

ORIGINAL ARTICLES

An Atypical Case of Neuralgic Amyotrophy with Respiratory Muscle Weakness: Case Report and Review of Literature*JM Reid¹, A Forster², PS Fitch³, FW Smith⁴, RJ Coleman²*¹ Institute of Neurological Sciences, Southern General Hospital, 1345 Govan Road, Glasgow G51 4TF² Department of Neurology, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZN³ Department of Respiratory Medicine, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZN⁴ Department of Radiology, Woodend Hospital, Eday Road, Woodend, Aberdeen AB15 6XS**Correspondence to**

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Abstract

This report is of an atypical case of neuralgic amyotrophy with a Horner's syndrome, bilateral brachial plexus, lumbar plexus and phrenic nerve involvement. The diagnosis is confirmed based on a classical history and examination findings with typical neurophysiological investigations for this condition. This report also highlights the novel use of positional magnetic resonance imaging to investigate patients with respiratory muscle weakness. This case report expands the recognised clinical features of neuralgic amyotrophy and the literature concerning atypical features of this condition is reviewed.

His vital capacity was 1.8 L (predicted 4.1 ± 1.0 L) sitting upright and 0.8 L sitting at 45 degrees. He was apyrexial with a pulse of 78/minute and blood pressure 174/73 mmHg.

He had a right Horner's syndrome (confirmed by relatives as new). He had asymmetric arm weakness affecting left shoulder abduction (UK Medical Research Council (MRC) classification of muscle power, grade 4/5), left elbow extension (MRC 4/5), left elbow flexion (MRC 2/5), and left wrist and finger extension (MRC 2/5). On the right he had elbow extension weakness only (MRC 4/5). He had mild bilateral hip flexion weakness (MRC 4/5). His upper limb reflexes were absent. His left knee jerk was absent and right knee jerk present with reinforcement; both ankle jerks were present and the plantar responses were flexor. He had loss of pin-prick sensation in the distribution of both axillary nerves.

Introduction

Neuralgic amyotrophy (NA), also known as Parsonage-Turner syndrome^{1,2} or brachial neuritis,³ is an idiopathic syndrome typically presenting with shoulder, arm or neck pain at the onset, followed by unilateral arm and/or shoulder weakness in the distribution of the upper or lower brachial plexus with minimal sensory loss.^{1,2} Turner and Parsonage proposed that NA was a form of mononeuritis multiplex.² This case report describes an atypical case of NA with a Horner's syndrome, bilateral brachial plexus, lumbar plexus and phrenic nerve involvement.

History

A 46 yr-old man developed a severe ache in his left arm that spread to the neck and both shoulders overnight. The following day he developed left arm weakness, paraesthesia over both upper arms and was unable to lie flat due to breathlessness. On the third day he attended hospital due to severe orthopnoea and new bilateral leg weakness. Two weeks previously he had symptoms of an upper respiratory tract infection that resolved. He had a past medical history of hypertension treated with bendroflumethazide and atenolol. There was no relevant family history. He was an ex-smoker (30 pack years) and drank 20 units of alcohol per week.

Examination

His O₂ saturation on air was 96% but he quickly became cyanosed on lying at 45 degrees. He had poor air entry at both lung bases. On sniffing he had bilateral sub-costal recession and he had a paradoxical abdominal wall motion on inspiration.

Investigations**(i) Neurological investigations**

Magnetic resonance imaging (MRI) of the cervical spine performed (using a 0.6 Tesla open scanner "Upright" scanner FONAR Melville NY) in the sitting position demonstrated no intrinsic cord abnormality or root compression. Cerebrospinal fluid testing on day 5 from symptom onset contained 2 polymorphs per μ l, with normal protein and glucose levels, and oligoclonal bands absent. Neurophysiological testing on the seventh day from onset of weakness showed no conduction block, normal distal motor latencies and normal motor conduction velocities (ulnar and median nerves tested). F wave studies were normal as were ulnar, median and radial sensory nerve action potentials (SNAPs). Electromyography (EMG) showed no voluntary activity in the left deltoid or triceps, and only a single voluntary motor unit was present in the left extensor digitorum communis (EDC). There was no evidence of a demyelinating polyneuropathy. Repeat nerve conduction studies (NCS) and EMG at three weeks showed traces of fibrillation and positive sharp waves, clearest in left EDC, indicative of denervation. Left radial SNAP had dropped from 25 μ V to 11 μ V, but was still present, suggesting wallerian degeneration of some fibres. At three months fibrillation and positive sharp waves in the affected muscles of the left arm were noted. Phrenic nerve studies performed in the upright position demonstrated a diaphragmatic compound muscle action potential (CMAP) amplitude recorded at the 7th intercostal space (as per the method described by Newsom-Davis)⁴ of 101 μ V on the left and 386 μ V on the right (normal range 160-500 μ V)⁴ with latencies of 10.2 ms and 7.0 ms (normal range 6.1-9.2 ms)⁴ respectively.

