Neuralgic amyotrophy is an uncommon condition characterised by the acute onset of severe pain in the shoulder and arm, followed by weakness and atrophy of the affected muscles, and sensory loss as the pain subsides. The diversity of its clinical manifestations means that it may present to a variety of different specialties within medicine. This article describes the epidemiology, aetopathogenesis, clinical features, differential diagnoses, investigations, treatment, course and prognosis of the condition.

Neuralgic amyotrophy was described by Dreschfeld in 1887. He reported recurrent episodes of the condition in two sisters. Several other reports followed, but it was Parsonage and Turner who clearly detailed the clinical aspects of the condition in a cohort of 136 patients in 1948. Many case reports and series of patients with neuralgic amyotrophy have been described, expanding the clinical variants and nomenclature. It has been referred to as the Parsonage-Turner syndrome, acute brachial neuropathy, acute brachial plexitis, brachial plexus neuropathy, cryptogenic brachial neuropathy, idiopathic brachial plexopathy, idiopathic brachial neuritis, localised neuritis of the shoulder girdle, multiple neuritis of the shoulder girdle, paralytic brachial neuritis, serum neuritis, shoulder girdle neuritis and the shoulder girdle syndrome.

The diversity of presenting features means that patients with neuralgic amyotrophy may be seen by orthopaedic surgeons, neurosurgeons, neurologists, internal medicine physicians, accident and emergency physicians, general practitioners, sports medicine specialists, obstetricians and respiratory physicians.

Neuralgic amyotrophy is approximately two to three per 100 000 person-years. It has been described in patients aged between three months and 81 years, with the highest incidence occurring in the third and seventh decades. Males are more commonly affected than females in ratios ranging between 2:1 and 11.5:1.

Aetiology
Neuralgic amyotrophy exists as an idiopathic and a hereditary form. Although the aetiology of the idiopathic form is unknown, various antecedent events, or factors which may trigger an immune-mediated process, have been proposed to contribute to its development. Infection has preceded the development of symptoms in 25% to 55% of patients. A history of antecedent immunisation has been recorded in 15% of cases. Strenuous exercise has been undertaken prior to the onset of symptoms in approximately 8% of cases in two large series. Post-surgical neuralgic amyotrophy is well-recognised after operations in areas remote from the shoulder girdle. It has occurred during pregnancy and postpartum.

Idiopathic neuralgic amyotrophy may be a result of an autoimmune process. A study showed that lymphocytes of patients with the condition increased their blastogenic activity in cultures with nerve extracts from different nerves of the brachial plexus and their branches, but not in cultures with extracts of nerves from the sacral plexus. Another study showed an increase in complement-fixing antibodies to peripheral nerve myelin in the acute phase in three patients with neuralgic amyotrophy. The results of these two studies have yet to be replicated.

The hereditary form of the condition is an autosomal dominant recurrent neuropathy affecting the brachial plexus. It is the first monogenic disease caused by defects in a septin family gene. Mutations in the gene septin 9 on chromosome 17q25 have been found in several families with hereditary neuralgic amyotrophy.
Gene septin 9 is a member of the cytoskeleton-related septin family, which is highly expressed in glial cells in neuronal tissues. Sequence alterations in septin 9 may disrupt various cellular processes, leading to abnormal cytoskeleton events and signalling.24

Clinical features
The characteristic clinical presentation is an acute, severe burning pain in the shoulder or arm lasting for several days or weeks, followed by muscle weakness, atrophy and sensory loss as the pain diminishes. However, this temporal profile is not universal. Symptomatic bilateral involvement of the brachial plexus occurs in approximately 30% of cases and is usually asymmetrical.7,10,16 Most of these patients note bilateral pain either simultaneously or within 24 hours.25,26 However, it is not uncommon for patients to present with bilateral neuralgic amyotrophy with only one side being symptomatic.27

Pain
Pain was the first symptom in 90% of cases in a study of 246 patients with neuralgic amyotrophy.16 The four loci for initial pain were in the shoulder or radiating from the shoulder to the arm (39.7%), from the neck radiating into the arms (35.4%), from the scapular or posterior chest wall region radiating to the arm or anterior chest wall or both (18.8%), or confined to a distribution in the lower plexus (6.1%). The pain is typically severe and unremitting, often waking patients from sleep. It is commonly worsened by movement of the shoulder or arm, resulting in patients holding the arm with the elbow flexed and the shoulder adducted.28 A helpful feature in distinguishing neuralgic amyotrophy from cervical radiculopathy is that with a Valsalva manoeuvre, the aggravation of the pain is typically less in the former.26 The pain may last for more than eight weeks.16 Minimal or no pain is uncommon in neuralgic amyotrophy.29

Weakness and atrophy
Weakness develops within 24 hours in approximately one third of cases.16 In approximately 70%, it occurs within the first two weeks of the onset of pain.10,16 It characteristically worsens as the pain subsides. Weakness affecting the distribution of the upper part of the brachial plexus, either with or without involvement of the long thoracic nerve is the most common pattern.7,10,16 The muscles commonly affected include the infraspinatus, supraspinatus, serratus anterior, biceps, deltoid and triceps.8,10,13,16,27 It is well recognised that individual nerves can be affected in isolation or several at a time, mimicking a ‘mononeuritis multiplex’ pattern.26 This may occur in 75% of cases.14 Isolated involvement of a particular nerve, for example, the anterior interosseous branch of the median nerve, has also been described.30,31 Unilateral or bilateral phrenic neuropathy resulting in paralysis of the diaphragm may occur in isolation or in association with other nerve involvement.32-35 Hemidiaphragmatic paralysis may be present on the contralateral side to the affected extremity.10 Involvement of cranial nerves VII, IX, X, XI and XII has also been reported.14,34,37

