Brachial neuritis

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Introduction

This article includes discussion of brachial neuritis, acute brachial neuropathy, acute brachial plexitis, acute brachial radiculitis, acute scapulohumeral paralysis, acute shoulder neuritis, brachial plexus neuropathy, cryptogenic brachial neuropathy, inflammatory brachial plexus neuropathy, localized neuritis of shoulder girdle, long thoracic neuropathy, multiple neuritis of shoulder girdle, neuralgic amyotrophy, paralytic brachial neuritis, Parsonage-Turner syndrome, and serratus magnus palsy. The foregoing terms may include synonyms, similar disorders, variations in usage, and abbreviations.

Overview

Brachial neuritis, also known as neuralgic amyotrophy, has a characteristic clinical presentation with sudden onset of pain in the shoulder or arm region followed by weakness and atrophy of shoulder girdle or arm muscles. Clinical variants may include upper limb mononeuropathies, lumbosacral plexus involvement, phrenic neuropathy with diaphragm dysfunction, and concomitant recurrent laryngeal or accessory nerve involvement. These variants are important to recognize to avoid unnecessary work-up or interventions and to direct appropriate treatment. In this article, the author discusses typical and variant clinical features, diagnostic approach, and the role of immune therapy and targeted rehabilitation in patients with brachial neuritis.

Key points

- Brachial neuritis, also known as neuralgic amyotrophy of Parsonage-Turner syndrome, is clinically characterized by acute onset of severe pain in the shoulder or arm, followed within days and weeks by weakness, reduced endurance, and wasting of affected muscles as well as variable sensory impairment due to involvement of the brachial plexus or its component nerves (Magee & Dejong 1960).
- Although the exact pathogenesis is unclear, available evidence points to an autoimmune pathogenesis, superimposed on a mechanically induced vulnerability of the nerves with an underlying genetic susceptibility (Spillane 1943). A large number of reports during that period helped to establish the full clinical spectrum of the disease and also gave rise to a variety of synonyms for this syndrome: "multiple neuritis of shoulder girdle," "localized neuritis of shoulder girdle," "acute brachial radiculitis," "acute brachial plexitis," and "acute scapulohumeral paralysis" (Spillane 1943; Tsairis et al. 1972). In their landmark paper, Parsonage and Turner analyzed 136 cases of brachial neuritis and noted that the essential clinical picture was simple but subject to modification (Parsonage and Turner 1948). They used the descriptive term "neuralgic amyotrophy" to avoid any assumptions about etiology or site of lesion. The syndrome received little attention in North American literature until Magee and Dejong reported 23 cases of paralytic brachial neuritis (Magee and Dejong 1960). Subsequently, Tsairis and colleagues reviewed a large series of patients with brachial neuritis to determine the natural history of the disease and advocated the term "brachial plexus neuropathy" (Tsairis et al. 1972). Other reports have further refined the clinical features and phenotypic variability of both idiopathic neuralgic amyotrophy and hereditary neuralgic amyotrophy (Byrne 1987; Cruz-Martinez 2002; van Alfen 2006). The entity continues to be recognized by different terms; however, "neuralgic amyotrophy," "brachial neuritis," "brachial plexus neuropathy," or the eponym "Parsonage-Turner syndrome" are most commonly employed.

Historical note and terminology

Brachial neuritis, characterized by acute pain and weakness with variable atrophy and sensory loss around the shoulder girdle, is a fairly well-defined clinical entity. Typical cases were reported as early as the end of the 19th century (Dreschfeld 1886), when the condition was often described as "serratus palsy." During the Second World War, an increased incidence of brachial neuritis was encountered in the civil population as well as in army personnel (Spillane 1943; Parsonage and Turner 1948). A large number of reports during that period helped to establish the full clinical spectrum of the disease and also gave rise to a variety of synonyms for this syndrome: "multiple neuritis of shoulder girdle," "localized neuritis of shoulder girdle," "acute brachial radiculitis," "acute brachial plexitis," and "acute scapulohumeral paralysis" (Spillane 1943; Tsairis et al. 1972). In their landmark paper, Parsonage and Turner analyzed 136 cases of brachial neuritis and noted that the essential clinical picture was simple but subject to modification (Parsonage and Turner 1948). They used the descriptive term "neuralgic amyotrophy" to avoid any assumptions about etiology or site of lesion. The syndrome received little attention in North American literature until Magee and Dejong reported 23 cases of paralytic brachial neuritis (Magee and Dejong 1960). Subsequently, Tsairis and colleagues reviewed a large series of patients with brachial neuritis to determine the natural history of the disease and advocated the term "brachial plexus neuropathy" (Tsairis et al. 1972). Other reports have further refined the clinical features and phenotypic variability of both idiopathic neuralgic amyotrophy and hereditary neuralgic amyotrophy (Byrne 1987; Cruz-Martinez 2002; van Alfen 2006). The entity continues to be recognized by different terms; however, "neuralgic amyotrophy," "brachial neuritis," "brachial plexus neuropathy," or the eponym "Parsonage-Turner syndrome" are most commonly employed.

