Unusual association of diseases/symptoms

Paraneoplastic subacute sensory neuronopathy in association with adenocarcinoma of the prostate

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Summary

Paraneoplastic syndromes arise infrequently in prostate cancer and paraneoplastic subacute sensory neuronopathy has not previously been reported in association with prostate cancer. When paraneoplastic syndromes occur, it is usually in the setting of small-cell carcinoma of the prostate or advanced, hormone-resistant disease. Here the authors report a 64-year-old man who developed a progressive, severe, sensory neuronopathy in the setting of a recently diagnosed stage T4 hormone-responsive prostate adenocarcinoma. Anti-Hu antibodies were positive and screening for a concurrent neoplasm at another site was negative. Sensory neuronopathy progressed, despite hormone responsiveness of his prostate adenocarcinoma, and resulted in a severe level of disability. His symptoms did not respond to intravenous corticosteroid therapy but there was a partial response to intravenous immunoglobulin.

BACKGROUND

Paraneoplastic neurological syndromes in association with anti-Hu autoantibodies are highly associated with small-cell lung carcinoma.¹ Paraneoplastic peripheral neuropathy in association with prostate cancer is very rare.² We found no reported cases of paraneoplastic subacute sensory neuronopathy in association with adenocarcinoma of the prostate in the literature. Here, we report a 64-year-old man who developed a severe sensory neuronopathy within months of being diagnosed with node positive metastatic adenocarcinoma of the prostate. Anti-Hu serology was positive. Despite a good response of his cancer to hormonal treatment, a paraneoplastic sensory neuronopathy developed which left him severely disabled within a few weeks of its onset.

CASE PRESENTATION

A 64-year-old bespoke furniture maker, previously fit and well, presented to his general practitioner with urinary frequency and urgency. He was a non-smoker with a 20 pack/year smoking history. His family history included his mother and father who had breast cancer and bladder cancer, respectively and his sister who had ovarian cancer. He was not taking any prescribed or over-the-counter medications or supplements. Rectal examination revealed an enlarged, hard prostate. His diagnostic prostate-specific antigen (PSA) level was 31.6 ng/ml. Transrectal ultrasound and biopsy revealed poorly differentiated adenocarcinoma of the prostate with a Gleason score of 9 (5+4). A CT scan showed pelvic and abdominal lymphadenopathy but bone scan showed no evidence of bone metastases. The patient was diagnosed as having stage IV prostate adenocarcinoma and treatment was given as follows: a 3-week course of flutamide followed by hormonal suppression treatment, with triptorelin. His PSA dropped to 1.8 ng/ml.

Two months later he began to notice tingling and numbness in his hands and feet and had to stop his regular running sessions. Over the following 4 weeks he began experiencing

difficulty using his left hand and was unable to work as a furniture maker. His Oncology outpatient appointment was brought forward and a wide-based gait was noticed as he walked into the consultation room. General physical examination was unremarkable. Neurological examination revealed normal cranial nerves and cognition. Trigeminal nerve sensation was normal. There was, however, a loss of reflexes, light touch, pin prick and joint position and vibration sense to his elbows and knees. Romberg's sign was positive. Strength and tone were normal. He was admitted to the ward for further investigation of a possible sensory neuropathy and cerebellar pathology. MRI brain was normal. CT thorax, abdomen and pelvis showed regression of nodal disease. Blood tests were sent for the detection of immunoglobulins, paraprotein, autoantibodies and paraneoplastic antibodies (anti Hu, Yo, Ma and Ri). Nerve conduction studies were performed. The patient was discharged with oncology and neurology outpatient follow-up.

One month later, the patient was admitted as an emergency. His symptoms were progressing; he felt numb from the neck down and was having difficulty in walking. He felt unsteady on his feet and complained his feet were scuffing the floor when he tried to walk. He felt he was unable to grip objects in either hand. Neurological examination revealed reduced sensation in all modalities: light touch, pin prick, joint position and vibration sense to the level of C3. He had pseudoathetosis in his hands. Cognitive function, cranial nerves and motor examination were normal. There was no postural drop in blood pressure. MRI spine revealed no evidence of spinal metastases or cord compression. Nerve conduction studies showed absent sensory responses from the upper and lower limbs. Motor conduction studies were normal in the upper limbs. Motor responses were, however, attenuated in the lower limbs and electromyography revealed signs of chronic denervation in keeping with a mild degree of chronic S1 and to a lesser degree L5 radiculopathy. Anti-Hu antibodies

were positive. Autoantibody screen (antinuclear antibody, extractable nuclear antigens, double-stranded DNA, cytoplasmic and perinuclear anti-neutrophil cytoplasmic antibody) was negative. He did not have a lumbar puncture. CT scan, again, showed a good response of his nodal disease to treatment and a whole body positron emission tomography (PET) scan did not show a pulmonary nor other occult neoplasm. These results confirmed a paraneoplastic sensory neuronopathy and anti-Hu antibodies in association with hormone responsive metastatic prostate cancer. He received two courses of methylprednisolone (1 g for 3 days) with no improvement in symptoms. A course of intravenous immunoglobulin (0.4 g/kg/day for 5 days) did result in some improvement and he was discharged home. He felt more steady on his feet and could walk short distances. This was not, however, measured objectively.

