Unusual association of diseases/symptoms

A case of neurosarcoidosis that presented with symptoms of Guillain–Barré syndrome

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Summary

This case report is of a patient who presented with clinical features suggestive of Guillain–Barré syndrome, who on investigation was found to have neurosarcoidosis. The patient was treated with high-dose corticosteroids and physiotherapy and he improved in condition substantially over 1 month. Neurosarcoidosis and its various presentations are discussed in the literature review.

BACKGROUND

Guillain–Barré syndrome (GBS) is a common cause of acute severe neuromuscular weakness. Prompt diagnosis is essential to allow appropriate treatment and distinguish it from other conditions (eg, myasthenia gravis, myositis). A confident initial diagnosis can be made on clinical grounds in most cases. However, appropriate investigation is needed to exclude other conditions which may rarely mimic GBS. In this case the findings of a significantly elevated white cell count in the cerebrospinal fluid (CSF) were inconsistent with the original diagnosis of GBS. This led to further investigation to diagnose his condition, and a significant impact on his subsequent treatment.

This case report reviews a patient who presented with symptoms of GBS that was later diagnosed as neurosarcoidosis. Neurosarcoidosis is a rare condition and this type of presentation is unusual with very few cases previously reported. The case therefore emphasises the need for full investigation of patients presenting with suspected GBS, and also adds to the literature on rare presentations of neurosarcoidosis.

CASE PRESENTATION

This 64-year-old Caucasian male presented with an 11-day history of bilateral and progressive thigh pain radiating to his back. Two days after the onset of pain, he developed numbness of his toes bilaterally, which ascended to the top of his legs over several days; this was associated with increasing weakness of the legs. He subsequently experienced sensory disturbances in both arms and arm weakness, worse on the right. At the time of transfer to the neuroscience ward 10 days after his symptoms began, he was unable to stand. At this stage, examination revealed normal ocular movements and mild neck flexion weakness. Tone was normal in all four limbs. Power was slightly reduced in the right upper limb with 4+/5 shoulder abduction and elbow extension, and 4/5 finger extension and flexion. In the lower limb, hip flexion was 3/5 on the right and 1/5 on the left, knee flexion and extension was 4/5 on the right and 3/5 on the left, and ankle flexion and extension

were 4+/5 bilaterally. Reflexes were present but reduced in the upper limbs, and absent in the lower limbs with down going plantars. There was no limb ataxia. Pinprick sensation was reduced below the right shin. Joint proprioception was reduced in the toes. About 14 days after initial presentation of symptoms, the patient developed bilateral asymmetric facial weakness. Medical history included hypertension and prostate cancer diagnosed a year before this presentation. He was taking aspirin, bendroflumethiazide, ramipril and doxazosin.

INVESTIGATIONS

The preliminary hospital investigations were not consistent with GBS: His initial lumbar puncture (LP) showed an elevated white cell count of 110 lymphocytes, the CSF protein level was 4.23 g/l (reference value <0.4 g/l), CSF glucose was borderline low compared to serum glucose (2.8 vs 5.7).

A first set of nerve conduction studies (NCS) carried out 3 weeks after onset of symptoms, indicated an acute demyelinating neuropathy with mildly prolonged distal motor latencies (DMLs) and F wave latencies and a reduced motor unit recruitment pattern. The second set of NCS, which were carried out 5 weeks after the onset of symptoms, displayed a non-uniform polyradiculopathy with now acceptable DMLs in all nerves, significantly prolonged F wave latencies and fibrillation potentials positive sharp waves in paraspinal muscles.

The abnormal findings on LP and NCS were suggestive of an inflammatory or malignant polyradiculoneuropathy.

MRI scans of the spine and brain, routine haematology, biochemistry, HIV, treponemal, Lyme disease tests and immunological tests (ANCA, autoimmune profile, serum and CSF angiotensin converting enzyme (ACE)) were all unremarkable. CSF TB culture was negative. CSF cytology displayed reactive changes with no evidence of malignancy.

Further investigations were carried out to provide a definitive diagnosis. Contrast enhanced scan of the thorax, abdomen and pelvis showed no significant abnormality.

A gallium scan (to identify evidence of systemic sarcoidosis) showed only changes consistent with inflammation of the nasal cavity. A lip biopsy showed several small non-caseating granulomata. Nerve biopsy revealed evidence of small vessel vasculitis. Although no granulomata were identified on the nerve biopsy, there were several epithelioid aggregations, which were thought to be associated with early granuloma formation. The only abnormality on quadriceps muscle biopsy was typical features of denervation, consistent with some of the abnormalities identified on the neurophysiological studies.

DIFFERENTIAL DIAGNOSIS

GBS was provisionally diagnosed. After the finding of a lymphocytosis in his CSF, GBS was excluded. The differential diagnosis included inflammatory or infective polyradiculoneuropathy (eg, HIV, syphilis, sarcoidosis) and malignant radiculopathy.

TREATMENT

Prior to histological evidence of his diagnosis, treatment was started because of progression of his condition. Lyme disease was not thought to be a probable cause, but he lives in an area where this condition is endemic. So, after the finding of a CSF lymphocytosis on day 10, he was started on intravenous ceftriaxone pending the results of more definitive investigations. Despite this treatment his condition progressed, that is, he developed facial weakness. It was therefore decided to initiate intravenous methylprednisolone 1 g/day for 3 days (starting on day 16) for a suspected non-infective systemic inflammatory condition. After the commencement of this treatment, the patient's condition stabilised. As he was neurologically stable, further steroid treatment was deferred until tissue biopsies could be performed. He was then started on oral prednisolone 5 weeks after the onset of symptoms (60 mg for 4 weeks, then a dose tapering to 10 mg over 4 months). Treatment with azathioprine also began at the same time as prednisolone (on an escalating dose to a treatment dose of 2 mg/kg/day). He experienced very severe pain in all limbs requiring morphine in the early stages of his illness. Subsequently gabapentin and amitriptyline were added. As his condition improved his analgesia was successfully withdrawn.