Byrne 1987;

Cruz-Martinez 2002;

van Alfen 2006)
Clinical manifestations

Presentation and course

Brachial neuritis has a typical clinical presentation with sudden onset of deep, sharp aching in the neck or around the shoulder girdle and upper arm. Pain often starts in the early morning and increases to an unbearable level (ie, NRS pain score 7/10 or higher) in a few hours. Infrequently, the pain occurs bilaterally and rarely (approximately 5% of cases) may be absent in an otherwise typical case of brachial neuritis. The duration of pain varies from a few days to several months. Patients develop weakness either simultaneously with the pain or after a variable period of several days to weeks. The severity of muscle weakness is variable. Muscle stretch reflexes are impaired or absent in weakened muscles. Atrophy of severely weak muscles usually ensues, and sensory loss is common but clinically less prominent (Parsonage and Turner 1948; Tsairis et al 1972; van Alfen and van Engelen 2006).

The disorder is more common in males (2:1) and, although it may occur at any age, is most common in the age range of 20 to 50 years. Antecedent events are reported in 28% to 83% of cases in different series and include various immune system activating events, such as upper respiratory infection, flu-like illness, hepatitis E, bacterial infections, vaccination, trauma or surgery in areas remote from the affected arm, fatigue, psychological stress, or strenuous exercise (Spillane 1943; Subramony 1988; van Alfen and van Engelen 2006). Recovery of nerve and muscle function usually begins within 1 month of onset of illness and can take from 3 months to 3 years (Parsonage and Turner 1948; Tsairis et al 1972; Devathasan and Tong 1980). But even though reinnervation occurs as expected in all but the most severely affected nerves, the functional prognosis is not good in over half of the patients. This is because altered shoulder biomechanics, scapular dyskinesia, and decreased endurance are common sequelae to brachial neuritis, which lead to persisting pain in affected and compensating muscles and interfere with the ability to keep up with daily demands of work, care, and hobbies or sports (van Alfen et al 2009a; Cup et al 2013; van Eijk 2016).

A wide array and distribution of possible symptoms has been reported for patients with brachial neuritis (Byrne 1987; England and Summer 1987; van Alfen 2011). However, several clinically relevant variants exist that benefit from timely recognition to facilitate appropriate management: a classic phenotype found in an estimated two thirds of the patients, a hereditary form, a pediatric form, a more extensive phenotype with concomitant phrenic nerve and often lumbosacral plexus involvement, and phenotypes that resemble isolated anterior or posterior interosseus nerve entrapment.

Classic brachial neuritis. The most common clinical presentation is a patient who wakes up late at night or early morning with a deep, stabbing pain in the scapular and shoulder joint region that becomes unbearable within a few hours. Problems with overhead reaching, exorotation of the arm, and pinch grip occur within a few days, but the exact onset can be hard to recall for the patient because of the intense pain. Patients often do not describe any discrete paresis but will say that “movements of the arm are more difficult than before.” Clinical examination will show abnormal scapula movement during anteflexion and abduction, weakness when reaching forward or exorotating the arm, and very often also a decrease in strength of the long thumb and index finger flexors and pronation of the flexed forearm (van Alfen 2007; van Alfen et al 2015). Initially, there is often (approximately 80%) some numbness and paresthesia in the axillary, lateral cutaneous nerve of the forearm and superficial radial nerve distribution. These findings point to the most common affected nerves: the long thoracic nerve, suprascapular nerve, and anterior interosseus nerve; in some there is axillary and musculocutaneous nerve (or possibly upper trunk brachial plexus) territory sensory involvement (Magee and Dejong 1960; Tsairis et al 1972; England and Sumner 1987; Cruz-Martinez et al 2002; van Alfen and van Engelen 2006). Asymmetric bilateral upper limb affection is not uncommon in brachial neuritis.

Anatomical variants. In a subgroup of brachial neuritis patients, the paresis mainly involves the middle and lower trunk nerves of the brachial plexus, often with severe weakness and wasting of the forearm and hand muscles and striking sensory and autonomic disturbances. The latter can cause a clinician to consider a complex regional pain syndrome, although the underlying focal neuropathy will usually become clear when further testing is done. This entity has been dubbed “distal neuralgic amyotrophy” (Vanneste 1999) and has a much longer recovery time and worse prognosis than the classic “proximal” phenotype.

Depending how the limits of brachial neuritis as a disorder are defined, other acute painful mono- or multifocal neuropathies have also been categorized under the umbrella term of neuralgic amyotrophy. Variants include isolated phrenic neuropathy, lumbosacral plexus neuropathy in nondiabetics, and acute anterior or posterior interosseus
neuropathy. Some patients have very extensive involvement of both brachial plexus plus other nerves, such as the phrenic nerve and lumbosacral plexus, and a few have involvement of cranial nerves, such as the recurrent laryngeal nerve or facial nerve. Some features of these anatomical variants are discussed below.

