

Severe Limb-Threatening Ischemia: Thoracic Outlet Syndrome

Archana Roy, MD, FACP

Thoracic outlet syndrome (TOS) is a well-described clinical entity that occurs in adults, with nerve compression being the most common presentation. The term TOS was introduced by Peet et al¹ in 1956 and was later defined by Rob and Standeven² as a set of symptoms that may exist due to compression on the brachial plexus and subclavian vessels in the region of the thoracic outlet. The wide variability of symptoms and lack of a single, accurate test that can confirm the diagnosis make TOS difficult to identify. It has been suggested that TOS may be the most frequently overlooked and misdiagnosed syndrome.^{3,4}

This article presents a case of TOS with rare arterial complications in a patient who was previously diagnosed with scleroderma and Raynaud's phenomenon. Coexistence of scleroderma with Raynaud's phenomenon makes the diagnosis of TOS particularly challenging; therefore, signs and symptoms helpful in differentiating Raynaud's phenomenon from ischemic complications of TOS are described. The etiology of TOS and diagnostic and therapeutic approaches are also reviewed.

CASE PRESENTATION

History

A 39-year-old woman presented to the emergency department with complaints of left hand pain, numbness, and bluish discoloration of her left ring finger. She awoke with these symptoms, which progressed over 8 hours before she presented. Her medical history was significant for scleroderma with Raynaud's phenomenon diagnosed a few years ago. She denied tobacco or alcohol use, exposure to cold, and use of any new medications. The patient worked as a secretary, and she denied history of recent hospitalization, surgery, or trauma. She had no risk factors for deep vein thrombosis.

Physical Examination

The patient's vital signs were normal. Skin examination showed thickening over the dorsum of the fingers and loss of substance from the finger pad without digital gangrene or ulcers. Cardiac, pulmonary, and abdomi-

nal examinations were unremarkable. Her left forearm and hand were cold, pale, and numb, and her left ring finger had bluish discoloration. Left arm pulses were not palpable. Unilateral symptoms with absent pulses suggested arterial occlusion rather than Raynaud's phenomenon. There was no swelling, engorged veins, or motor deficits of the left arm.

Laboratory and Imaging Studies

Complete blood cell count, metabolic panel, and screening coagulation tests were normal. Chest radiograph did not show any abnormalities. Arterial occlusion was suspected, and urgent angiogram was performed. Angiography showed that the mid left subclavian artery was tortuous and irregular, with a short focal 50% stenosis at its mid distal aspect. There was abrupt occlusion of the left brachial artery at the level of the proximal mid humerus, suggestive of a thrombus. Extensive collateral vessels reconstituted the left brachial artery at the mid distal humerus. Just above the left elbow joint, there was abrupt occlusion of the left brachial artery with reconstitution of the left interosseous artery consistent with a second thrombus. Delayed imaging showed a diminutive and irregular left ulnar and radial artery, with extremely sluggish flow almost up to the level of the wrist. There was markedly limited filling of the arteries of the wrist and palmar arch and no significant filling of any of the digital arteries. When the patient's left arm was extended in an extremely abducted position, there was complete occlusion of the left mid subclavian artery. Fluoroscopic examination of the patient's cervicothoracic junction demonstrated a small left cervical rib.

Diagnosis and Treatment

The patient's symptoms were thought to be related to thromboembolic occlusion of the left arm arteries caused by the cervical rib. Standard anticoagulation was started as soon as the diagnosis was made. She

Dr. Roy is an assistant professor of medicine, Mayo Clinic College of Medicine, and consultant, Division of Hospital Medicine, Mayo Clinic, Jacksonville, FL.

underwent surgical resection of the cervical rib without complications and with complete resolution of her symptoms. Later, the patient revealed that she had slept with her left arm hyperabducted the night before admission. Prolonged and complete occlusion of the left mid subclavian artery in the hyperabducted position followed by multiple distal emboli was most likely the cause of her symptoms.

DISCUSSION

Etiology

TOS is caused by obstruction of the neurovascular bundle of the arm as it passes from the thoracocervical region to the axilla. Three anatomical areas make up the thoracic outlet: (1) the scalene triangle, which comprises the spaces between the scalene muscles as they attach to the first rib; (2) the costoclavicular space, which is the space bordered by the clavicle, first rib, and costoclavicular ligament anteriorly and the posterior border of the middle scalene muscle posteriorly; and (3) the subcoracoid space, which is the space beneath the pectoralis minor muscle and the coracoid process.

