FEATURE ARTICLE

Neurogenic thoracic outlet syndrome: An often overlooked but treatable condition

Rely primarily on a patient's history and your physical examination findings in considering the diagnosis. Physical therapy, tricyclic antidepressants or SNRIs, and botulinum toxin type A injections can help control symptoms.

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Ms. R, a 25-year-old woman who sustained a whiplash injury in a car accident within the year, schedules an office visit for evaluation of pain she has been experiencing for 7 months in the right side of her neck and the trapezius. The pain radiates down the medial aspect of her right arm to the 4th and 5th digits, and it worsens when she brushes her hair or lifts bags of groceries. She feels her quality of life is significantly impaired because her limited arm movement makes it hard to hold her 1-year-old child. She also experiences headaches more frequently than she did before the accident.

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A complex pain syndrome

This patient's clinical presentation of pain radiating from the neck to the arm and hand following trauma to the neck is typical of nerve irritation associated with neurogenic thoracic outlet syndrome (NTOS).[1] The disorder is complex and characterized by different neurovascular signs and symptoms involving the upper limbs.[2] Trauma from an external kinetic force is not the only cause of NTOS. Stresses from repetitive movement can also be at fault. Assembly line workers, violinists, and data entry professionals are especially vulnerable given the nature of their work. Athletes using frequent overhead arm motion in their sport (eg, volleyball players, baseball pitchers, weightlifters, swimmers) are also at risk for this syndrome.

Estimates of thoracic outlet syndrome frequency vary widely, from 3 to 80 cases per 1000 individuals.[3] NTOS mainly affects patients in the third and fourth decades of life and has a female to male ratio of 3.5-4:1.[4] Although NTOS is not common, family physicians are likely to be the first to evaluate patients who have symptoms and a history suggestive of the disorder. A lack of distinctive clinical indicators can make diagnosis difficult. But disregarded, this often underappreciated syndrome can lead to functional impairment, emotional upheaval, and impaired quality of life. For individuals with severe symptoms, the adverse impact on quality of life has been compared with that of patients suffering from chronic heart failure.[5]

A brief tour of the anatomy involved

Thoracic outlet syndrome manifests as "upper extremity symptoms due to compression of the neurovascular bundle by various structures in the area just above the first rib and behind the clavicle."[6] This neurovascular bundle consists of the trunks of the brachial plexus and the subclavian vessels. As these vital structures course from the neck into the upper arm, potential sites for compression include the interscalene triangle, costoclavicular triangle, and subcoracoid space deep to the pectoralis minor tendon. In 1956, Peet and colleagues first coined the term *thoracic outlet syndrome* (TOS) to encompass previously described disorders involving compression of these neurovascular structures.[7] Compression of the brachial plexus, a hallmark of NTOS, can occur in all 3 of these anatomic spaces. But most cases involve compression within the interscalene triangle.[3]

Congenital abnormalities, including first ribs and fibrous bands, may also be sources of neurovascular compression. Although present in less than 1% of the population, cervical ribs and associated fibrous bands usually lie within the middle scalene muscle, thereby narrowing the space within the scalene triangle through which the nerve roots of the brachial plexus pass.[1]

Factors that can precipitate NTOS

Virtually any injury that causes chronic cervical muscle spasm, such as hyperextension-flexion injuries, may precipitate NTOS.[8,9] Whiplash injury, exercise-induced scalene muscle hypertrophy, hypertrophied anterior scalene muscles, and repetitive work-related injuries can bring on the syndrome. Risk factors for NTOS are not entirely understood, although many patients with NTOS exhibit a congenital predisposition, such as cervical ribs, in addition to a history of trauma or repetitive stress on the scalene muscles. Chronic stress of the cervical musculature, specifically the anterior scalene and middle scalene muscles (ASM and MSM, respectively), is strongly implicated in the development of NTOS and chronic pain. Cervical muscle spasm involving the ASM and MSM places traction on the brachial plexus/thoracic outlet.[8] The mainstay of current minimally invasive treatment targets these muscles in an attempt to decrease spasm.[10-14]

Clinical presentation

Pain is a foremost feature of NTOS, although other symptoms can include sensory loss, shoulder and neck discomfort, arm paresis or edema, headache, and even sympathetic nervous system impairment.[8]

Arm exertion and elevation aggravate the symptoms, which typically occur after exercise rather than during exercise. Pain often radiates from the shoulder down along the inner aspect of the arm. Patients may also have pain in the neck, anterior chest wall, trapezius, or mastoid. Occipital headaches secondary to brachial plexus compression along C5–C7 are common.