Anterior and posterior interosseus nerve entrapment have traditionally been viewed as entrapment neuropathies in the proximal forearm region. However, evidence points to a more multifocal inflammatory origin in many cases, with a clinical course and diagnostic findings compatible with the phenotype of neuralgic amyotrophy (Pham et al 2014; Maldonado et al 2016).

A subset of patients, usually middle-aged males, has been identified who suffer extensive bilateral brachial plexus involvement with concomitant phrenic nerve and often unilateral lumbar plexus involvement and also have elevated liver enzymes at onset (van Alfen and van Engelen 2006). Additional work suggests an association between this extensive phenotype and hepatitis E virus infection (van Eijk et al 2014; Dalton et al 2016; Scanvion et al 2017).

Idiopathic lumbosacral plexopathy can also occur without brachial plexus or other nerve involvement. Although lumbosacral plexopathy is a frequent finding in diabetics, it is rare or under recognized in the nondiabetic population (Dyck and Windebank 2002). Its clinical features and recovery are very similar to that of brachial plexus neuritis, although the prognosis for reinnervation may be worse in the longest leg nerves (ie, peroneal and tibial).

Unilateral or bilateral diaphragm paralysis is present in about 7% of neuralgic amyotrophy patients and may predominate in the clinical picture (Tsairis et al 1972; Mulvey et al 1993; Tsao et al 2006). Isolated and recurrent phrenic nerve palsy following shoulder pain is recognized as a variant of brachial neuritis and may present with severe dyspnea of sudden onset (Gregory et al 1990; Lahrmann et al 1999; Kumar et al 2004). A retrospective analysis of 33 patients with idiopathic phrenic neuropathy found that 17 of these patients had clinical features of brachial neuritis (Tsao et al 2006).

Other clinical features. Classic brachial neuritis is easily recognizable from a patient's history by its onset and typical pain, proximal upper extremity symptoms, sequence of events, and a focused clinical exam. Diagnostic criteria were initially put forward for the hereditary variant for research purposes (Stogbauer et al 2000) and have been modified to include evolving genetic knowledge (van Alfen et al 2012) and the classic idiopathic phenotype (van Alfen et al 2015).

Recurrent attacks are not uncommon in idiopathic brachial neuritis. At least 25% of the patients suffer a recurrent episode within the first 5 to 10 years after their initial symptoms. There is currently no way to predict or prevent these recurrences. About 1 in 10 patients with brachial neuritis has a positive family history for the disorder that leads to a diagnosis of hereditary neuralgic amyotrophy. Onset in hereditary neuralgic amyotrophy is usually around the age of 20 years; nerves outside the brachial plexus are more often involved, and patients on average suffer more recurrences and have a worse prognosis than patients with the idiopathic variant. In hereditary neuralgic amyotrophy, the trait that predilects whether a patient will develop a focal neuritis is inherited in an autosomal-dominant fashion. Hereditary neuralgic amyotrophy is genetically heterogeneous, but to date only mutations or duplications in the SEPT9 gene on chromosome 17q25 have been found to be associated with the phenotype. SEPT9 alterations are found in 30% to 55% of families with hereditary neuralgic amyotrophy. How SEPT9 changes predispose someone to episodes of focal neuritis is unknown (van Eijk et al 2016).

Brachial neuritis can occur in all age groups and has also been described in children from birth to adolescence (van Alfen et al 2000; Host and Skov 2010). In neonates, there is an association with concomitant osteomyelitis of the humerus. Recognizing the disorder can be a challenge in young children because of limitations in eliciting a specific history and difficulties carrying out a detailed neurologic examination. Recovery of nerve function appears to occur more quickly than in adults and occurs in about 65%, usually within a year.

Prognosis and complications

The initial nerve trunk pain lasts 2 to 3 weeks on average but can last from a few hours to a few months. It will usually respond only partially to even a combination of strong analgesics (van Alfen and van Engelen 2006). The multifocal paresis will often start to recover after 2 to 4 months, with recovery of nerve function depending on the extent of axonal degeneration within each of the affected nerve fascicles. Most patients will attain about 70% to 90% recovery of nerve function over the course of 2 to 3 years, but many cannot use their strength fully because of an ineffective
compensating movement pattern (termed "scapular dyskinesia" if it involves shoulder blade stabilization) that follows the initial paresis. In practice, we find that many patients have relatively good serratus anterior strength if the muscle is tested selectively (ie, trunk upright, arm elevated to 80 degrees abduction in the scapular plane with elbow flexed, examiner pushing against elbow) but show clear medialization and winging during automatic reaching movements (for an example, see this video). The combination of altered shoulder biomechanics, decreased exercise intolerance of the affected limb, and subsequent overuse of both weak and compensating muscle groups is the main reason many patients develop a second type of persistent musculoskeletal pain after their initial nerve trunk pain episode. Long-term assessment of functional status in patients with neuralgic amyotrophy, however, has revealed significant pain and fatigue in 25% to 30% of patients and impairment in daily life activities in over 50% (van Alfen 2009).

