

Chronic inflammatory demyelinating polyneuropathy associated with intestinal tuberculosis

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Received: August 15, 2006 Revised: February 27, 2007 Accepted: April 1, 2007

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an increasingly common but under-recognized neurological disorder. It is immune mediated, and usually has a relapsing and remitting course. However, the initial presentation may be rapid. It can be associated with significant morbidity and mortality, particularly if there is a delay in diagnosis and treatment. It has been associated with both infective and non-infective etiologies. We present a case of CIDP associated with ileocecal tuberculosis (TB), presenting with progressive motor weakness and significant weight loss. The patient's symptoms improved to some extent with intravenous immunoglobulin and steroid, but improved significantly after being started on anti-TB therapy. However, his symptoms relapsed when he stopped his anti-TB treatment prematurely whilst continuing the immunosuppressive therapy. Upon resuming the anti-TB therapy, he made a good recovery. CIDP associated with TB has only been reported once. Our case highlights the need to consider TB in patients with neurological disorders.

Key words: Immunosuppression; Polyradiculoneuropathy, chronic inflammatory demyelinating; Tuberculosis, gastrointestinal

Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an increasingly common, but under-recognized immune-mediated neurological disorder [1-3]. Patients typically present with bilateral progressive motor weakness with or without sensory deficits. Half of those affected present with a relapsing and remitting course, but the initial deterioration may be rapid, resembling Guillain-Barré syndrome (GBS). Without treatment, CIDP is associated with significant morbidity and mortality. Therapies with intravenous immunoglobulin, plasmapheresis, and steroids have been shown to arrest or reduce disease progression [1]. CIDP associated with tuberculosis (TB) infection has only been reported once [4]. We report a case of CIDP associated with intestinal TB.

Case Report

A 70-year-old man was admitted with a 4-day history of weakness in all 4 limbs with minimal sensory deficit. He did not have any preceding symptoms suggestive of a viral infection or any acute gastrointestinal disorder. He had also had a similar episode more than a month prior to the current presentation. The first episode had resolved spontaneously and he had not sought any medical attention. He also reported significant weight loss over the last few months. His background medical history included bronchial asthma, hypertension, benign prostate hypertrophy, and right nephrectomy for a complicated stone disease more than ten years previously. The initial suspicion of the referring doctor was of polymyositis due to an elevated creatinine phosphokinase level and prominent proximal muscle weakness. He was referred to the neurology unit for further evaluation. On examination, he was found to be malnourished, and to have a mild to moderate degree of muscle wasting with significant motor weakness — both proximally and distally, of the upper limbs (Medical Research

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Council [MRC], grade II) and lower limbs (MRC, grade 0). Reflexes and sensations were normal. Laboratory investigations showed a mildly elevated erythrocyte sedimentation rate (27 mm/h) and hypoalbuminemia (23 g/L). Repeat creatinine kinase and other investigations, including blood sugar, renal function, remaining liver profiles, and complete blood count, were normal. Chest radiography showed bilateral apical fibrosis consistent with previous pulmonary TB. Similar to the first episode, he recovered spontaneously and was discharged for further evaluation on an outpatient basis.

The patient was readmitted within a few days of discharge with similar complaints. Clinical examinations showed similar findings, except the reflexes were now generally reduced and Babinski's sign was positive on the right side. Two days after admission, he became acutely short of breath and was not able to maintain his oxygen saturation (persistently less than 90%). He was transferred to the intensive care unit for further management. His condition deteriorated rapidly and he required ventilator support. He was treated for presumed respiratory muscle involvement complicated by aspiration pneumonia. Repeated blood investigations were similar to the previous admission. Tumor markers, that included carcinoembryonic antigen, carbohydrate antigen 19-9, prostate-specific antigen, and alpha-fetoprotein, were normal. Ultrasound scan examination of the abdomen showed a solitary left kidney, liver cyst, and enlarged prostate. High resolution computer tomography of the chest confirmed the bilateral apical fibrosis of old pulmonary TB. There was no evidence of pulmonary embolism. Repeated sputum examinations and cultures were negative for acid-fast bacilli. A nerve conduction study showed prolonged conduction velocities, prolonged F waves and decreased action potentials of the median, ulnar, and common peroneal nerves. The abnormalities were predominantly of the demyelinating type. Muscle biopsy was negative for polymyositis. A lumbar puncture showed mildly elevated protein at 0.66 g/L (normal, 0.10 to 0.40 g/L) without pleocytosis. Viral antigen tests were negative. Autoimmune markers, Venereal Disease Research Laboratory test and human immunodeficiency virus serology were negative. Differential diagnoses of CIDP, polyradiculopathy or paraneoplastic neuropathy were considered. In view of the possibility of CIDP, the patient was given pulse intravenous methylprednisolone (1 g daily for 3 days) followed by azathioprine (50 mg daily) maintenance therapy. He was extubated on the sixth day and later transferred to the neurology ward.

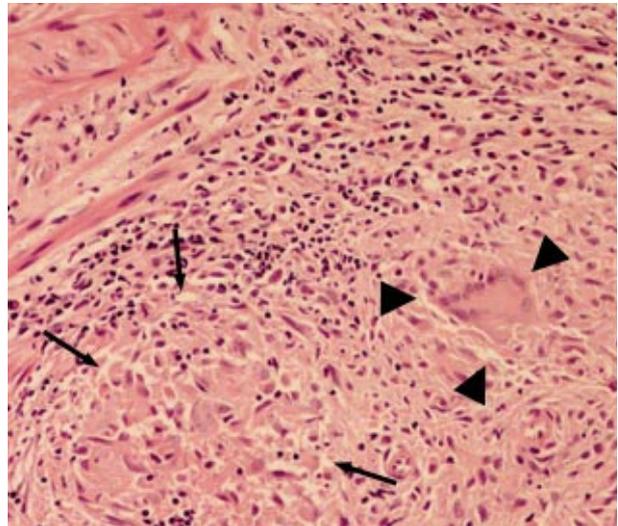


Fig. 1. Caseating granuloma (arrows) and giant Langerhans' cell (arrowheads) [hematoxylin and eosin stain, $\times 20$].