An estimated 95% of TOS cases are neurogenic in origin,[15] with arterial or venous anomalies accounting for the remainder. True NTOS, characterized by objective findings consistent with brachial plexus compromise, account for just 1% of NTOS cases. The other 99% of neurogenic cases lack objective findings, are more difficult to define, and are deemed nonspecific NTOS.[16]

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Diagnosis

Physical examination findings are most important

A thorough history and physical examination are the basis for NTOS diagnosis.[17]

Palpation may elicit tenderness over the scalene muscles, subcoracoid space, anterior chest wall, or trapezius. There is often decreased sensation to light touch in the fingers, especially over the 4th and 5th digits.[2] Light percussion over the brachial plexus in the neck may elicit tingling or a "pins and needles" sensation—the Tinel sign—in the affected nerve distribution. These findings, as well as worsening symptoms with other provocative maneuvers, can help distinguish NTOS from other pathologies, such as carpal tunnel syndrome or degenerative disorders of the cervical spine.

Additional provocative tests (eg, Adson maneuver, nerve tension tests) have unknown reliability and specificity for NTOS. However, these examinations can assist in assessing patients. Some experts believe the elevated arm stress test (EAST) most consistently elicits NTOS symptoms.[17] To perform the EAST, abduct the patient's affected arm 90 degrees in external rotation while having the patient open and close the hand slowly over 3 minutes. A patient with NTOS typically reports neck and shoulder pain with paresthesias, often occurring in the medial aspects of the arm, forearm, and last 2 fingers.

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Of note, a considerable proportion of the population will compress their radial pulse on hyperabduction maneuvers, but they do not have vascular TOS. Patients who present with neurogenic symptoms and have diminished pulse upon hyperabduction of the arm are frequently mislabeled as having vascular TOS. This sign, however, should make you suspect that the thoracic outlet could be tight and that the constellation of the neurogenic symptoms with the physical exam findings could be consistent with neurogenic TOS.

Imaging has limited usefulness

An x-ray of the chest or neck can identify cervical and anomalous first ribs.[18] A growing body of research has also focused on using magnetic resonance imaging (MRI) to evaluate patients with suspected NTOS.[19] In general, MRI and computed tomography (CT) are more useful for identifying other symptomatic conditions than for establishing a diagnosis of NTOS.[3]

Diagnostic anterior scalene block

One of the more effective methods for confirming a diagnosis of NTOS is the intramuscular anterior scalene block. The block temporarily paralyzes the muscle in spasm and allows the first rib to descend, which decompresses the thoracic outlet. Symptom reduction in response to the block correlates well with outcomes for surgical decompression. The block may be performed under guidance with electromyography (EMG), ultrasound, and, more recently, CT. Data on CT guidance indicate that this imaging modality minimizes such complications as brachial plexus block, dysphonia, and Horner's sign.[4]

Electrodiagnostic studies more useful in excluding other disorders

There is no solid evidence to suggest that electrodiagnostic testing such as EMG and nerve conduction velocity (NCV) have diagnostic utility for NTOS, and results are often normal in patients with the syndrome.[2,8] EMG and NCV are helpful to exclude other neurologic abnormalities, such as radiculopathy, carpal tunnel syndrome, cubital tunnel syndrome, polyneuropathy, and motor neuron disease.[6]

Additionally, the medial antebrachial cutaneous (MAC) nerve conduction study has been identified as a sensitive test to detect milder cases of NTOS.[2] It measures the sensory function of the lower trunk of the brachial plexus. Results of this test can be abnormal in patients whose EMGs and NCVs are normal. MAC studies may help to provide objective evidence of NTOS, but more research is needed to validate this test before its routine use can be recommended.