Other often-found complications are rotator cuff tendon irritation because of off-centered movement of the glenohumeral joint that is caused by an imbalance in strength and motion of the scapular movers; deltoid muscle and rotator cuff action; and subsectoral nerve entrapment of the inferior and middle trunks caused by habitual shoulder adduction, elevation, and anteflexion in the painful arm. Subsectoral entrapment causes paresthesias and altered sensation in the medial forearm and hand, especially during activities where the arm is adducted or anteflexed (eg, working behind a computer or desk, sleeping on one's side). Symptoms mimic those of carpal tunnel syndrome or ulnar neuropathy, and additional EMG or ultrasound testing may be necessary to exclude these other common causes.

Recovery of diaphragm function caused by phrenic neuropathy is often protracted. A minority of patients recover within a few months, but in many it can take up to 3 or 4 years for any improvement to occur, and a subgroup will not recover at all (Hughes et al 1999; unpublished cohort observations).

**Clinical vignette**

A 37-year-old male was referred for electrodiagnostic evaluation of weakness in his left hand due to possible anterior interosseus nerve compression. Review of the patient's symptoms revealed a history of acute, severe pain in the left shoulder region 2 months prior to evaluation. Pain was worse on movement and was partly relieved by analgesics. A radiograph of the left shoulder joint was reported to be normal. There was no history of trauma, antecedent infection, or immunization. The intensity of pain decreased after 2 to 3 weeks, at which time he noted tingling and numbness over the outer aspect of forearm and weakness of the left thumb. Examination revealed marked weakness of the flexor pollicis longus and flexor digitorum profundus; the patient was not able to form an 'O' with the thumb and index finger. In addition, there was atrophy of the left infraspinatus muscle, winging of the right scapula, and decreased biceps and supinator reflexes on the left. There was no weakness of intrinsic hand muscles. The patient also reported that he had similar pain and weakness of the right shoulder 8 years earlier, with spontaneous recovery. He denied any family history of similar weakness.

Electrophysiologic study revealed normal motor and sensory nerve conduction of the median and ulnar nerves, reduced sensory nerve action potential amplitude of the lateral antebrachial cutaneous nerve, and compound muscle action potential of the anterior interosseus nerve on the left. Needle EMG showed active denervation in the supraspinatus, infraspinatus, flexor pollicis longus, and pronator quadratus. Chronic neurogenic changes were present in the right serratus anterior, probably related to the previous episode. Nerve ultrasound showed a focal increase in nerve size of the left median nerve in the distal upper arm, with an hyperechoic appearance of the epineurium surrounding a single fascicle. The typical history of neuritic pain and deficits in the distribution of the suprascapular, anterior interosseus, and lateral cutaneous nerve of forearm, with the typical finding of focal nerve inflammation on ultrasound, favored the diagnosis of neuralgic amyotrophy. Conservative treatment included analgesics and physical therapy. Follow-up at 3 months revealed significant improvement but an impaired ability to keep up in his job as an office clerk because of increasing pain around the shoulder and neck during the day.

**Biological basis**

**Etiology and pathogenesis**

Although the exact pathophysiological mechanism of brachial neuritis is unknown, the disorder is thought to occur from an interplay between a genetic predisposition, a mechanical vulnerability of the different nerve elements, and a subsequent autoimmune trigger for the attacks (van Alfen et al 2012). Even if the clinical picture of brachial neuritis is characteristic, the localization of the lesion appears to be multifocal rather than constrained to the brachial plexus itself. Localization confined to the region of brachial plexus does not explain several clinical and electrodiagnostic
observations: (1) isolated involvement of nerves, such as long thoracic, spinal accessory, or phrenic, which exit from the nerve roots proximal to the plexus; (2) severe denervation in the distribution of nerves arising from one part of the plexus with sparing of other nerves from the same trunk or cord; and (3) dissociated involvement of muscles supplied by the same nerve. Such findings can be attributed to a lesion distally in the peripheral nerves or a discrete proximal lesion of the fascicular fibers destined to constitute those nerves (Spillane 1943; Wilbourn 1985; England and Sumner 1987). With the advances of nerve imaging techniques using magnetic resonance neurography and high-resolution nerve ultrasound, it has become clear that the inflammatory nerve lesions can involve the peripheral nervous system at different levels, from the extrafascicular roots and interscalene brachial plexus elements to single peripheral nerves in the shoulder and upper arm regions (Aranzy et al 2015; Abraham et al 2016; Bäumer et al 2016; Lieba-Samal et al 2016). Overall, 4 patterns of involvement can be identified: (1) mononeuropathy, (2) mononeuropathy multiplex, (3) plexus with mononeuropathy, or (4) multiple combinations (Cwik et al 1990; Moghekar et al 2007), and brachial neuritis can be considered to consist of a phenotypic spectrum rather than one particular phenotype (van Alfen 2011).

