Paraneoplastic Orthostatic Tremor Associated with Small Cell Lung Cancer

H.J. Gilhuis^a H.J. van Ommen^a B.J.M. Pannekoek^b P.A.E. Sillevius Smitt^c

Departments of ^aNeurology and ^bPulmonology, Reinier de Graaf Group Hospital, Delft, and
^cDepartment of Neurology, Erasmus University Medical Centre, Rotterdam, The Netherlands

Dear Sir,

Paraneoplastic neurological syndromes (PNS) are disorders associated with cancer that are not directly related to the tumour or its metastases. Presumably, immunological factors play an important role in the aetiology of PNS. Ectopic expression of neuronal antigens by the tumour provokes an immune reaction that subsequently cross-reacts with similar antigens in the nervous system [1, 2]. Often, but not always, the serum of patients with PNS contains paraneoplastic antineuronal antibodies, such as the anti-Hu antibody. In PNS, all parts of the nervous system may be affected resulting in a wide variety of presenting symptoms. We describe for the first time a patient who developed severe orthostatic tremor (OT) as the sole presenting paraneoplastic manifestation of small cell lung cancer (SCLC). Treatment with chemotherapy was followed by marked clinical improvement.

Case Report

A 55-year-old, otherwise healthy woman was referred for a severe tremor of the head, arms and legs, gradually becoming worse within a week. The tremor was induced by standing and did not disappear while walking. However, the symptoms disappeared when she sat or laid down. She had no history of drug abuse or use of medication, but reported a 40-pack-year smoking history. Neurological examination re-

vealed a wild and disabling shaking of the arms, legs and head while attempting to stand or walk. The shaking had a frequency of 3–5 Hz. When she lay down, the examination was completely normal. No other neurological symptoms were present. Routine laboratory tests (including thyroid functions, calcium and phosphate), EEG and MRI of the brain were normal. Six weeks after the beginning of symptoms, she became progressively dyspnoeic and lost weight. An SCLC in the right upper lobe with lymph node and liver metastases was diagnosed. Anti-Hu antibodies were present in serum (titre of 1:3,200). A few days after the initiation of chemotherapy, the shaking gradually disappeared, and within a week only a slight tremor of the hands remained. She was able to stand and walk again till she died of respiratory failure 9 months later.

Discussion

We present a patient with subacute onset, disabling OT, who was subsequently diagnosed with SCLC. According to the recently published diagnostic guidelines for PNS [3], the aetiology of the OT in our patient is definitely paraneoplastic because of its close temporal relation to the diagnosis of SCLC, the presence of anti-Hu antibodies and the regression of symptoms after chemotherapy.

OT is a rare clinical syndrome in which a rapid (14–16 Hz) regular lower limb tremor causes unsteadiness on standing that is relieved when sitting or walking. OT is generally considered to be an idiopathic disorder (primary OT), although it has also been described in patients with Parkinson's disease, hydrocephalus, pontine lesions, head trauma and cerebellar degeneration [4–6]. A positron emission tomography study in primary OT suggested increased blood flow in the cerebellum bilaterally and in the thalamus and lentiform nuclei contralateral to an arm with 16-Hz tremor, suggesting involvement of the cerebellum [7].

In contrast to primary OT, the tremor in our patient had a frequency of 3–5 Hz and did not decrease on walking. Also, this tremor involved all limbs and the head, and was so disabling that our patient was confined to her bed. In our patient, the symptoms were caused by an anti-Hu-associated paraneoplastic syndrome, probably affecting the brainstem and/or cerebellum.

The most common paraneoplastic syndromes associated with anti-Hu antibodies include sensory neuropathy (54–55%), cerebellar degeneration (10–22%), limbic encephalitis (9–15%) and brainstem encephalitis (16%) [1, 2]. The most prevalent underlying neoplasm is SCLC [1, 2]. So far, OT has not been reported as an anti-Hu-antibody-associated paraneoplastic syndrome.

The exact role of anti-Hu antibodies in the pathogenesis of PNS remains unclear.

Pathological examination of the nervous system generally shows neuronal cell loss and inflammatory infiltrates in affected areas with inflammatory infiltration in the interstitial and perivascular spaces [8–10].

Although paraneoplastic cerebellar degeneration and brainstem encephalitis are usually accompanied by signs of a multifocal encephalomyelitis [1], this tremor was the sole paraneoplastic symptom. Interestingly, the symptoms improved dramatically after chemotherapy. Neurological improvement is rarely seen in PNS, with the exception of patients with limbic encephalitis [2]. In our patient, early chemotherapy may have limited irreversible cerebellar damage.

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