CASE: Ms. R's exam findings

On physical examination, Ms. R has tenderness over the right anterolateral neck, just posterior to the sternocleidomastoid muscle. She has normal light touch and pinprick sensation in the right upper extremity. Strength is 4+/5 in the right arm and 5/5 in the left arm. Elevated arm stress testing reveals a reproduction of her symptoms at 15 seconds. MRI of her neck is negative for stenosis, disc bulge, or prior surgery. EMG conduction testing of her right arm is normal. Chest x-ray is negative for a cervical rib. Duplex scan of her right carotid, internal jugular, and axillary vessels is negative for stenosis and thrombosis.

Treatment

The clinical variability of NTOS is wide, and much debate continues regarding treatment strategies for these patients.

Medications and physiotherapy are first-line options

The initial approach to treating NTOS is conservative. A typical plan involves behavior modification, a course of physical therapy, and medication. Because NTOS displays neuropathic features, tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors (SNRIs), and membrane stabilizers (eg, gabapentin) may help to manage symptoms. Nonsteroidal anti-inflammatory agents and muscle relaxants are frequently prescribed for pain, as well. If pain persists and a patient's quality of life continues to be impaired, sustained-release opioids may prove useful.[8]

Minimally invasive approaches

An area of increasing focus is nonsurgical, minimally invasive techniques to decompress the interscalene space. Injection of medications into the cervicothoracic musculature is a strategy aimed at diminishing pressure within the interscalene space by relaxing the scalene muscles, thereby decreasing compressive symptoms and nerve irritation.[2] Agents include local anesthetics, corticosteroids, and, more recently, botulinum toxin type A (BTX-A). Modalities employed to ensure accurate injection have included anatomical landmarks, EMG, ultrasound, CT, or a combination of ultrasound/EMG or fluoroscopy/EMG.

Although local anesthetics may help to reduce pain, relief is brief. Such injections are more useful in confirming the diagnosis, predicting surgical outcomes, assessing candidacy for BTX-A therapy, and determining the reversibility of symptoms.[2]

BTX-A. This toxin, derived from *Clostridium botulinum,* has been a scientific curiosity since its discovery in 1897. Its mechanism of action targets the neuromuscular junction, blocking the release of acetylcholine from presynaptic terminals. By the mid-1980s, BTX-A emerged as an effective therapy for strabismus and blepharospasm.[20] Since that time, BTX-A has been approved to treat hemifacial spasm, cervical dystonia, glabellar lines, hyperhidrosis, and chronic migraine.

BTX-A works by reducing muscle overactivity and, possibly, decreasing pain and inflammation. BTX-A injected into the anterior scalene muscle alone, or into more than one scalene muscle along with the upper thoracic or chest wall muscles, has effectively reduced symptoms of NTOS.[10,21]

Histologic studies demonstrate that injury to either the anterior or middle scalene muscles contributes to most of the pathology in NTOS.[1,10] Muscle fibrosis is the most significant histologic finding, showing that scar tissue occurs 3 times more frequently than other pathologic changes.[10] Interestingly, some animal data suggest that BTX-A may improve wound healing in injured muscles and reduce the risk of scarring. Human studies show benefit from BTX-A injection into muscles affected by radiation fibrosis syndrome.[10]

Cervical muscle spasm and, probably, fibrosis place traction on the brachial plexus/thoracic outlet and lead to muscle and nerve edema, neural compromise, and spatial narrowing of the outlet. The application of BTX-A to targeted scalene muscles can ease the symptoms of NTOS.

Although the use of BTX-A for NTOS is off label, so is its use for many other non–FDA-approved applications. Due to its history of safety and therapeutic benefit, BTX-A is also used to treat piriformis syndrome, lateral epicondylitis, achalasia, and oromandibular dystonia.

In clinical practice, doses of BTX-A injections into the ASM range between 12 and 25 units[10]; however, much study and debate continues regarding the optimal dosage, targeting of muscle groups, and patient selection. Symptomatic relief can last up to 6 months, although the average duration of pain relief is slightly beyond 3 months,[8] which is the approximate duration of action of BTX-A in other applications.[22]

Larger doses of BTX-A, more frequent use, and higher protein load increase the chance that patients will develop neutralizing antibodies.[22] Antibodies often diminish the duration of action and the maximal therapeutic effect of BTX-A. Therefore, it's prudent to use the lowest effective dose over the greatest time interval while still aiming for a reasonable duration of pain relief. Author PC does not repeat dosing until 3 months have passed.