Several congenital and acquired abnormalities can compromise these spaces, thus leading to TOS. Common causes of TOS include bony abnormalities, such as cervical ribs or an anomalous first rib; a large transverse process of the seventh vertebra; or abnormal soft tissue structures, such as fibrous band, ligaments, or hypertrophic scalene muscle. Cervical rib causes a chronic intermittent extrinsic compression of subclavian vessels leading to stenosis, tortuosity, and irregularity that predisposes to thromboembolism. Ischemia may be precipitated when there is complete occlusion of blood flow due to either thromboembolism or hyperabduction of the arm. An estimated 0.12% to 1% of the general population has a cervical rib; however, less than 10% of patients with a cervical rib develop TOS and even fewer develop vascular complications.⁵

Sagging musculature related to aging, obesity, or heavy breasts are common but underappreciated causes of TOS. Abnormal posturing, such as that caused by carrying a heavy backpack or sitting with marked forward angulations of the upper trunk and neck, may also contribute to TOS.⁶ Structural abnormalities, such as traumatic laxity of the costoclavicular joint and separation of the sternoclavicular joints, may also cause TOS.

Pathophysiology

Neurovascular complications in TOS occur from long-standing and intermittent vascular compression. Compression of the subclavian vein in TOS can cause transitory hand edema or pain and pallor during hy-

perabduction. However, venous thrombosis can also occur after prolonged compression (eg, after vigorous shoulder activity). Pulmonary embolism resulting from TOS-related thrombus has been described.⁷ Major arterial pathologic changes caused by TOS can be classified as follows⁸: (1) subclavian artery stenosis at the thoracic outlet; (2) poststenotic dilation of subclavian artery or aneurysm formation; (3) partial or complete thrombosis of subclavian artery; (4) embolic complications to the axillary, brachial, radial, and ulnar arteries; and (5) microembolic complications to the digital, palmar, or interosseous vessels. In patients with chronic intermittent compression, collateral circulation usually develops to maintain circulation of the upper extremity.

Clinical Presentation

Patients with TOS may present with neurologic, vascular (venous or arterial), or combined symptoms (**Table 1**). Neurologic manifestations include pain and paresthesia in the affected limb, followed by sensory and motor deficit in advanced cases. Vascular presentation includes either venous occlusion characterized by swelling or edema, pain, cyanosis, and venous engorgement in the affected limb or arterial occlusion characterized by pallor, pulselessness, and coldness of the limb associated with pain and numbness, as was seen in the case patient. Busetto et al⁹ developed the nerve, artery, and vein (NAV) classification of TOS (**Table 1**) that defines the severity of compression of these 3 structures.⁹ **Table 2** lists the clinical manifestations and suggested treatments of TOS in various stages.

Arterial Thoracic Outlet Syndrome Versus Primary Raynaud's Phenomenon

Typically, the diagnosis of arterial TOS is made only after a thromboembolic complication has already occurred and is rarely made early in its course. Initially, symptoms can be mild and may be overlooked by both the patient and physician. In advanced cases or when the diagnosis has been delayed, major arterial occlusion and potentially limb-threatening ischemia can occur. Raynaud's phenomenon, characterized by episodic pallor, coldness, and cyanosis, occurs in almost all patients with scleroderma. It may occur many years before skin changes of scleroderma are evident. Therefore, it is important to distinguish primary Raynaud's phenomenon from ischemic complications of TOS, which could be an early manifestation of bilateral cervical ribs.¹⁰ Raynaud's phenomenon usually presents bilaterally, and distal pulses remain intact. Often, there is a clear history of cold exposure. Pulselessness is not a feature of Raynaud's phenomenon. In contrast, arterial occlu-

sion is characterized by pulselessness, pallor, and coolness of the affected limb. Pain and paresthesia develop later and suggest critical ischemia and threat to limb viability. When motor weakness or paralysis begins to develop, the potential for limb loss is very high. Arterial complications are rare but serious, as they can rapidly lead to limb loss. Therefore, urgent diagnostic work-up and treatment are crucial.

Diagnostic Evaluation

Upper extremity ischemia has many causes, and a complete history and physical examination is the first step in determining the differential diagnosis. As occupational history and recreational activities may precipitate TOS, patients should be questioned about these activities in detail. Physical examination should include palpation and auscultation of the supraclavicular regions, Doppler pressure at the brachial and wrist levels, careful inspection of the fingers and nail beds, and detailed neurologic examination. Positional bruit and diminished pulses are helpful in increasing clinical suspicion, but many asymptomatic patients may have these findings.