OUTCOME AND FOLLOW-UP

This treatment was followed by a steady and significant improvement in the patient's symptoms. Before treatment, the patient was bed-bound, was unable to lift his right leg more than a few inches off the bed and unable to lift his left leg completely; 2 weeks after the commencement of steroid therapy the patient was able to lift both legs off the bed and walk the length of the ward with the assistance of a frame. He has subsequently continued to improve and 12 months after his initial symptoms was able to walk 1 mile unaided. His facial weakness has fully resolved.

DISCUSSION

Neurosarcoidosis is a rare but severe form of sarcoidosis. The disease can manifest with involvement of the central nervous system (CNS), the cranial nerves, the peripheral nerves and muscle.

GBS is an acute inflammatory demyelinating condition of the nerve roots, plexus and peripheral nerves. It manifests with symmetrical flaccid paralysis, which ascends the patient's body to a variable extent.¹ Patients usually present with progressive sensorimotor limb symptoms, with or without cranial nerve involvement. If severe, GBS can cause autonomic dysfunction and ventilatory failure. CSF analysis by LP is one of the key investigations in suspected GBS. In GBS, the CSF reveals a raised protein level of more than 0.4 g/l in the absence of significantly elevated cell count (although CSF protein can be normal in the first week). Clinically, peak deficits are reached by 4 weeks after the onset of symptoms, with recovery beginning 2–4 weeks after the peak of the illness; a progressive course after 4 weeks excludes GBS as a diagnosis.

Due to the low prevalence of neurosarcoidosis and a lack of understanding of its aetiology, clinical aids such as criteria and protocols have been difficult to construct. However, Zajicek *et al*² have proposed criteria for the diagnosis of neurosarcoidosis – with patients falling into definite, probable or possible.

Definite: clinical presentation suggestive of neurosarcoidosis with exclusion of other possible diagnoses and the presence of positive nervous system histology.

Probable: clinical syndrome suggestive of neurosarcoidosis with laboratory support for CNS inflammation (elevated levels of CSF protein and/or cells, the presence of oligoclonal bands and/or MRI evidence compatible with neurosarcoidosis) and exclusion of alternative diagnoses together with evidence for systemic sarcoidosis (either through positive histology, including Kveim test, and/or at least two indirect indicators for Gallium scan, chest imaging and serum ACE).

Possible: clinical presentation suggestive of neurosarcoidosis with exclusion of alternative diagnoses where the above criteria are not met.

Therefore, using the above criteria, the patient can be classified as having probable neurosarcoidosis.

Neurosarcoidosis is a rare disease: 10% of sarcoidosis patients have neurological involvement, the prevalence of neurosarcoidosis is estimated at 4 per 100 000.³ Due to the rarity of the disease, knowledge of the symptoms of neurosarcoidosis has been gained from only a handful of case-series reports.^{4–7}

According to the literature, neurosarcoidosis causes cranial neuropathies in 50–75% of patients, with facial palsy being the most common (65% unilateral, 35% bilateral).² It has also been reported that patients presenting with a facial nerve palsy alone have a better prognosis than those presenting with a polyneuropathy.⁹ Other symptoms reported include tonic-clonic seizures in 10–15% of patients,¹⁰ meningitis in 3–26% of patients,¹¹ localised granulomatous mass lesions of the CNS,^{8 12} spinal cord involvement,¹³ psychiatric disorders in 20% of patients,¹⁴ movement disorders¹¹ and peripheral nerve and muscle disease in 15% of patients.¹¹

Only a small number of cases of neurosarcoidosis presenting with GBS-like symptoms have been reported.^{15 16} Past case-reports on neurosarcoidosis presenting with GBS-like symptoms report a variable prognosis, from complete recovery after 3 months¹⁵ to death despite prednisolone therapy.¹⁶

Treatment of neurosarcoidosis remains controversial. Due to the rarity of the disease there are no randomised controlled trials to provide evidence on which to base treatment decisions. However, there is evidence of benefit of steroid use in sarcoidosis,¹⁷ therefore, due to the similar disease process steroids are also used in neurosarcoidosis. Steroid treatment remains controversial in GBS due to lack of evidence of significant benefit.¹⁸ Burns *et al*¹⁹ reported on 57 cases of biopsy-proven neurosarcoidosis. They concluded that corticosteroid treatment of neurosarcoidosis was recommended with the aim of ameliorating a patient's symptoms, as opposed to the actual disease process. Burns *et al*¹⁹ also concluded that a short time period between the onset of symptoms and treatment leads to an improvement in a patient's neuropathic state. In our patient, the diagnosis of GBS had been ruled out; therefore steroid treatment was indicated. Azathioprine has also been used as a treatment for neurosarcoidosis with varying effectiveness.^{20–23} It is difficult to identify the reason for the patient's improved condition – it may be due to the treatment with prednisolone and azathioprine, or the disease may have spontaneously resolved by its own accord.

Learning points

- ▶ Systemic diseases, such as neurosarcoidosis, can present in varied and unexpected ways.
- ▶ Although the symptoms and signs should form the basis of the patient's diagnosis, use of appropriate targeted investigations can lead to the correct diagnosis in a challenging case.

Competing interests None.

Patient consent Obtained.

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