(ii) Respiratory investigations

Chest X-ray was reported to show an elevated left hilum and "poor inspiratory effort". Arterial blood gas on air was pH 7.43, pCO₂ 5.5, pO₂ 11.0. His vital capacity varied between 1.5 and 2.3 L. Peak inspiratory mouth pressure was 28 cm H₂O (predicted 95). Spirometry at 3 months had not improved.

(iii) Other investigations

Full blood count was normal apart from a mean corpuscular volume of 102 fl. Blood film showed macrocytes and stomocytes consistent with alcohol excess. Alanine aminotransferase level was 105 μ /L (normal range 1-40), gamma glutaryl transferase 280 μ /L (normal range 4-35) with normal bilirubin and alkaline phosphatase levels. The following tests were either normal or negative: urea and electrolytes, glucose, C reactive peptide, thyroid function, vitamin B12, clotting, Hepatitis B and C serology, Lyme and syphilis serology, auto-immune profile (including anti-nuclear and anti-neutrophilic cytoplasmic antibodies), serum electrophoresis, blood lead level, serum angiotensin converting enzyme, creatine kinase, urinary porphyrins, routine urinalysis.

Progress

His vital capacity was monitored and he received a course of intravenous immunoglobulin (0.4g/kg/day for five days). Arm pain was treated with gabapentin. He had difficulty sleeping at night unless he was upright and he was able to sleep supine with overnight non-invasive ventilation. His condition did not deteriorate. He developed wasting of the affected muscles noted at review at three months. On review six months after presentation he was still having significant orthopnoea and required non-invasive ventilation for adequate sleep. The strength in his legs returned to normal but the right Horner's syndrome and bilateral asymmetric arm weakness persisted. His knee jerks were now present but he remained areflexic in the arms with spinothalamic sensory loss in the distribution of the axillary nerves bilaterally. At 18 months his arm strength had returned to normal but the Horner's syndrome and orthopnoea persisted.

Discussion

Given the typical history of severe shoulder, neck and arm pain followed by arm weakness, no evidence of a demyelinating polyneuropathy and supportive features of brachial neuritis on NCS/EMG, this case is consistent with a diagnosis of an atypical form of NA with bilateral brachial and lumbar plexus involvement, phrenic neuropathy and a Horner's syndrome. An alternative diagnosis would be acute motor axonal neuropathy (AMAN), an axonal variant of Guillain Barré syndrome. However AMAN causes an ascending symmetrical paralysis, frequent cranial nerve involvement and sensory disturbance and pain are rare.^{5,6} Clearly the patient had clinical and physiological evidence of left phrenic nerve dysfunction with hemidiaphragmatic weakness as phrenic nerve studies demonstrated a low CMAP amplitude and a delayed latency on the left.

NA is a poorly understood, usually monophasic condition affecting the brachial plexus presenting with a combination of severe shoulder, neck and/or arm pain, weakness, and minimal sensory loss.^{1,2} It frequently has a sudden nocturnal onset and the pain lasts days to weeks. It has an incidence 1.6/100,000/year,⁷ with an onset at any age and a male preponderance.⁸ The pathological basis of NA is unclear but it

has been associated with vaccinations (especially tetanus), strenuous exercise, minor trauma, infectious diseases (e.g. parvovirus, cytomegalovirus, Epstein-Barr virus, human immunodeficiency virus, etc.), pregnancy and surgical procedures.^{1,2,3,7,8} Two of these risk factors, strenuous exercise and recent viral illness, were present in this case. In other reported cases, nerve biopsy shows axonal loss^{3,9} and NCS typically shows multifocal axonal lesions in the brachial plexus or its branches although proximal conduction block has been reported.¹⁰ Proximal conduction of the brachial plexus was not tested except using F waves. Therefore, the possibility that there was proximal conduction block as seen in three out of eight patients in the aforementioned study cannot be excluded. EMG shows evidence of denervation in the affected muscle groups.¹¹ Mild numbness in an axillary nerve distribution, as seen in this case, is recognised in roughly one third of patients with NA.^{1,2,3,7,8,12} Typically there is unilateral weakness in the proximal upper limb muscles maximal within a few days. Bilateral involvement has been reported in 5-30%.^{1,2,3,7,12} The upper brachial plexus is involved more commonly than the lower plexus.^{3,8}

Several clinical variants of NA are recognised. There can be involvement of an isolated peripheral nerve (e.g. long thoracic nerve)¹³ or cranial nerve (e.g. recurrent laryngeal nerve)^{14,15,16,17} in NA. Phrenic nerve involvement was reported in 7 out of ninety nine cases of NA in one series;³ the diaphragmatic weakness can be unilateral or bilateral and is not always on the same side as the brachial neuritis.³ Lumbosacral involvement is recognised but rare.^{15,18} There is also an autosomal dominant form of NA (hereditary NA) with recurrent attacks that is linked to chromosome 17q25.¹⁹ Mutations in the SEPT9 gene at this locus have recently been described.²⁰ Hereditary NA can affect lower cranial nerves, phrenic or intercostal nerves, and affects the lumbosacral plexus in 12% of attacks.¹⁹ One case of a brachial neuritis and Horner's syndrome is reported in hereditary NA.¹⁹

