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Sarcoidosis presenting with an acute Guillain-Barré syndrome

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Summary: A 28 year old Caucasian male presented with an acute Guillain-Barré syndrome and bilateral facial weakness. He had an abnormal chest radiograph. Lumbar pucture revealed acellular fluid with a raised protein count and lung function tests showed a restrictive ventilatory defect. The patient deteriorated and required mechanical ventilation for 14 days. Steroids and plasmapheresis were not used and the patient spontaneously recovered. Two months after presentation limb power was almost normal but there was residual partial bilateral facial weakness. The chest radiograph remained abnormal and repeat lung function tests showed a persistent restrictive ventilatory defect and a reduced gas transfer coefficient. A transbronchial biopsy revealed non-caseating granulomata. The association between neurosarcoidosis and Guillain-Barré polyneuropathy is discussed and the literature reviewed.

Introduction

Sarcoidosis is a multi-system disorder of unknown aetiology most commonly affecting young adults and presenting most frequently with bilateral hilar lymphadenopathy, pulmonary infiltration, ocular and skin lesions. Between 5 and 10% of patients will have neurological involvement.[1,2] Neurosarcoidosis comprises cranial nerve palsies, neurophthalmological problems, intra-cranial space-occupying lesions, hypothalamic and pituitary lesions, meningitis, cerebellar ataxia, peripheral nerve palsies, mononeuritis multiplex or a polyneuropathy.[1] The following case of acute polyneuropathy in association with sarcoidosis illustrates a rare association between these two conditions.

Case report

A 28 year old Caucasian male was admitted with a one week history of aching discomfort and paraesthesiae in his back, arms and thighs. In the 48 hours before admission he had noticed increasing weakness of his arms and legs, with difficulty in walking. Prior to this illness he had been well apart from a flu-like illness beginning 2 weeks before his admission. On examination the patient had bilateral facial nerve palsies and was unable to close either eye. He had a mild dysarthria and dysphagia with nasal regurgitation of fluids. In the limbs power was globally reduced to MRC grade 4* with reduced tone and absent tendon reflexes; sensation was intact. Examination of the chest and abdomen was normal.

Investigations including full blood count, urea, electrolytes, liver enzymes, blood glucose and immunoglobulin quantification were normal and a test for urinary porphyrins was negative. The chest X-ray was abnormal with widespread reticulo-nodular shadowing throughout both lung fields, sparing the apices. Pulmonary function tests revealed a mild restrictive defect. The diffusing capacity (DLCO) was 69% of predicted normal. At lumbar puncture the opening pressure was normal and the cerebrospinal fluid was acellular with a protein concentration of 0.8 g/l. Simultaneous blood and cerebrospinal fluid sugars were normal. Motor and sensory nerve conduction studies showed evidence of slowed conduction velocities and delayed F waves in the lower limbs.

A provisional diagnosis of Guillain-Barré syndrome with an atypical pneumonia was made and erythromycin was begun. Over the ensuing 72 hours the patient became progressively weaker - MRC grade 2* in both arms and legs. He was electively ventilated as his forced expiratory volume in one second (FEV_1) had begun to fall; dropping rapidly over 4 hours to below 1 litre. Mechanical ventilation was required for 14 days. Plasmapheresis was not performed and corticosteroids were not used. He made a rapid recovery and 2 weeks after discharge from the intensive care unit he was able to walk unaided.

*M.R.C. Grading; 4 = movement which is possible against gravity plus resistance but which is weaker than normal: 2 = movement which is possible with gravity eliminated.

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Two months later his limb power was almost normal but he had a residual partial bilateral facial palsy. His chest X-ray remained abnormal. Paired serology for mycoplasma, legionella, psittacosis, coxiella, cytomegalovirus, herpes simplex, measles, adenovirus and influenza A and B were all negative. Repeat respiratory function tests showed a persistent restrictive defect and impaired diffusing capacity. A transbronchial biopsy revealed numerous non-caseating sarcoid granulomata.

