Clinical Reports

Pseudotumour cerebri in a patient with Castleman’s disease

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Summary: A patient with systemic Castleman’s disease (angiofollicular lymph node hyperplasia) including bone changes and peripheral neuropathy, is described. She also had pseudotumour cerebri, and, as this association has been reported previously, it is unlikely to be due to chance.

Introduction

Castleman’s disease (angiofollicular lymph node hyperplasia) is often associated with systemic manifestations,1 although central nervous system involvement is unusual. We describe such a patient in whom pseudotumour cerebri occurred and in whom the degree of papilloedema fluctuated with disease activity.

Case report

A 40 year old West Indian woman was admitted in 1977 with severe headaches for 10 days, blurring of vision and a blackout, and was found to have bilateral papilloedema. An electroencephalogram, isotope brain scan and left carotid angiogram were normal. Lumbar puncture was normal apart from a raised pressure of 38 cm water. A diagnosis of pseudotumour cerebri was made; she was started on acetazolamide and cerebrospinal fluid was drained four times to reduce the pressure. In 1978, a fluorescein angiogram confirmed that intracranial pressure was still raised, although she was clinically asymptomatic with normal visual fields, and minimal residual disc swelling.

She was readmitted in 1979, still on acetazolamide, with a 6-month history of 22 kg weight loss, malaise, lethargy, nausea, more frequent headaches and irregular menstruation. On examination she had a palpable liver edge and spleen, and widespread lymphadenopathy, and a chest X-ray showed bilateral pleural effusions with paratracheal and mediastinal lymphadenopathy. Peripheral nerve conduction studies confirmed a symptomless motor and sensory peripheral neuropathy. A radiological bone survey revealed sclerotic changes in three vertebral bodies and a lytic lesion in the left acetabulum, and electrophoresis of serum showed an IgG paraprotein band; other immunoglobulin levels were normal. However, histological appearances of biopsy specimens of bone marrow and of a sclerotic vertebra were both normal. Mild primary myxoedema and a low serum B12 level were found, but tests of gastrointestinal function and a computed tomographic head scan were normal.

At mediastinoscopy a lymph node biopsy was performed and the histological appearances were of angiofollicular lymph node hyperplasia consistent with Castleman’s disease (Figure 1a, b). She was treated with prednisolone, acetazolamide, thyroxine and hydroxycobalamin.

One year later she was readmitted on the same treatment with further weight loss and inability to walk due to progression of her peripheral neuropathy. She also complained of gradual painless blurring of vision associated with increasing headaches. She had axillary lymphadenopathy with hepatosplenomegaly, and again severe papilloedema. Her prednisolone and acetazolamide were stopped. A thoracotomy was performed with
clearance of the right hilar nodes and thymectomy. Histology again confirmed angiofollicular lymph node hyperplasia. Within 4 weeks of surgery some improvement in her neuropathy was confirmed by electromyography. Prednisolone 20 mg daily was restarted together with chlorambucil 5 mg daily and she gradually improved; her weight returned to normal, and she could walk again, but was left with a mild sensory neuropathy to just above the ankles. Since 1983 her optic fundi have been normal.

She remains in remission on 5 mg prednisolone daily and 5 mg chlorambucil on alternate days.

Discussion

Pseudotumour cerebri is characterized by bilateral papilloedema with absence of hydrocephalus or a space-occupying lesion. For a more specific diagnosis four criteria have been proposed: (i) intracranial pressure greater than 20 cm water, (ii) normal cerebrospinal fluid composition, (iii) signs and symptoms of raised intracranial pressure and (iv) normal radiological studies. A large number of conditions have been associated with this syndrome, but using these strict criteria a recent review suggests that only a few of the cases concerned were adequately documented. These included steroid treatment and withdrawal, hypoparathyroidism, hypo- and hyper-vitaminosis A, iron deficiency, severe anaemia and several drugs. Our case with Castleman's disease now also fulfils the criteria for this diagnosis.

Castleman's disease, or angiofollicular lymph node hyperplasia, was described in 1956 and is characterized histologically by lymphoid nodules with germinal centres containing hyaline material associated with central blood vessels. It is of unknown aetiology. More recently there have been reports of multisystem involvement with manifestations including anaemia, sclerotic bone changes, neuropathy, nephrotic syndrome, thrombotic thrombocytopenic purpura and acute haemolytic anaemia, and these have been classified as multicentric angiofollicular lymph node hyperplasia, which is a variety of the original Castleman's disease. The patient we describe has a benign monoclonal gammopathy and peripheral neuropathy. Both have been described in Castleman's disease, and a further subset has been suggested, comprising the POEMS syndrome (Peripheral neuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, and Skin changes). Disease progression is variable and may be stable, relapsing, aggressive or develop into malignant lymphoma. The case described started with an aggressive course but following surgery and with chemotherapy has remained stable for 5 years.

Central nervous system involvement in Castleman's disease is uncommon. An intracranial tumour with the histological features of Castleman's disease has been described, as has temporal arteritis and an encephalopathy. There was a single case report of pseudotumour cerebri associated with Castleman's disease in 1978, and this is probably therefore the second case reported, although in a recent series it was commented, without clinical details, that one patient did have pseudotumour cerebri. In the first case, the patient presented with visual symptoms

Figure 1 (a) Section of enlarged node showing Castleman-type follicle composed of a central vessel and large eosinophilic cells surrounded by lymphocytes. Around the follicle vessels prominent endothelial cells are present, together with some eosinophilic extra-cellular matrix. H&E ×250. (b) Higher magnification of another follicle to show a vessel with prominent endothelial cells. H&E ×400.
and was found to have an abdominal mass. Carotid angiograms were normal and cerebrospinal fluid pressure was raised. She received no specific treatment and at that time had slowly progressed over 3 years with no change in the papilloedema. In the other mentioned case the patient followed a relapsing course and was treated with cyclophosphamide, vincristine, procarbazine, bleomycin and prednisolone before death, but no other details were given. In our patient the pseudotumour cerebri appeared before clinical evidence of Castleman’s disease, but the degree of papilloedema fluctuated with disease activity. With surgical hilar node clearance and prednisolone and chlorambucil therapy the disease and pseudotumour cerebri have remained stable for 5 years.

Note added in proof
She has recently been admitted with bone pain, apparently due to infiltration of the ribs, and so the disease is probably now progressing.

References
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