Parsonage-Turner syndrome

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Abstract
Parsonage-Turner is a clinically defined syndrome that is easily confused with other neck and upper extremity abnormalities. Affected patients present with a characteristic pattern of sudden and acute pain across the top of the shoulder, lasting a few hours to a fortnight, followed by flaccid paralysis of some muscles of the shoulder girdle. Features supporting strongly diagnosis of Parsonage-Turner disease include:

- discrepancy for muscles wasting and denervation between muscles innervated by the same nerve;
- patchwork distribution of muscles denervation for muscles that are innervated by several nerves or nerve trunk arising from the brachial plexus
- dissociation between sparing of the sensory nerve action potential and muscles denervation depending from the same mixed nerves.

The incidence has been estimated at approximately 1.64 in 100,000, with a peak rate between the third and fifth decades and a slight male predominance. Although different precipitating factors, such as infection, trauma, surgery, immunization, and autoimmune mechanisms, have been suspected and incriminated in the occurrence of Parsonage-Turner syndrome, the etiology remains unknown. Prognosis is generally favorable, with about 75% of complete recovery within 2 years. Treatment is symptomatic and is based on analgesic drugs and physical therapy.

Keywords

Disease name and synonyms
Parsonage-Turner disease was first reported under different names, such as:

- Localised neuritis of the shoulder girdle (1)
- Seratus magnus paralysis (2)
- Multiple neuritis of the shoulder girdle (3)
- Acute brachial radiculitis (4-5)

In 1948, Parsonage and Turner described similar conditions and isolated a distinct clinical
syndrome under the neutral term of "Neuralgic amyotrophy; the shoulder-girdle syndrome" (6). Subsequently, further appellations have been proposed, such as:
- Paralytic brachial neuritis (7-8)
- Acute shoulder neuritis (9)
- Acute scapula-humeral palsy (10)
- Brachial plexus neuropathy (11)

This terminology underlines the persistent lack of knowledge concerning the pathogenic process and the localization of lesions in this syndrome. Nevertheless, the "Parsonage-Turner syndrome" (12) appellation has the advantage of referring to a well-recognized and a well-identified clinical entity, without addressing the issues of localization or pathogenic process.

**Excluded diseases**

**Hereditary neuralgic amyotrophy (HNA) or Hereditary brachial plexus neuropathy (HBPN)**

Familial occurrences of the Parsonage-Turner syndrome led to the individualization of Hereditary neuralgic amyotrophy (HNA) or Hereditary brachial plexus neuropathy (HBPN). Clinical features of HNA are identical to those of the sporadic form. Family history, a marked tendency of relapse, cases beginning more frequently in childhood, and in some cases, minor dysmorphic features, enable distinguishing the hereditary forms from the sporadic variety (13). An autosomal-dominant transmission mode linked to 17q25 locus is admitted in most HNA families (14), but recent data tend towards a genetic heterogeneity (15).

**Hereditary neuropathy with liability to pressure palsies (HNPP)**

HNPP is a distinct genetic disorder and recurrent brachial plexopathy might be its only expression (16).

**Diabetic amyotrophy**

Proximal diabetic neuropathy, which consists of muscle-weakness and, exceptionally, wasting in the proximal part of the lower limbs, involves the scapulo-humeral region (17).

**Neuralgic amyotrophy as a complication of serotherapy**

This entity, known since 1910, is clinically identical to Parsonage-Turner syndrome, except that the delay between pain and paralysis is shorter, and sometimes preceded by generalized urticaria. This condition is usually considered distinct from Parsonage-Turner syndrome because of the well-identified precipitating factor. However, numerous authors consider it as the prototypic form of the Parsonage-Turner syndrome, and use this argument to support the involvement of an immune mechanism in Parsonage-Turner syndrome (6-13-18-19-20-21-22-48-49).

**Neuralgic amyotrophy of the lumbar plexus**

Similar conditions involving lumbo-sacral plexus rather than brachial plexus have been described. Although the clinical features and evolution are very similar, pelvis belt neuralgic amyotrophy is excluded from Parsonage-Turner syndrome (23).

**Diagnosis criteria / definition**

Parsonage-Turner disease is a rare and clinically defined syndrome of unknown etiology, which consists of sudden pain followed by muscle-weakness and wasting of the shoulder girdle and upper arm. Usually "without any constitutional disturbance, pain starts suddenly across the top of the shoulder-blade (…) and lasts from a few hours to a fortnight (…) Then, a flaccid paralysis of some of the muscles of the shoulder girdle and often of the arm develops". Sensory impairment is more often limited to "a patch of numbness over the outer side of the upper arm. When the paralysis appears, the severe pain usually stops" (6).