A magnetic resonance imaging scan of the spine only showed mild spondylosis of the lumbar spine. In view of the significant weight loss, endoscopic evaluations were organized to assess for underlying gastrointestinal malignancies. Upper gastrointestinal endoscopy only showed a mild esophagitis (Los Angeles Classification Grade A). Colonoscopy showed mildly erythematous ileocecal valve and a sigmoid polyp. The terminal ileum could not be entered and was not examined. Polypectomy showed tubular adenoma without any malignant features. Surprisingly, the biopsies of the ileocecal valve showed Langerhans' giant cells, caseating granuloma, and chronic inflammatory infiltrations consistent with TB. Ziehl-Neelsen staining for acid-fast bacilli was negative (Fig. 1). In view of the histological findings and the chest radiographic changes, he was started on anti-TB therapy (rifampin 450 mg daily, isoniazid 300 mg daily, ethambutol 800 mg daily, pyrazinamide 1 g daily, and pyridoxine 25 mg daily). The patient showed marked improvement and was mobile with assistance on discharge. He had continued to improve when he was seen 3 months after discharge.

The patient was again readmitted 4 months following discharge with lower limb weakness. He admitted to stopping his anti-TB medications a month ago, when he felt ill, but had continued with the immunosuppressive medications. Anti-TB treatment was restarted without additional steroid or immunoglobulin therapy and he showed marked improvement in symptoms again. He was last seen after completing 12 months of therapy and remained well without any neurological deficits.

His immunosuppressive therapy was continued for a further few months after completion of his TB treatment.

Discussion

CIDP is an increasingly common neurological disorder that can affect patients of all ages. However, it is still often under-recognized. There are diagnostic criteria available to help in making a firm diagnosis [5-8] and these stress the importance of clinical findings and nerve conduction studies. These often show neurological abnormalities resembling that of acute GBS, but lasting more than 2 months [5-8]. Nerve biopsy and cerebrospinal fluid examinations may also be required. Our patient fulfilled the criteria set out by the Neuropathy Association Guidelines and the European Federation of Neurological Societies/Peripheral Nerve Society [2,7]. It is important to recognize this condition early as response to steroids, intravenous immunoglobulin, or plasmapheresis is reportedly very good at this stage [9, 10]. Delay in treatment can lead to significant morbidities and even mortality. However, in spite of early treatment, many are still affected in the long term [11].

The etiology of CIDP is unknown, but there are reports of associations with infections, inflammatory disorders, and malignancies [1,3,4,12-15]. Association with TB infection has only been reported once in the English literature [4]. This was a case of CIDP associated with pulmonary TB in a man with Marfan's syndrome that was initially diagnosed as acute GBS. There was no evidence in our case to suggest any other etiology. Investigations for viral infections, underlying malignancies, and metabolic disorders were all negative. The magnetic resonance imaging scan showed only mild spondylosis of the lumbar spine. The association in our case was further strengthened by the temporal trend; the initial improvement with therapy and then the recurrence of motor weakness on the premature stopping of the anti-TB treatment by the patient, followed subsequently by a remarkable improvement on restarting treatment. At all times, the patient had continued with his immunosuppressive therapy.

The exact pathogenesis of CIDP is unknown but it is believed to be due to a molecular mimicry leading to the immunological attack of peripheral nerves [1-3]. The pathogenesis is probably similar to that described for GBS. This concept of molecular mimicry is further supported by studies showing dramatic response to immunosuppressant therapies. For this reason, we continued with immunosuppressive therapy along

with the anti-TB therapy. Despite adequate treatment duration for the TB infection, our patient continued to have residual weakness that only recovered fully with prolonged immunosuppressive therapy. This suggests that the underlying inflammatory process was still occurring despite removal of the inciting etiology. However, diagnosis needs to be made early, which necessitates a high level of suspicion. Benefits of treatment are usually seen when treatment is given early in the course of illness.

Neuropathies in association with TB infections are uncommon, but have been previously reported to occur due to associated malnutrition, alcoholism, and the neuropathic effects of medication [2]. However, direct involvement of the nervous system has been reported as a result of meningeal involvement, direct nerve root involvement, and granuloma affecting optic or peripheral nerves [13-15].

Similar to the TB involvement of other organs, presentation can be delayed leading to a delay in diagnosis. This is further compounded by a lack of suspicion and the nonspecific protean manifestations. In this case, the patient did not have any respiratory symptoms despite the chest X-ray findings, or any gastrointestinal complaints to suggest underlying active TB infections. Furthermore, multiple sputum smears and cultures were repeatedly negative. The histological findings were also unexpected, as colonoscopy only showed mild irregularity of the ileocecal valve.

In conclusion, this case highlights an important association between TB infection and CIDP. Although the association in our case could be coincidental, causative link cannot be excluded. The response to anti-TB therapy and the temporal trend observed further strengthen the odds of this association. Therefore, it is important for physicians to consider TB infections in patients presenting with neurological symptoms, particularly if they have risk factors and have features consistent with TB infections. This is especially significant as recent years have seen a resurgence in TB infections due to the human immunodeficiency virus pandemic and the changes in population demographics due to migration.

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