Rare disease

Paraneoplastic sensorimotor neuropathy associated with regression of small cell lung carcinoma

E Mawhinney,¹ O M Gray,² F McVerry,¹ G V McDonnell¹

¹ Department of Neurology, Royal Victoria Hospital, Belfast, UK

² Department of Neurology, Craigavon Area Hospital, Portadown, Craigavon, UK

Correspondence to E Mawhinney, EI_0@hotmail.com

Summary

An elderly female smoker presented with nausea and anorexia. Imaging and histopathology were consistent with a diagnosis of small cell lung cancer (SCLC). She subsequently developed a progressive sensorimotor neuropathy with high titres of anti-Hu antibodies. Development of the neuropathy was associated with marked regression in the lung neoplasm. Repeat investigation with radioimaging and bronchoscopy showed no evidence of neoplasia. Paraneoplastic sensorimotor neuropathies are commonly associated with SCLC particularly in the presence of anti-Hu antibodies. Regression of SCLC with anti-Hu antibodies has only been reported twice previously. The authors believe this case supports the theory that anti-Hu antibodies confer anti-tumour activity causing tumour regression.

BACKGROUND

Anti-Hu antibodies indicate an underlying neoplasm in 88% of cases.¹ Of these, 81% are small cell lung cancers (SCLC).¹ Patients with SCLC and no clinical paraneoplastic syndrome have anti-Hu antibodies in their serum in approximately 17% of cases.²⁻³ They cause a spectrum of neurological paraneoplastic syndromes, including cerebellar ataxia (10%), limbic encephalitis (9%), polyradiculopathy, Lambert-Eaton syndrome, opsoclonus-myoclonus syndrome and, most commonly, sensory neuropathy (54%).¹⁻⁴

It has been previously reported that, of patients presenting with neuropathy associated with anti-Hu antibodies, 5% are acute onset, 55% subacute and 40% progressive. At onset, symptoms are symmetrical in 65%, asymmetrical in 25% and multifocal in 10% of patients.⁵ The Hu antigens are normally expressed throughout the central and peripheral nervous system. In SCLC, one of these antigens, Hu-D, may also be expressed by tumour cells. Although the exact pathogenesis is unclear, it is thought that when this occurs the Hu antigens are recognised by the immune system as 'non-self' triggering the paraneoplastic response.

The natural course of SCLC is usually aggressive with a 10-year survival of 13%.⁶ The development of a paraneoplastic syndrome as the presenting complaint of an underlying SCLC explains why anti-Hu antibodies are associated with earlier tumour stage and prolonged survival.¹⁻² Recent reports also suggest that anti-Hu antibodies are associated with increased chemosensitivity.¹

CASE PRESENTATION

An elderly female smoker presented with nausea, anorexia, weight loss and lethargy. She was found to be hyponatraemic and initial investigation confirmed the syndrome of inappropriate antidiuretic hormone secretion. Investigation was initiated to identify a cause. Subsequent

chest x-ray revealed a right hilar mass and on CT of the chest, a lobulated mass in the right middle lobe with subcarinal and hilar lymphadenopathy was seen. Combined CT/positron emission tomography (CT PET) confirmed a mass arising in the bronchus intermedius invading the mediastinum (figure 1 and video 1). A provisional diagnosis was primary SCLC. Washings performed at bronchoscopy showed atypical cells suggestive of SCLC. However, a definite histological diagnosis could not be confirmed despite several attempts at biopsy. In the absence of a definite cell type she was treated conservatively by the oncology team with observation and interval CT scanning. She received no chemotherapy or radiotherapy. She remained well and attended for CT follow-up 7 months later. Interestingly, this showed almost complete resolution of the mass and lymphadenopathy. Within weeks she presented with a 2-week history of distal dysaesthesia and weakness. She had difficulty attending to personal hygiene and was unable to mobilise without an aid. Neurological examination revealed an ataxic sensorimotor neuropathy with mild weakness.

Video 1 Initial CT PET scan prior to symptomatic onset of neuropathy. 10.1136/bcr.01.2009.1486v1

INVESTIGATIONS

Nerve conduction studies were consistent with a severe axonal sensorimotor neuropathy. Extensive workup revealed only strongly positive anti-Hu antibodies. MRI of brain and cerebrospinal fluid was normal. Interestingly, chest x-ray was normal. CT and CT PET showed almost complete resolution of previous appearances with only a small residual hilar node (figure 2 and video 2). Bronchoscopy was normal and both histopathology and cytology showed no abnormal cells. A diagnosis of paraneoplastic sensorimotor neuropathy with anti-Hu antibodies and regression of SCLC was made.

Figure 1 Initial CT PET scan prior to symptomatic onset of neuropathy.

Video 2 CT PET following development of neuropathy showing resolution of the mass arising from the right main bronchus. 10.1136/bcr.01.2009.1486v2

OUTCOME AND FOLLOW-UP

Treatment with intravenous immunoglobulin (0.4 mg/kg daily for 5 days) and intravenous methylprednisolone and subsequent oral corticosteroids resulted in a degree of improvement in muscle strength and sensory symptoms. Following a period of rehabilitation, she regained independence for activities of daily living. Following discharge, her neurological symptoms deteriorated with worsening distal dysaesthesia and weakness and she became increasingly dependent. She died at home 18 months later. No postmortem examination was performed.

DISCUSSION

We describe an elderly woman who develops a lung neoplasm histologically suggestive of a SCLC. On subsequent development of a paraneoplastic sensory neuropathy with high titres of anti-Hu antibodies, the lung tumour regresses with no evidence of neoplasia on radioimaging (CT and PET) or bronchoscopy. There is subsequent steady decline in her neurological state until her death 18 months later.

There has only been one previous case reported of spontaneous tumour regression associated with anti-Hu antibodies in patients with histologically proven SCLC. The patient, a 43-year-old woman presented with weight loss, dyspnoea and fatigue. Chest x-ray revealed a right hilar mass and paratracheal lymphadenopathy. Biopsy of a supraclavicular node confirmed SCLC. She subsequently developed a progressive paraneoplastic syndrome with high titres of anti-Hu antibodies. A repeat chest x-ray revealed almost complete resolution of her neoplasm prior to starting chemotherapy.⁷

A second report described a 71-year-old woman with a left pulmonary nodule on CT; however, bronchoscopy was normal. She developed a sensory neuropathy with associated anti-Hu antibodies; a presumed diagnosis of SCLC with paraneoplastic sensory neuropathy was made. Within 4 months she had radiological evidence of complete resolution of her lung mass without any active treatment.⁸

The spontaneous remission of a non-SCLC has also been described in a 75-year-old woman who presented with an anti-Hu antibody peripheral neuropathy. The lung neoplasm was identified by imaging and confirmed by biopsy. Twelve months later the neuropathy had progressed but there was no evidence of the tumour on CT imaging.⁹

Figure 2 CT PET following development of neuropathy showing resolution of the mass arising from the right main bronchus

Learning points

- ▶ Anti-Hu antibodies are strongly associated with underlying neoplasia and can cause a range of clinical paraneoplastic syndromes.
- ▶ Anti-Hu antibodies can be associated with earlier diagnosis and increased chemosensitivity.^{2 3}
- ▶ To date, the mechanism of tumour regression in anti-Hu syndromes remains unexplained.
- ▶ The authors believe that the temporal association of the development of the paraneoplastic syndrome and anti-Hu antibodies with spontaneous tumour regression in this case is strongly suggestive that an anti-tumour immune-mediated response is the underlying mechanism.

Competing interests None.

Patient consent Not obtained.

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