**Differential diagnosis**

At the disease onset, the pain around the shoulder girdle may be a sign leading to misdiagnosis, as acute pain can occur in numerous other shoulder affections (13-24), such as:
- Rotator cuff tears
- Adhesive capsulitis
- Calcific tendonitis
- Shoulder arthritis
- Local bone affection
- Cervico-brachial neuralgia
- Herpes Zoster

When muscles are subsequently affected with paralysis and wasting, other conditions involving the second motor neurone can be discussed, especially:
- Discogenic nerve root compression
- Tumors of the spinal cord or brachial plexus
- Infiltrative tumor of the nerve root or brachial plexus such as Pancoast-Tobias syndrome
- Outlet syndrome such as neuralgia of the supra scapular nerve, the long thoracic nerve, or the thoracic outlet syndrome
- Traumatic compressive nerve injuries
- Cervical artery dissection
- Anterior poliomyelitis
- Amyotrophic lateral sclerosis

The acute onset of pain followed by its rapid resolution or decrease, as weakness and paralysis occur, constitute a disease pattern characteristic of Parsonage Turner syndrome.
However, electro-physiological and imaging studies are useful in distinguishing the above conditions from Parsonage-Turner syndrome (6-11-13-24).

**Frequency**

Firstly described in military personnel during the Second World War, Parsonage-Turner syndrome seems rare. In the general population of Rochester, Minnesota, the incidence has been estimated at about 1.64 in 100,000 (25). Ages of affected patients range from 3 months to 84 years (26), with the highest incidence occurring between the third and fifth decades (6-7-11-27-28-29-30), and the average age at onset has been estimated to 38 years from review of literature series(31). A male predominance is reported in the civilian population, with a male-to-female ratio ranging from 1.74:1 to 4:1 (11-25-26).

**Clinical description**

Local pain around the shoulder girdle is the prevalent presenting symptom (6-7-8-10-11). It is usually sudden and often severe, insufferable, sometimes awakening patients during the night. It worsens progressively for some hours or even two days. Described as a constant severe ache associated with tenderness of the muscles, the pain is not affected by coughing. However, it is accentuated by arm movements and muscular pressure, but almost unaltered by movements of the neck. The pain is commonly distributed across the back of the scapula and the tip of the shoulder. It often radiates down the outer side of the arm and up along the neck, and seldom spreads down as far as the outer side of the forearm, below the elbow. There is no exact correlation between the localisation of the pain and the distribution of the subsequent muscle paralysis. However, in general, pain radiating below the elbow is associated with involvement of the biceps or triceps, and radiation into the neck involves the sternocleidomastoid and trapezius. Similarly, most of the patients with bilateral paralysis also initially suffer from bilateral pain. Usually the severe pain lasts from a few hours to three weeks, and then disappears rather suddenly while the muscular wasting and weakness occur. A less severe pain may persist considerably longer. Severe pain may sometimes last days or even weeks after appearance of the weakness. Occasionally, muscular weakness and pain occur simultaneously. Although lack of pain is extremely uncommon in Parsonage-Turner syndrome, it has been already reported in the original series of Parsonage and Turner(6). As the pain subsides, flaccid paralysis of some muscles of the shoulder girdle, and often of the arm, develops (6-7). Usually, muscle weakness appears suddenly, but sometimes gradually increases over two or three days, or even one week in rare cases. Paralysis is of lower motor neurone type, with flaccidity and rapid wasting of the affected muscles. Tendon reflexes might be affected, depending on the severity and extent of muscular paralysis and wasting. Hypoactive reflexes are frequently encountered, and fasciculations are occasionally seen (6-7-8-10-11).