Genetics. About 10% of brachial neuritis patients have a positive family history for the disorder. At the individual level, the signs and symptoms are the same as in the idiopathic form, but attacks tend to recur more often and more regularly involve nerves outside the brachial plexus (van Alfen and van Engelen 2006). Hereditary brachial neuritis or hereditary neuralgic amyotrophy is associated with missense mutations or duplication of a region within the SEPT9 gene on chromosome 17q in about 55% of North American families (van Alfen et al 2012). It is unknown how SEPT9 alterations lead to recurrent peripheral nervous system abnormalities. As no abnormalities in SEPT9 were found in 45% of the families, hereditary neuralgic amyotrophy must be genetically heterogeneous, but no other locus has been identified thus far. No genetic changes have been found in patients with idiopathic brachial neuritis (Klein et al 2009), but given the recurrence rate of 25% within 5 to 10 years, it is plausible to assume an association with predisposing genetic factor in idiopathic neuralgic amyotrophy as well.

Immunology. A variety of antecedent and precipitating factors have been recognized in all large series and case reports, but their role in the causation of the disease has not been elucidated, and the etiology of sporadic brachial neuritis remains unknown. The antecedent factors can be classified into (1) infections: nonspecific viral illnesses, influenza, Coxsackie virus, Epstein-Barr virus, Q fever, Mycoplasma pneumoniae, bacterial pneumoniae, typhoid, syphilis, HIV disease, dengue fever, and Lyme borreliosis (Parsonage and Turner 1948; Tsairis et al 1972; Post et al 2002; Tsao et al 2004; Wendling et al 2009; Verma et al 2011; Finney and David 2012). One study identified a concurrent hepatitis E infection in about 10% of patients with acute brachial neuritis (van Eijk et al 2014; van Eijk et al 2017); (2) immunizations: tetanus toxoid, diphtheria, swine flu, immune sera, and recombinant DNA hepatitis B vaccination (Reutens et al 1990; Stratton et al 1994); (3) surgery and child birth (Dumitru and Liles 1989; Malamut et al 1994; Lederman and Wilbourn 1996); and (4) miscellaneous: strenuous exercise, lumbar puncture, radiologic contrast administration, allergy desensitization, heroin addiction, severe asthma, interferon therapy, botulinum toxin injection for writer's cramp, Hodgkin disease, chemotherapy, hypersensitive reaction to lamotrigine, and thrombolytic therapy (Subramony 1988; Mulvey et al 1993; Sheean et al 1995; Hennessy et al 1998; Moghekar et al 2007).

Some evidence of an immune-mediated process has been observed in the form of altered lymphocyte subsets, with a decrease in CD3 values and an increase in the CD4:CD8 ratio. Increased blastogenic activity of lymphocytes was observed in cultures containing extracts from brachial plexus nerves but not from the sacral plexus; serratius anterior paralysis was correlated with the blastogenic response to an extract from the long thoracic nerve (Sierra et al 1991). Based on the temporal relationship of these events to the onset of disease, autoimmune mechanisms have been postulated; however, evidence to support this hypothesis is scanty, largely because of the inaccessibility of the anatomical structures involved. In addition, oligoclonal bands in the CSF and lymphocyte sensitization to brachial plexus nerves have been demonstrated, suggesting an immune-mediated process (Pierre et al 1990; Sierra et al 1991). The presence of multifocal mononuclear infiltrates in brachial plexus biopsies and antiganglioside antibodies in sera of patients with brachial neuritis further supports an immune basis (Suarez et al 1996; van Eijk et al 2011).

Biomechanical factors. About 10% of brachial neuritis attacks are reported to be preceded by physical strain of the upper extremity. Some patients experience an attack in the weeks following the occurrence of a (MRI-verified) cervical radiculopathy. It is speculated that attacks may have a predilection for certain peripheral nervous system segments, such as the upper trunk of the brachial plexus, because these segments are subject to more mechanical strain than other nerves. This everyday “wear and tear” may cause the blood-nerve barrier to be less tight in these spots, allowing the immune system access to peripheral nervous system tissue that is usually shielded from it. This may allow an autoimmune attack to develop (van Eijk et al 2016). In addition, biomechanical factors may also allow for torsion of
some affected nerves, such as the radial nerve, as has been demonstrated from several surgical studies (Pan et al 2014; Aranyi et al 2015).

Pathology. Pathologic studies are limited to occasional brachial plexus or superficial radial nerve biopsies. They have revealed epineural perivascular mononuclear T-cell infiltration and active multifocal axonal degeneration without vessel wall inflammation or necrosis, and perineural thickening (Suarez et al 1996; Klein et al 2002). In isolated cases, a B-lymphocyte germinal center has been found surrounding epineural and endoneurial vessels in a brachial plexus fascicle. Surgically excised nerve segments in brachial neuritis patients showed signs of moderate to marked inflammation, with scattered CD81 T-lymphocytes in nerve fibers and fascicles, abundant CD68 macrophages, and CD20 B-lymphocytes surrounding the endo- and perineurial vessels as well as variable degrees of axonal loss and replacement by fibrous tissue (Pan et al 2014). There is no evidence that brachial neuritis is caused by a peripheral nervous system vasculitis.