The choice and urgency of diagnostic tests depends on the clinical situation. For patients presenting with signs and symptoms of ischemia, the most definitive test should be performed immediately. Arteriography of the entire upper extremity is usually the most reliable test and is considered the gold standard for providing direct evidence of the site and nature of occlusion. Noninvasive testing, such as plain radiography, computed tomography (CT), magnetic resonance imaging (MRI) or angiography (MRA), or duplex ultrasound scan, are helpful in making the diagnosis of TOS in noncritical situations.

Plain radiograph of the chest may demonstrate a supplementary rib, but it has limited specificity because the rib is often an incidental finding. Further testing is required to establish a causal relationship with vascular symptoms. CT has higher sensitivity in detecting an extra cervical rib and defining the relationship of any bony abnormality with vascular structures. Three-dimensional CT imaging can better delineate the structures of the thoracic outlet.¹¹ Helical CT arterial and venous angiogram with postural maneuvers can provide accurate information regarding the location and mechanism of vascular compression.^{12,13}

MRI is the imaging modality of choice for evaluating the anatomy of the brachial plexus. However, elevation of the arm or hyperabduction maneuvers may be required to demonstrate compression of vascular or neurologic structures to diagnose TOS, which may not be possible in a conventional MRI scanner due to lim-

Table 1. Nerve, Artery, Vein (NAV) Classification of Thoracic Outlet Syndrome

| Nerve (brachial plexus and sympathetic fibers) compression | |
|---|--|
| N0 | No symptoms or signs of injury |
| N1 | Only mild sensory symptoms, no paresthesia (negative EMG, nerve conduction velocity, and SSEP recording) |
| N2 | Severe sensory symptoms, pain or sympathetic irritation, mild electrical abnormalities (conduction velocity loss) |
| N3 | Motor symptoms, weakness and muscular atrophy, serious electrical abnormalities |
| Subclavian axillary artery compression | |
| A0 | No symptoms or signs of injury |
| A1 | Intermittent compression, claudication, no local anatomic lesion, negative ultrasound of arm |
| A2 | Minimal anatomic local lesion: minimal stenosis with mild poststenotic dilation (< twice the diameter of normal artery lumen), ultrasound shows irregularity of arterial wall, positive CT and MRI |
| A3 | Severe anatomic local lesion, intimal damage with aneurysmal evolution (poststenotic dilation twice the diameter of normal artery) |
| Subclavian axillary vein compression | |
| V0 | No symptoms or signs of injury |
| V1 | Chronic intermittent compression, irregular appearance of arm swelling without any sign of acute or chronic thrombosis, negative ultrasound |
| V2 | More advanced disease, not amenable to surgical revascularization, chronic thrombosis (> 2 wk) with long segment of vein obstructed (> 20 mm) confirmed by venography |
| V3 | More advanced disease with predictable surgical revascularization: chronic obstruction with short segment of venous obstruction (< 10 mm) that is acute (< 5 days) or subacute (6–15 days) confirmed by venography |

CT = computed tomography; EMG = electromyography; MRA = magnetic resonance angiogram; MRI = magnetic resonance imaging; SSEP = somatosensory evoked potential.

Adapted with permission from Busetto A, Fontana P, Zaccaria A, et al. Vascular thoracic outlet syndrome staging and treatment. *Acta Neurochir Suppl* 2005;92:29–31.

ited space. An open MRI scanner may obviate some of these limitations.^{14,15} MRA is the procedure of choice for patients presenting with predominantly vascular symptoms. Duplex scan (ultrasound combined with Doppler velocity waveforms) can diagnose occlusion of large vessels, such as subclavian or axillary vessels, but is not helpful in the evaluation of small vessels.^{15,16} Moreover, duplex scanning has limited reliability due to high false-positive and false-negative rates.¹⁷ Venography is the most reliable diagnostic test for venous TOS.¹⁸

The usefulness of electrodiagnostic testing in neurologic TOS remains controversial. Electrodiagnostic

Table 2. Staging and Treatment of Thoracic Outlet Syndrome Based on NAV Classification

| Stages | Signs and Symptoms | Suggested Treatment |
|------------------------------|---|---|
| Stage 1: N0–N1, A0–A1, V0–V1 | Intermittent neurovascular compression | Conservative treatment, education |
| Stage 2: N2, A0–A1, V0–V1 | Early neurologic involvement without irreversible neurologic damage | Physical therapy; if ineffective, then minimally invasive surgery |
| Stage 3: N3, A2, V2 | Advanced neurologic and/or vascular damage | Minimally invasive decompression surgery |
| Stage 4: N2–N3, A3, V3 | Advanced neurologic and/or vascular damage | Requires more extensive surgery: A3—decompression plus arterial reconstruction or thromboembolectomy plus decompression surgery V3—initial thrombolysis followed by decompression surgery, venous angioplasty (for residual obstruction) N2—sympathectomy N3—neurolysis, brachial embolectomy |

A = artery; N = nerve; V = vein.