OUTCOME AND FOLLOW-UP

He was readmitted 2 months later as he was getting more unsteady on walking and unable to mobilise independently. PSA was 4.7 ng/ml and testosterone was 0.4 ng/ml. After a further 3 days course of intravenous immunoglobulin he felt that his symptoms stopped progressing and he was discharged home. 6 months later he is able to mobilise short distances in his bungalow with a frame. He lives independently with the use of functional aids. He feels he is gradually getting worse and is uncertain as to how long he will manage to be independent. He shows no symptoms or signs of a lung neoplasm. His PSA is now 4.4.

DISCUSSION

Paraneoplastic neurological syndromes are most commonly associated with small-cell lung cancer, they are also well described in breast and gynaecological cancers and lymphoma. They can affect any part of the nervous system, onset is usually rapid and can render a previously fit patient unable to walk within a few weeks.³ The pathophysiology of paraneoplastic neurological syndromes is thought to be caused by autoimmune processes triggered by the cancer and directed against antigens common to both cancer and the nervous system.

Paraneoplastic syndromes in prostate cancer usually occur in the context of very advanced, castrate resistant disease and have a poor outcome. In over 70% of cases, the syndrome develops in the early stages of prostate cancer and is the first clinical manifestation of disease; in 20% the syndrome is the first sign of development to a castrate resistant state in established prostate cancer.² There are a wide range of paraneoplastic syndromes reported in the literature and symptoms usually resolve after initial treatment of the underlying malignancy.

Lucchinetti *et al* in their study of 162 patients with anti-Hu antibodies identified four patients with prostate cancer. Cancer was found in 142 patients, 132 of whom had small-cell lung cancer.¹ There are three documented cases of paraneoplastic peripheral neuropathy in the literature with prostate cancer; two with metastatic small-cell carcinoma of the prostate^{4 5} and one describes a paraneoplastic symmetrical mixed polyneuropathy with adenocarcinoma of the prostate.⁶ It is possible that there was an undetected small-cell lung cancer especially in view of his smoking

history. He has, however, 1 year later not shown any signs or symptoms of lung cancer.

Paraneoplastic subacute sensory neuronopathy, or dorsal root ganglionitis, is characterised by rapidly progressive, asymmetric and frequently painful sensory symptoms with a profound proprioceptive loss which affects upper limbs more than lower limbs. It typically begins with loss of vibration sense and joint position sense followed by impairment in pain and temperature sensation. At the time the patient is first examined there is usually loss of sensation across all modalities causing disabling ataxia which is worse with eye closure and associated with pseudoathetoid movements of the fingers. All sensory modalities are affected while motor function is preserved. Nerve conduction studies show low sensory nerve action potentials with normal motor studies. Histologically there is loss of dorsal root ganglion cells and lymphocytic infiltration. Onset is usually over weeks to months often rendering a previously fit patient bedbound. In most cases only treatment of the tumour is associated with stabilisation of disease or an improved outcome. Immunomodulatory treatments such as corticosteroids, plasma exchange and intravenous immunoglobulin are generally unsuccessful.⁷ In the absence of anti-Hu autoantibodies the differential diagnosis of a subacute sensory neuronopathy includes Sjogren's syndrome, idiopathic, cisplatin toxicity and pyridoxine abuse.

Paraneoplastic subacute sensory neuronopathy is usually associated with small-cell lung cancer, colon, lymphoma or uterine sarcoma. It has not previously been described in association with prostate cancer. In this patient the paraneoplastic syndrome was not associated with advanced hormone-resistant disease and as evidenced by the PET scan there were no other malignancies present. The other unusual feature of this case is that the syndrome developed once the prostate cancer had been diagnosed and had already responded well to hormonal treatment.

Learning points

- Paraneoplastic syndromes arise infrequently in prostate cancer.
- Subacute paraneoplastic sensory neuronopathy can occur in prostate cancer.
- These syndromes may not resolve following treatment of the underlying neoplasm.
- More research into the pathophysiology of these syndromes will elucidate the complex interactions between prostate cancer and the immune system.

Competing interests None.

Patient consent Obtained.

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