Epidemiology

Brachial neuritis has long been considered an uncommon neuromuscular disorder. The annual incidence was previously estimated to be 1.64 cases per 100,000 population in a retrospective cohort sample (Beghi et al 1985); however, there were also signs that the actual incidence might be higher (Spillane 1943; Parsonage and Turner 1948; MacDonald et al 2000; van Alfen and van Engelen 2006). A prospective study in the general population that provided a short clinical instruction for general practitioners regarding the recognition of the classic phenotype found an incidence rate of 1 per 1000 per year (van Alfen et al 2015).

The male-to-female ratio has been similar among various cohort studies and is approximately 2:1. Although cases have been reported at all ages (3 months to 71 years), the disease seems to be most prevalent in the 20- to 50-year-old age group (Parsonage and Turner 1948; Beghi et al 1985), with a mean age of onset of 40 years for the idiopathic form and around 25 years in the hereditary form. Brachial neuritis is a sporadic disorder, but occasional epidemic clusters have been reported (Bardos and Somodska 1961). In a retrospective study of nontraumatic brachial plexopathies, neuralgic amyotrophy constituted 48% of the cases (Mullins et al 2007).

Prevention

Although biomechanical strain (eg, sports or heavy labor) and immunologic events (eg, infections, immunizations, or childbirth) are reported to have triggered attacks in many cases, and these factors are implied in the pathophysiology, no practical recommendation can be given to prevent further attacks from occurring. Brachial neuritis patients are, therefore, advised to get the necessary vaccinations because the chance that they will become ill while travelling is probably much bigger than the chance that an attack will occur after such a vaccination. Of note, the incidence of brachial neuritis related to the administration of immune sera has probably decreased with marked decline in the use of such agents. There are also no special measures that a midwife or gynecologist need to take during delivery, as it does not seem to make any difference if women with brachial neuritis deliver naturally or via a caesarean section, and an epidural is not any more or less safe than other forms of pain control.

Differential diagnosis

In a typical case of brachial neuritis with acute severe neuropathic pain and patchy paresis that involves the long thoracic, suprascapular, and anterior intersosseus nerve, there is usually no other diagnosis to consider. However, some patients may have this phenotype as a consequence of a direct peripheral nervous system infection with Borrelia burgdorferi or HIV, so for patients in risk groups, these possibilities need to be evaluated. When patients present with more uncommon phenotypes, if painless attacks occur, or when symptoms are progressive in time or anatomical distribution, brachial neuritis needs to be distinguished from other diseases involving the brachial plexus as well as lesions outside the brachial plexus that lead to pain or atrophic paralysis around the shoulder girdle and arm.

In its initial stages, brachial neuritis may be (and often is) misdiagnosed as rotator cuff tendonitis or subacromial bursitis. However, these glenohumeral pathologies will cause pain in the shoulder joint and lateral upper arm on both active and passive movement attempts, and no paresis is found in other upper extremity muscles. Isolated peripheral nerve lesions may be mistaken for entrapment neuropathies, especially if they involve the anterior or posterior intersosseus nerve. Importantly, several studies looking at MRI abnormalities in anterior and posterior intersosseus nerve syndrome found inflammatory lesions in median and radial nerve fascicles in the upper arm, respectively, rather than
amyotrophy, relieving pain in 60% of the patients (Pham et al 2014; Bäumer et al 2016), and another study found that all 123 patients with suspected nontraumatic anterior interosseous nerve palsy had multifocal nerve involvement on careful clinical, EMG, and MRI examination that fit the phenotype of brachial neuritis (Maldonado et al 2016). Brachial neuritis is often mistaken for a cervical radiculopathy initially; however, careful clinical examination will reveal patchy, multifocal involvement of nerves that cannot be explained by affaction of a single root. Cervical spine abnormalities on MRI should be interpreted with care as degenerative changes are present in a very large proportion of the general population (Nakashima et al 2015).

In patients with pain and progressive symptoms, a malignancy such as metastasis, a Pancoasts syndrome or neurolymphomatosis needs to be ruled out by means MRI or PET-CT imaging. If progression is painless, multifocal inflammatory demyelinating neuropathy (also called MADSAM neuropathy or Lewis-Sumner syndrome) and multifocal motor neuropathy need to be considered, and EMG and nerve imaging studies should be performed accordingly (Goedee 2017). Brachial neuritis may be associated with various systemic diseases, such as systemic lupus erythematosus, giant-cell arteritis, polyarteritis nodosa, infectious mononucleosis, Hodgkin disease, cytomegalovirus infection, and inflammatory bowel disease (Subramony 1988). Brachial neuritis is distinguished from poliomyelitis by cutaneous sensory symptoms, a normal CSF, and absence of constitutional symptoms.