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testing may provide useful information in the evaluation of suspected distal compression such as at the carpal tunnel or cubital tunnel level. Somatosensory evoked potentials are a more sensitive measure to assess brachial plexus nerve compression.¹⁹

Treatment

Treatment of TOS depends on the type, severity, and acuity of the presentation (Table 2). It can be managed conservatively or surgically.

Conservative management. In the absence of critical vascular or neurologic compromise, the appropriate approach is conservative management, which can be effective in 50% to 90% of patients.⁵ The goals of therapy are: decreasing compression on the brachial plexus, restoring mobility of the neurovascular bundle, and correcting muscle imbalance in the cervicospinal region. Approaches include physical therapy to strengthen the muscles surrounding the thoracic outlet, patient education regarding posture correction, and avoiding hyperabduction of the arm. If prolonged use of the arm in a hyperabducted position is required, the person should be advised to have frequent breaks in a neutral arm position. Successful conservative treatment of TOS must address the brachial plexus nerve compression at all levels and correct muscle imbalance in the cervicospinal region as well as address other concomitant conditions, such as cervical nerve root impingement, cervical disc disease, rotator cuff tendonitis, and epicondylitis. Attention to only 1 component of TOS may not result in total relief of symptoms.²⁰

Surgical management. Vascular complications of TOS

require surgical treatment that always involves decompression and may include vascular repair. In patients with arterial TOS, prompt relief of the obstruction is the treatment of choice for patients with ischemic complications. Thromboembolectomy can be attempted when there is occlusion of large blood vessels. Arterial reconstruction or bypass surgery is indicated if thromboembolectomy is ineffective or incomplete. The decompression procedure of TOS includes excision of the cervical rib together with all muscles and other soft tissue structures. The reconstructive vascular procedure includes repair of artery (resection and anastomosis). Stenting of the subclavian artery is another alternative in a patient with mild to moderate stenosis without thrombus.

Management of distal embolic disease is difficult. Distal emboli are often multiple and diffuse. The more distal the embolic occlusion, the harder it is to re-establish adequate perfusion, and major digital and extremity amputation is sometimes unavoidable.⁸ Depending on the extent and chronicity of thrombi and presence and absence of collateral flow, symptoms of ischemia and pain can occur. Sympathectomy may be a valuable adjunct in some patients with chronic severe pain related to distal embolism.⁸

Treatment of venous TOS includes management of the clot, extrinsic compression, and the intrinsic damage to the vein. Standard anticoagulation with heparin is the treatment of choice for venous thrombosis. In patients with venous thrombosis caused by TOS, standard anticoagulation treatment, even with a decompression procedure, is associated with severe residual symptoms. Thrombolytic therapy appears to result in better out-

comes.²¹ If the thrombus is only a few days old, the success rate is between 80% and 100%. The older the clot, the lower the success rate. Therefore, many authors recommend early thrombolytic therapy and a period of anticoagulation, followed by late surgical decompression; transcatheter thrombolytic therapy with subsequent early surgical decompression is the preferred alternative. Once the thrombus is lysed, further treatment depends on follow-up venography. Thrombolysis should be followed by a minimum of 3 months of anticoagulation. In patients with more than 50% of residual stenosis vein patch, angioplasty should be considered.¹⁸

CONCLUSION

TOS is caused by compression of subclavian vessels and/or the brachial plexus in the region of the thoracic outlet. Diagnosis of vascular TOS can be difficult, especially when scleroderma with Raynaud's phenomenon is concomitant. Although rare, arterial TOS can be devastating if the diagnosis is overlooked or delayed. Patients with arterial TOS may be at risk of limb-threatening ischemia. Therefore, surgical decompression with arterial reconstruction should be performed as soon as any arterial pathology is discovered. Excellent outcome can be expected with timely diagnosis and treatment. **HP**

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