Depending on the supposed anatomical site of the lesion, several patterns of weakness are reported: weakness involving muscles that are innervated by either one peripheral nerve, several peripheral nerves, one or several nerve-root, or a combination of nerve-roots and peripheral nerves. The most frequent pattern of weakness corresponds to the involvement of several peripheral nerves, among which axillary, suprascapular, long thoracic and musculocutaneous nerves are the most commonly affected (6-7-8-10-11). Radial (11-7), anterior intersosseous (7-10-33-36), and median nerves (37), are also occasionally reported to be affected. The involvement of the phrenic nerve, resulting in diaphragm paralysis with dyspnea is rarely, but classically, reported. This involvement is probably underestimated, as it is frequently associated with asymptomatic presentation. Regarding nerve-root involvement pattern, C5 and C6 are the most commonly affected; C4 and C7 are also involved, but more rarely. Accordingly, the weakness will affect the deltoid, which is the muscle the most frequently involved, and the supraspinatus, infraspinatus, serratus anterior, biceps, triceps, and wrist and finger extensors (6-7-8-11-38-39). Muscle involvement is usually unilateral, although bilateral involvement is not uncommon, with an asymmetrical pattern of affected muscles. Weakness and pain area do not coincide perfectly. Muscular atrophy occurs rapidly in different degrees of severity. The resulting clinical feature is a patchwork of weakness and atrophy in one or several muscles, principally around the shoulder blade.

In the early stages of the affection, many patients report a localised numbness, although there is no residual sensory impairment at the later stages when weakness has already appeared (6-7). Sensory impairment at the later stages is usually mild and the most commonly involved area is a small strip over the outer side of the upper arm, corresponding to the distribution of the circumflex nerve. Nerve-root distribution of muscle weakness is usually associated with sensory impairment occurring down the outer side of the arm and forearm in
the C5-C6 cases, and extending to the neck side when C4 root is involved. In fact, areas of sensory impairment correspond to the distribution of the nerve or nerve-root supposedly affected, which is itself based on distribution of weakness. However, in several cases, the degrees of sensory impairment and weakness corresponding to the distribution of the same nerve do not correlate (6-7-8-10-11-25-26-28-31).

From the observation of few cases in which sensory impairment was absent and the pattern of muscles affected by weakness did not correspond to any peripheral nerve or nerve root distribution, Parsonage and Turner (6) suggested that the lesion could probably also affect the spinal cord (anterior horn cells).

Management and treatment
Prognosis is generally good, since recovery of strength and sensation usually begins spontaneously, as early as 1 month after symptoms onset, with about 75% of complete recovery within 2 years (11). However, the period of time for complete recovery is very variable, ranging from 6 months to 5 years (7-24). It seems that the delay in recovering strength depends on the severity and duration of pain, weakness, or both (6-8-11-39).

Furthermore, patients with involvement of proximal and upper trunk lesions have the most rapid recovery (11). Although not very common, relapse might nevertheless occur within a few months to several years after full recovery (6-7-8-11-38-40-41). In general, complete restoration to normal strength and function usually occurs within five years.

However, prognosis is influenced by the duration of the resulting incapacity, some patients having experienced impairment persisting sometimes thirty years after the onset (31). The occurrence of diaphragmatic forms must be taken into account in the diagnostic approach of dyspnea. No specific treatment has yet been proved efficient in Parsonage-Turner syndrome. In the early stages, pain may require treatment. Common analgesic drugs are usually sufficient. However, in many cases, high pain intensity requires morphine administration. Corticosteroids administration does not provide any significant benefit, with the exception of a few patients who experienced some pain relief (11). Rest is recommended (42), and immobilization of the affected upper extremity may be helpful in relieving the pain and in preventing stretching of the affected muscles (10-43).

As pain subsides, physical therapy is recommended. Passive range of motion exercises of the shoulder and elbow (38-43) are suggested to maintain full range of motion. Active rehabilitation is undertaken only when some recovery of the affected muscle(s) is already obtained. Furthermore, all the upper body muscles should undergo rehabilitative exercises, and not only those presenting clinical weakness (42). It is also recommended that strength recovery reaches a plateau before patient returns to sports (44).

However, the recovery delay does not seem to be improved by these physical therapies (11). Surgical stabilization of the scapula to the thorax, or tendon transfers have been performed with benefit in patients who did not achieve recovery (43).

Etiology
The exact cause of brachial neuritis remains unknown. Numerous authors have proposed various precipitating events or factors. These factors, suggested to contribute to the development of brachial neuritis, are found in approximately 30 to 85% of the cases (1-6-7-8-11-26-28-35), 3 to 14 days preceding the onset of pain. The most frequently reported factors are infection, viral diseases, trauma, heavy exercise, surgery, immunization, and autoimmune mechanisms (vaccinations, serotherapy, foreign serum injection, subcutaneous injections of allergens, immunogenic substances, pregnancy) (6-7-8-10-11-13-27-28-30-32-33-34-45).