Sensory involvement
Sensory involvement may occur in 78% of cases.16 Hypoesthesia or a combination of paraesthesia and hypoesthesia are the most common complaints.16 Seen most often over the deltoid and lateral aspect of the upper arm and the radial aspect of the forearm.10,13,16,27 Isolated sensory manifestations have been described in eight patients; in three, the lateral cutaneous nerve of the forearm was affected, while partial involvement of the distal median nerve was documented in the other five.38

Autonomic dysfunction
Signs of involvement of the peripheral autonomic nervous system, such as vegetative and trophic skin changes, oedema at the onset of the attack, temperature dysregulation, increased sweating and changes in nail or hair growth were documented in approximately 15% of a series of 246 cases.16 In addition, one patient with hereditary neuralgic amyotrophy suffered a persistent Horner’s syndrome combined with involvement of the brachial plexus.39

Craniofacial and cutaneous findings
Minor dysmorphic features including hypotelorism, palate and unusual skin folds have been observed in some patients with the hereditary form of the condition.40,41

Differential diagnosis
The diagnosis of neuralgic amyotrophy can be challenging, especially in the early stages. There are many differential
diagnoses (Table 1). It can mimic other conditions which cause acute pain and weakness around the shoulder. The pain can be so severe that patients may be investigated for myocardial infarction. The correct diagnosis is important to avoid unwarranted treatment, including inappropriate surgery.

**Investigations**

Blood tests occasionally reveal abnormalities including elevated liver enzymes and positive antiganglioside antibodies, although the significance of these remains unclear. Examination of the cerebrospinal fluid is usually normal, although mildly elevated protein, slight pleocytosis and oligoclonal bands have been reported. A chest radiograph is useful to exclude a Pancoast tumour of the lung and may detect an elevated hemidiaphragm caused by involvement of the phrenic nerve. An MRI of the cervical spine may reveal cervical disc disease or cervical root lesions, and of the shoulder may identify other causes of pain at this site such as rotator cuff tears, labral tears, impingement syndromes or other local lesions. Abnormalities in the musculature of the shoulder girdle related to denervation may be detected. The mechanism and time course of changes in the signal intensity of the muscles on MRI are not fully understood. In the acute phase of denervation, the intensity may be normal. The earliest detectable change in denervated muscles is a diffuse increase of the T2-weighted signal as a result of oedema, without a T1-weighted change. In the subacute and chronic stages of denervation, the T2-weighted changes persist and muscle atrophy may develop. Atrophy is suggested by a reduced muscle mass and an increase in the intramuscular linear T1-weighted signal because of fatty infiltration, which may return to normal several months after the chronic stage. An increased T1-weighted signal in the supraspinatus, infraspinatus and deltoid muscles at initial presentation and T1-weighted changes of atrophy without fatty infiltration during follow-up, were reported in three cases. A retrospective study of 27 patients with neuralgic amyotrophy showed T1- and T2-weighted signal changes in the muscles compatible with predominant involvement of the supraspinalis (supraspinatus and infraspinatus) and axillary (deltoid and teres minor) nerves. These changes matched or nearly matched electromyographic changes where these were available. Similarly, in another retrospective study of 26 cases, T1- and T2-weighted signal changes were most commonly seen in the supraspinatus, infraspinatus, deltoid and teres minor muscles.

Conventional MRI of the brachial plexus is not sensitive enough to identify pathological changes in neuralgic amyotrophy. Of 50 patients studied in one series, focal T2 hyperintensities in two patients and focal thickening of the plexus in one patient were detected. Magnetic resonance neurography provides better image resolution. Using this technique in an acute case of neuralgic amyotrophy, the affected brachial plexus was found to be thickened and hyperintense, while in a chronic case there was also hyperintensity.

Electrophysiological evaluation is useful for the diagnosis of neuralgic amyotrophy and to distinguish it from cervical root lesions. It is helpful in localising the symptoms to the brachial plexus. Nerve conduction studies and needle electromyography are best performed at least three weeks after the onset of symptoms. Nerve conduction velocities are usually normal, although proximal conduction block has been recorded, although the primary pathology is thought to be axonal degeneration. In three of five cases with proximal conduction block, there was complete resolution of the block when the studies were repeated three to nine months later, suggesting that in some cases demyelination may predominate in the early stages. Delayed distal latencies and a decreased amplitude of compound muscle action potentials may also be seen. Electromyography reveals acute denervation, indicating axonal degeneration, with positive sharp waves and fibrillation potentials three to four weeks after the onset of symptoms. Electromyography performed three to four months after the initial symptoms may show chronic denervation and early reinnervation with polyphasic motor unit potentials.

**Treatment**

Corticosteroids may reduce the time to the start of improvement of weakness, although treated patients appeared to suffer more attacks than untreated ones. Corticosteroids may reduce pain in the early stages. Analgesics may also be helpful, with a combination of a non-steroidal anti-inflammatory and an opiate appearing to be best. Physiotherapy and rehabilitative exercises are recommended as the pain subsides and the weakness improves, although these measures have not been shown to hasten recovery.

**Course and prognosis**

Some studies have recorded that between 80% and 90% of patients had recovered after two to three years. However, others have suggested a less favourable outcome with less than 50% of patients recovering fully from pain or weakness after six years. Recurrence has been reported in between 5% and 26% of patients with idiopathic neuralgic amyotrophy, although referral bias may have affected the study with the higher figure.

**References**