Several studies have shown BTX-A injection into the ASM alone, or into more than one scalene muscle along the upper thoracic or chest wall muscles, to be effective in NTOS patients.[8] In a prospective longitudinal study by

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Christo et al, patients underwent CT-guided BTX-A injections of the ASM.[10] After 3 months, patients experienced a 29% decrease in their pain as well as an approximate 15% reduction in their visual analog scale score. A prior study by Torriani and colleagues also showed similar promising results, but the mean duration of improvement after BTX-A injection was 31 days.[21]

To date, only one randomized controlled trial involving BTX-A for TOS has been completed.[11] Interestingly, it failed to detect a clinically or statistically significant reduction in pain for subjects treated with BTX-A. This study had several limitations, thus making it difficult to interpret the results. For instance, patients in the BTX-A treatment group had experienced, on average, nearly 6 years of symptoms. The investigators noted that many of these patients had already developed chronic pain with central sensitization, making it unlikely that a single intervention would significantly reduce pain. Injections were also guided with EMG as opposed to more precise modalities, such as MRI, CT, or ultrasound.[10,11,23]

Surgical decompression of the thoracic outlet is an option for patients who have not obtained adequate relief with conservative therapies.

Surgical intervention

Surgical decompression of the thoracic outlet is an option for patients who have not obtained adequate relief with conservative therapies.[24] However, the benefits of surgery are controversial given the difficulties in objectively establishing a diagnosis, a lack of uniform indications for surgery, variations in surgical technique, and a lack of objective postoperative outcomes metrics.[25] Many studies are based on small sample sizes and do not report long-term data.

A variety of surgical techniques, used for more than 50 years in the treatment of NTOS, include scalenectomy alone, first rib resection alone, or first rib resection with scalenectomy (FRRS). Overall, surgical success rates can be as high as 90% with low complication rates, but persistent disability in 60% of patients one year following surgery with more than a 30% complication rate has also been reported.[26,27]

Predictors of success with surgery. Predicting which patients will benefit from surgical intervention has been a challenge for surgeons and pain specialists. Recent studies have looked at patient selection and factors that may be associated with surgical failure. Rochlin et al retrospectively reviewed 161 patients with NTOS who underwent surgical intervention (182 FRRS procedures) from 2003 to 2011, and looked for evidence of unresolved, recurrent, or contralateral neurogenic symptoms after FRRS.[28] Patients with poorer outcomes tended to be older and actively smoking, have more comorbid pain syndromes and neck or shoulder disease, and have experienced a long duration of symptoms.

Caputo et al showed that younger patients tend to be better surgical candidates.[29] In this retrospective review of 189 patients undergoing supraclavicular decompression (scalenectomy, brachial plexus neurolysis, and first rib resection, with or without pectoralis minor tenotomy) for NTOS, adolescents had more favorable preoperative characteristics and enhanced 3-month and 6-month functional outcomes than adults.[29]

In general, preoperative factors associated with a poor postoperative course are active smoking, age >40 years, and a need for opioids to control pain.[30] A need postoperatively for opioids or injections of BTX-A, steroids, or local anesthetics likely indicates that surgery has failed.[30] Strict patient selection for surgery has become a critical determinant of the NTOS treatment algorithm.

CASE: Ms. R obtains pain relief

Ms. R was treated with physical therapy for 2 months, NSAIDs, and a muscle relaxant. She noted a 20% improvement in pain, but she requested more relief. A CT-guided anterior scalene block was then performed, producing 50% relief of her symptoms. Next, she was offered the choice of decompressive surgery or BTX-A therapy, and she elected to try BTX-A. She was treated with 25 units of BTX-A injected into the anterior scalene muscle. At the 2-month follow-up, Ms. R reported 60% relief of her pain, improved functional use of her arm, and better strength.

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