Discussion

Neurological involvement is uncommon in sarcoidosis occurring in between 5 and 10% in published series.[1-3] Peripheral nerve involvement comprises 15% of these cases and may take the form of isolated cranial or peripheral nerve palsies, mononeuritis multiplex or a polyneuropathy.[1,4] Manifestations of sarcoid neuropathy include paraesthesiae, root pains, weakness and wasting of muscles and absence or depression of tendon reflexes.[5] Neuralgia, symmetrical or asymmetrical, is a frequent symptom. The exact pathogenesis of the polyneuropathy is not well defined. Oh[6] described a 58 year old patient with subacute polyneuropathy. A sural nerve biopsy showed non-caseating granulomas in the epineural and perineural spaces, periangitis and panangitis together with axonal degeneration. Corticosteroids produced a marked clinical improvement. It was thought that the neural injury was due to mechanical compression by the granulomata. On the other hand, Nemni *et al.*[7] did not find abnormalities of the myelin sheath at the paranodal region caused by compression. Electromyographic studies on neurologically asymptomatic sarcoidosis patients show low amplitude of evoked sensory potentials in one or more nerves, suggesting that subclinical nerve lesions are common in sarcoidosis.[8] Examination of the cerebrospinal fluid in neurosarcoidosis is unhelpful. Raised pressure, pleocytosis and elevated protein levels are found in one half of patients.[1,9]

The neurological picture in this case is typical of an acute Guillain-Barré polyneuropathy. While this disease has been described as a complication of sarcoidosis there are only 5 previously reported cases. The first[10] was a 25 year old woman with biopsy proven sarcoidosis involving hilar and scalene nodes with interstitial lung disease. One year after initial presentation she developed an acute symmetrical motor and sensory polyneuropathy, the cerebrospinal fluid was acellular with a raised protein content. Following treatment with prednisolone and isoniazid the neuropathy resolved completely within 3 months and the appearances of her chest radiograph improved. In further cases in males aged 11[11] and 25[12] years, sarcoidosis was diagnosed on the basis of bilateral hilar lymphadenopathy with positive lymph node or bronchial biopsies. Both developed severe symmetrical polyneuropathy over 14 – 17 days with an acellular cerebrospinal fluid in association with an elevated protein. In one this occurred 2 months after the diagnosis of sarcoidosis,[12] in the other simultaneously with diagnosis of sarcoidosis.[11] A 51 year old male who presented with a 3 week history of leg weakness was areflexic and had absent sensation over the legs and trunk. Sarcoidosis was diagnosed on lymph node biopsy.[5] The patient died despite prednisolone therapy. A possible fifth case has also been reported.[13]

It is accepted that steroid therapy in sarcoidosis is indicated for active ocular disease, progressive pulmonary involvement (either symptomatic or causing significant pulmonary function disturbances), persistent hypercalcuria or hypercalcaemia, with or without renal insufficiency, nervous system involvement and disfiguring dermatological lesions.[14] In this respect there are clear indications for using steroids in this case. On the other hand the use of steroids in acute Guillain-Barré syndrome is controversial[15] and may be associated with a detrimental outcome.[16] We did not use steroids in this patient as he had a rapidly progressive presentation and showed a rapid recovery; by the time he underwent transbronchial biopsy he had recovered virtually all of his neurological deficit.

It seems unlikely that the acute symmetrical polyneuropathy in our patient was due to granulomatous involvement in view of the acellular cerebrospinal fluid and rapid onset of symptoms and recovery. Table I shows features that may be helpful in distinguishing neurosarcoidosis from Guillain-Barré syndrome. The data on the prevalence of sarcoidosis is poor but estimates range from 3 – 50 cases per 100,000 population.[17] The incidence of Guillain-Barré is 1 – 2 per 100,000 population.[18] With a conservative estimate of the prevalence of sarcoidosis in the United Kingdom of 5 per 100,000 one would expect the coincidental occurrence of the two diseases every 20 – 40 years. It therefore remains entirely possible that the case described represents only this coincidental chance and not a manifestation of neurosarcoidosis.

Table I Comparison of neurosarcoidosis and Guillain-Barré syndrome

	Neurosarcoidosis	*Guillain-Barré syndrome*
Age at presentation	20 – 40	20 – 70
Sex incidence	equal	equal
Facial nerve palsy	+	–
Cerebellar ataxia	+	– Miller Fisher { +
Cranial nerve palsy	+	– variant { +
Papilloedema	+	(+) rare
Uveitis	+	–
Respiratory muscle weakness	–	+
Abnormal chest radiograph	+	– (rarely atypical pneumonia)
Skin lesions	+	–
Bone cysts	+	–
Positive Kveim	+	–
Negative tuberculin	+	–
Hypercalcaemia	+	–
CSF protein ↑	+ (50% of cases)	+
CSF ACE ↑	+	–
CSF lysozyme ↑	+	–
CSF β_2 microglobulin ↑	+	–
Sural nerve biopsy	granulomata, periangitis panangitis, axonal degeneration	normal/demyelination in severe cases
Steroid therapy	Helpful	Possibly detrimental
Plasmapheresis	Untried	Helpful

CSF = cerebrospinal fluid; ACE = angiotensin converting enzyme.

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