**Diagnostic workup**

There is no definitive "litmus" test that can unequivocally rule in or rule out brachial neuritis. In typical cases with a classic presentation, the diagnosis can usually be made clinically, and no further testing is required. However, when there is uncertainty about the diagnosis for whatever reason (eg, an uncommon phenotype or presentation, unfamiliarity with the disorder, uncertainty about the course of symptoms, or presence of additional morbidities that cloud the clinical picture) it is recommended to seek additional diagnostic confirmation by performing a tailored EMG examination (Wilbourn 1985) and/or imaging of the plexus and upper extremity nerves using MRI or ultrasound (Pham et al 2014; Lieba-Samal et al 2016).

Routine laboratory studies on blood, urine, and CSF examination are unremarkable in brachial neuritis and do not add to the diagnostic workup. In patients who are at risk for *Borrelia burgdorferi* or HIV, serologic testing is required to rule out a direct infection of the peripheral nervous system. For patients, especially middle-aged men, with an extensive clinical phenotype (eg, bilateral brachial plexus involvement and phrenic nerve affection), hepatitis E virus serology and PCR confirmation may reveal acute hepatitis E infection as a trigger of the symptoms.

Although mild elevation in CSF protein has occasionally been noted and oligoclonal bands in CSF have been found (Devathasan and Tong 1980; Pierre et al 1990; van Alfen and van Engelen 2006), lumbar puncture is rarely indicated for brachial neuritis unless there is a need to rule out intrathecal infection or malignancy.

On EMG examination, routine motor and nerve conduction studies are often within normal limits (van Alfen et al 2009b), although decreased amplitudes can be found in clinically affected nerves. Because of the limited sensitivity of sensory conduction studies, a normal sensory examination does not necessarily point to a radicular origin of symptoms. To further complicate matters, patients with brachial plexitis can also show paraspinol signs of denervation. However, a careful needle EMG examination of clinically affected muscles will show the multifocal origin of the pathology to support a diagnosis of brachial neuritis.

Imaging of the brachial plexus with either ultrasound or MRI may show focal areas of nerve swelling and changes in signal intensity in clinically affected nerves that are compatible with inflammation or repair (Gaskin and Helms 2006; Scalf et al 2007; Corato et al 2014; Park et al 2014; Aranyi et al 2015; Lieba-Samal et al 2016). Both techniques may also show denervation, atrophy, and fibrotic changes in the affected muscles, depending on the disease stage. The sensitivity and specificity of these techniques is yet unknown.

**Management**

**Drug treatment.** In the acute phase, adequate pain control is a priority for most patients. The initial nerve trunk pain, which typically has a Numeric Rating Scale (NRS) score for pain of 7/10 or higher, usually does not respond to first-line, over-the-counter analgesics, such as acetaminophen or an NSAID. A combination of a long-acting opioid analgesics with a nonsteroidal anti-inflammatory drug was found to be most effective in a large cohort study of neuralgic amyotrophy, relieving pain in 60% of the patients (van Alfen and van Engelen 2006). Co-analgesics usually take too
long to become effective and are not advised. For the secondary types of pain that many brachial plexitis patients go on to suffer, medication or even invasive pain treatments are usually ineffective in the long term, and other factors, such as altered movement patterns, strain, and keeping an overall energy balance, need to be addressed.

When patients are seen early and the pain is still severe, a short course of corticosteroids may help relieve pain and enable recovery. Oral prednisolone or prednisone 60 mg/day (or 1 mg/kg/day for children or patients over 100 kg), for a week followed by tapering with 10 mg/day for the next week may be used for this purpose. The sooner corticosteroids can be started, the higher the chance they will help decrease symptoms (van Eijk et al 2009). Clinically, a responder can be described as someone in whom the severe pain largely disappears within 24 hours after starting steroids. In practice, it is advisable to start as soon as possible, preferably within the first week but no later than after 2 weeks and not when the pain is already decreasing by itself. Chronic steroid use is not warranted in brachial plexitis.

Immunomodulatory treatment is generally not indicated because brachial neuritis is a monophasic illness with a relatively good spontaneous recovery of nerve function. Several small case series suggest intravenous immunoglobulins may be effective, but costs are high, and in some of the patients described it is unclear whether the course really differed from expected given the natural history of the disorder (Tsao et al 2004; Nakajima et al 2006; Johnson et al 2011; Naito et al 2012).

In hepatitis E virus-associated acute brachial neuritis, experts recommend that in acute cases with progressive symptoms, treatment with ribavirin and prednisone should be started (Dalton et al 2016), although the outcome with that treatment seems variable (van Eijk et al 2017).

Rehabilitation. Persistent pain, decreased endurance of the affected limbs, severe fatigue, and impairment of daily life activities are present in a large proportion of brachial plexitis patients (Cup et al 2013). Many patients in the subacute and chronic phase continue to use analgesics and can make only limited use of their arms during walking, keyboard use, or overhead tasks without an increase in pain. No indications were found in this disorder for either underlying psychopathology, a chronic pain syndrome, or chronic fatigue syndrome (van Alfen et al 2009). Residual symptoms are strongly correlated with altered biomechanics of the shoulder girdle, and altered movement patterns can lead to strain of the paretic and compensating muscles, even when weakness is no longer present. As this causes persistent myalgia and fatigue, any rehabilitation program for brachial plexitis should address these issues specifically (van Eijk et al 2016).