Pain usually resolves in NA within 1 to 2 weeks of onset but recovery from the weakness takes months or years. The prognosis for recovery from brachial weakness in NA is good with 36% making a recovery within one year and 75% within two years.^{2,3} Upper brachial plexus neuropathies make a more rapid and complete recovery than lower brachial plexus neuropathies.³ Some diaphragmatic recovery occurs following phrenic neuropathy but may take up to 3 years.²¹ Longer nerves tend to show poorer recovery.²¹

The use of positional MRI in this clinical scenario is noteworthy. The patient caused diagnostic uncertainty because he presented with a combination of features not previously described together in NA. On initial assessment the possibility of an acute intrinsic cervical cord lesion was considered. Because of severe postural respiratory impairment the patient was referred to Aberdeen's positional MRI scanner and was scanned in a seated position. If positional MRI had not been available the patient would have required intubation and ventilation with exposure to all the associated risks.

Conclusion

This case demonstrates a novel presentation of NA with a combination of rare features that are recognised in NA but have never been reported simultaneously in a single case. This widens the phenotype of NA and, as Turner and Parsonage proposed, suggests that NA should be thought of as a form of mononeuritis multiplex² rather than an isolated brachial neuritis. This case also demonstrates the novel use of positional MRI in a patient with severe respiratory muscle weakness.

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References

1. Parsonage MJ, Turner JWA. Neuralgic amyotrophy. The shoulder-girdle syndrome. *Lancet* 1948; i: 973-8.
2. Turner JWA, Parsonage MJ. Neuralgic amyotrophy (paralytic brachialis neuritis). *Lancet* 1957; ii: 209-12.
3. Tsairis P, Dyck PJ, Mulder DW. Natural history of brachial plexus neuropathy. Report on 99 patients. *Arch Neurol* 1972; 27: 109-17.
4. Newsom-Davis J. Phrenic nerve conduction in man. *J Neurol Neurosurg Psychiatry* 1967; 30: 420-26.
5. McKhann GM, Cornblath DR, Griffin JW, et al. Acute motor axonal neuropathy: a frequent cause of acute flaccid paralysis in China. *Ann Neurol*. 1993; 33: 333-42.
6. Paradiso G, Tripoli J, Galicchio S, et al. Epidemiological, clinical, and electrodiagnostic findings in childhood Guillain-Barre syndrome: a reappraisal. *Ann Neurol*. 1999; 46: 701-7.
7. Beghi E, Kurland LT, Mulder DW, et al. Brachial plexus neuropathy in the population of Rochester, Minnesota, 1970-1981. *Ann Neurol* 1985;18: 320-3.
8. McCarty EC, Tsairis P, Warren RF. Brachial neuritis. *Clin Orthop* 1999; 368: 37-43.
9. van Alfen N, Gabreels-Festen AA, Ter Laak HJ, et al. Histology of hereditary neuralgic amyotrophy. *J Neurol Neurosurg Psychiatry* 2005; 76: 445-7.
10. Lo Y-L, Mills KR. Motor root conduction in neuralgic amyotrophy: evidence of proximal conduction block. *J Neurol Neurosurg Psychiatry* 1999; 66: 585-90.
11. van Alfen N. The trouble with neuralgic amyotrophy. *Practical Neurology* 2006; 6: 298-307.
12. Magee KR, DeJong RN. Paralytic brachial neuritis. Discussion of clinical features with review of 23 cases. *JAMA* 1960; 174: 1258-62.
13. England JD, Summer AJ. Neuralgic amyotrophy: an increasingly diverse entity. *Muscle Nerve* 1987; 10: 60-68.
14. Pierre PA, Laterre CE, Van den Bergh PY. Neuralgic amyotrophy with involvement of cranial nerves IX, X, XI and XII. *Muscle Nerve* 1990; 13: 704-7.
15. Byrne E. Extended neuralgic amyotrophy syndrome. *Aust N Z J Med* 1987; 17: 34-8.
16. To WC, Traquina DN. Neuralgic amyotrophy presenting with bilateral vocal cord paralysis in a child: a case report. *Int J Pediatr Otorhinolaryngol* 1999; 48: 251-4.
17. Sanders EA, Van den Neste VM, Hoogenraad TU. Brachial plexus neuritis and recurrent laryngeal nerve palsy. *J Neurol* 1988; 235: 323.
18. Awada A, Obeid T, Al Jumah M, et al. Atypical brachial plexopathy with pseudotumor cerebri. *Eur J Neurol*. 1999; 6: 103-5.
19. van Alfen N, van Engelen BG, Reinders JW, et al. The natural history of hereditary neuralgic amyotrophy in the Dutch population: two distinct types? *Brain*. 2000; 123: 718-23.
20. Kuhlenbaumer G, Hannibal MC, Nelis E, et al. Mutations in SEPT9 cause hereditary neuralgic amyotrophy. *Nat Genet*. 2005; 37:1044-6.
21. Hughes PD, Polkey MI, Moxham J, et al. Long-term recovery of diaphragm strength in neuralgic amyotrophy. *Eur Respir J* 1999; 13:379-84.