge because diverse cancer related neurological complications, or a previous neuropathy aggravated by the tumour or its treatment, may mimic a paraneoplastic neuropathy.

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- 1 Croft PB, Wilkinson M. The incidence of carcinomatous neuromyopathy in patients with various types of carcinoma. *Brain* 1965;88:427–34.
- 2 Antoine J-C, Mosnier J-F, Absi L, *et al*. Carcinoma associated paraneoplastic peripheral neuropathies in patients with and without anti-onconeural antibodies. *J Neurol Neurosurg Psychiatry* 1999;67:7–14.
- 3 Molinuevo JL, Graus F, Reñé R, *et al*. Utility of anti-Hu antibodies in the diagnosis of paraneoplastic sensory neuropathy. *Ann Neurol* 1998;44:976–80.
- 4 Vincent D, Dubas F, Hauw JJ, *et al*. Nerve and muscle microvasculitis in peripheral neuropathy: a remote effect of cancer? *J Neurol Neurosurg Psychiatry* 1986;49:1007–10.