Although commonly admitted, the contributing role of these factors has not been proved and remains hypothetical. The particular case of post-serotherapy neuralgic amyotrophy (18-19-20-21-22) must be underlined. This well-known condition is an occasional complication of serum injection. Although incompletely elucidated, the physiopathology of this process lies in the occurrence of perineural oedema, similar to the mechanism involved in urticaria in serum sickness (6). Several authors consider that neuralgic amyotrophy following foreign serum injection should not be distinguished from the Parsonage-Turner syndrome (48-49).

In a way similar to post-serotherapy neuralgic amyotrophy, and on the basis that numerous immune events are recognized as precipitating factors for Parsonage-Turner disease, an allergic or hypersensitivity reaction mechanism is commonly suggested in the etiology of the disorder (6-9-28-45). Rare cases reported in anatomo-pathological studies are suggestive of an inflammatory-immune pathogenesis (50). Furthermore, some authors underline that the particular evolution of Parsonage-Turner disease, i.e. sudden pain onset and spontaneous recovery, is similar to the
inflammatory dysimmune process of the delayed over-sensitiveness type (30).
Several studies provide additional evidence for an allergic or autoimmune mechanism. Sierra et al (51) showed that blood lymphocytes in patients with neuralgic amyotrophy are specifically sensititized to brachial plexus nerves. In addition, Vriesendorp et al (52) determined that complement-fixing antibodies to peripheral nerve myelin and terminal complement activation products are increased in serum of patients in the acute phase of neuralgic amyotrophy.

**Diagnostic methods**
The Parsonage-Turner disease is a clinical syndrome and there is no existing diagnostic study providing a specific result that allows diagnosis confirmation. The results of most of laboratory studies are normal, and their aim is to eliminate conditions in differential diagnosis. There is no evidence for an inflammatory or infectious process. Cerebrospinal fluid is usually normal or might show a slight increase in the total protein (8-11-28). Imaging studies such as brachial plexus and cervical MRI are helpful in eliminating any local pathological process, which is associated with a differential diagnosis condition. High intensity signals on T2-weighted images in shoulder muscles before development of muscle atrophy have been described, but are not specific (46). Electromyographical studies are more useful as they give the precise pattern of muscles involvement, and subsequently the hypothetical localisation of the nerve lesion(s). They can also be helpful in detecting sub-clinical involvement of unsuspected muscles, or in ruling out a traumatic or compressive nerve or trunk lesion. In neuralgic amyotrophy, electromyographical findings usually reveal acute denervation resulting from an axonal neuropathy. However, some rare studies reported evidence of proximal conduction block, suggesting focal proximal demyelination (47).

The following features are highly suggestive of Parsonage-Turner disease diagnosis:
- discrepancy for muscles wasting and denervation between muscles innervated by the same nerve;
- patchwork distribution of muscles denervation for muscles that are innervated by several nerves or nerve trunk arising from the brachial plexus;
- dissociation between sparing of the sensory nerve action potential and muscles denervation depending from the same mixed nerves.

Similarly, diaphragmatic denervation supports also diagnosis of Parsonage-Turner disease (31). Diaphragmatic involvement may also be revealed by radiography or ultrasonography imaging of the thorax, even if there is no clinical evidence for a diaphragmatic weakness.

**Unresolved questions**
Although some arguments are in favor of a possible immune mechanism, the etiopathogenesis of Parsonage-Turner disease remains unknown. Furthermore, the rare cases of conduction block reported suggest a possible focal demyelination (47-53), which may occur during the early stage of the affection, when electromyographical studies are rarely performed. Moreover, the precise location of the lesion on the nerve root, either among the brachial plexus, or in the nerve trunk is also uncertain. Particularly, the cases with distal muscles involvement may result from a partial plexus trunk lesion or a distal terminal nerve lesion (31). Thus, the diversity of appellations for Parsonage-Turner diseases reflects entirely these uncertainties as to the localization and the pathogenic process.

More recently, many cases of clinical variations of Parsonage-Turner disease have been reported (37-54). These variants forms include focal and distal forms, sensory isolated forms, and some involve cranial nerves (31). Therefore, it seems that the nosographic framework of neuralgic amyotrophy is widening, and that the condition should be considered as a multifocal neuropathy involving mostly, but not only, nerves of the upper extremity.

**References**