"Routine" physical therapy for shoulder disorders, which is usually aimed at strengthening the rotator cuff muscles and maintaining glenohumeral range of motion, has been found to be ineffective or to worsen symptoms in half of the patients with brachial plexitis (Cup et al 2013). A more comprehensive and multidisciplinary rehabilitation strategy showed improvement in activities, performance, and participation in 75% of the patients (Ijspeert 2013). The program uses physical and occupational therapy, and focuses on disease-specific patient education, regaining scapulothoracic and glenohumeral coordination (ie, technique rather than strength training), gradually increasing exercise tolerance, optimizing ergonomics and efficiency of arm use, and recognizing and respecting the limits of physical functioning.

Surgery. For patients with severe, Sunderland grade IV nerve damage who have intraneural scarring that prevents axonal sprouting and reinnervation, surgical neurolysis or excision and grafting of the damaged nerve segment may help recovery (Pan et al 2011; Pan et al 2014). Such lesions can be inferred when there is a severe paresis or paralysis with a lack of any recovery after 6 to 12 months and the appearance of a scarred, string-of-beads-like or torsioned appearance on nerve ultrasound. In selected cases with axillary nerve damage that shows no signs of recovery, a radial-to-axillary nerve transfer can be considered to restore some deltoid muscle function.

Special considerations

Pregnancy

Pregnancy and childbirth have been recognized as precipitating factors for the development of brachial neuritis, especially the familial variety. The clinical course and prognosis are similar to other cases of brachial neuritis (Dumitr and Liles 1989). Patients with diaphragm dysfunction are at a higher risk for pulmonary compromise due to pregnancy-related changes in lung function (Faust and Wilson 1992). There are no special measures that a midwife or gynecologist can or needs to take during delivery as it does not seem to make any difference if women with brachial neuritis deliver naturally or via a caesarean section, and an epidural is not any more or less safe than other forms of
pain control.

**Anesthesia**

Although surgical procedures constitute a well-known precipitating event, the role of surgery and anesthesia in the pathogenesis of brachial neuritis is unclear (Parsonage and Turner 1948; Malamut et al 1994). The possibility of traction or compressive injury to the brachial plexus during surgery is excluded on the basis of delayed onset of pain and weakness. Surgery has been performed without complications in the setting of brachial neuritis; however, special attention to preoperative evaluation and choice of anesthesia is required if there is diaphragm paralysis (Ennis and Bednar 1992; Faust and Wilson 1992).

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**References especially recommended by the author or editor for general reading.**

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**ICD and OMIM codes**

**ICD codes**

ICD-9:
Brachial neuritis or radiculitis NOS: 723.4

ICD-10:
Brachial neuritis or radiculitis NOS: M54.1

**OMIM numbers**

Hereditary neuralgic amyotrophy (neuritis with brachial predilection): #162100

**Profile**

**Age range of presentation**

01-23 months
02-05 years
06-12 years
13-18 years
19-44 years
45-64 years
65+ years

**Sex preponderance**

male>female, >2:1
male>female, >1:1

**Family history**

family history may be obtained

**Heredity**

heredity may be a factor
autosomal dominant

**Population groups selectively affected**

none selectively affected

**Occupation groups selectively affected**

none selectively affected
Differential diagnosis list

hereditary neuralgic amyotrophy
acute poliomyelitis
diseases involving brachial plexus
lesions outside brachial plexus
systemic diseases
systemic lupus erythematosus
giant cell arteritis
polyarteritis nodosa
infectious mononucleosis
Hodgkin disease
cytomegalovirus infection
HIV infection
inflammatory bowel disease
neoplasms
radiation plexopathy
hereditary neuropathy with predisposition to pressure palsy
poliomyelitis
cervical root syndromes
vertebral artery dissection
isolated lower cranial nerve lesions
rotator cuff tendonitis
subacromial bursitis
peripheral nerve lesions
entrapment neuropathies

Associated disorders

Cytomegalovirus infection
Ehlers-Danlos syndrome
Familial neuralgic amyotrophy
Giant cell arteritis
Hepatitis E virus infection
HIV infection
Hodgkin disease
Idiopathic brachial neuritis
Infectious mononucleosis
Lamotrigine sensitivity
Polyarteritis nodosa
Systemic lupus erythematosus

Other topics to consider

Brachial plexus palsy in neonates
Charcot-Marie-Tooth disease types CMT2, CMT4, CMT with intermediate conduction velocities, and others
Epstein-Barr virus infections of the nervous system
Headache associated with AIDS
Neurologic complications of chemotherapy
Peripheral nerve complications of HIV-1 infection

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