

CASE REPORT

# Thoracic Outlet Syndrome Secondary to Localized Scleroderma Treated With Botulinum Toxin Injection

ELIZABETH N. LE, JULIE A. FREISCHLAG, PAUL J. CHRISTO, AVNEESH CHHABRA, AND FREDRICK M. WIGLEY

## Introduction

Localized scleroderma is characterized by thickening of the skin and subcutaneous tissue. Depending on clinical and pathologic findings, localized scleroderma is classified into different subtypes: plaque morphea, generalized morphea, bullous morphea, linear scleroderma, deep (pansclerotic) morphea, and mixed subtypes (1,2). Plaque and generalized morphea are superficial, where skin involvement is generally limited to the dermal layer (1). Bullous morphea involves fibrosis of the superficial or deep subcutaneous layer that leads to lymphatic obstruction and bullae formation (3). Linear scleroderma and deep morphea can involve the dermis, subcutaneous tissue, fascia, muscle, and underlying bone (1).

Unlike systemic sclerosis, localized scleroderma usually does not involve internal organs; however, nearly one-quarter of patients with localized scleroderma have evidence of extracutaneous involvement (4). This can cause significant functional difficulties (4). These extracutaneous manifestations can involve the musculoskeletal, neurologic, vascular, ocular, gastrointestinal, respiratory, cardiac, and renal systems (4). We report for the first time, to our knowledge, a case of linear scleroderma associated with thoracic outlet syndrome (TOS). The patient was treated with conservative measures and periodic botulinum toxin injections.

Elizabeth N. Le, BS, Julie A. Freischlag, MD, Paul J. Christo, MD, MBA, Avneesh Chhabra, MD, Fredrick M. Wigley, MD: Johns Hopkins School of Medicine, Baltimore, Maryland.

Dr. Wigley has received consultant fees, speaking fees, and/or honoraria (more than \$10,000 each) from Actelion Pharmaceuticals, Novartis, United Therapeutics, and Asahi Kasei Pharma.

Address correspondence to Fredrick M. Wigley, MD, Johns Hopkins University, 5200 Eastern Avenue, Suite 4100, Mason F. Lord Building, Center Tower, Baltimore, MD 21224. E-mail: fwig@jhmi.edu.

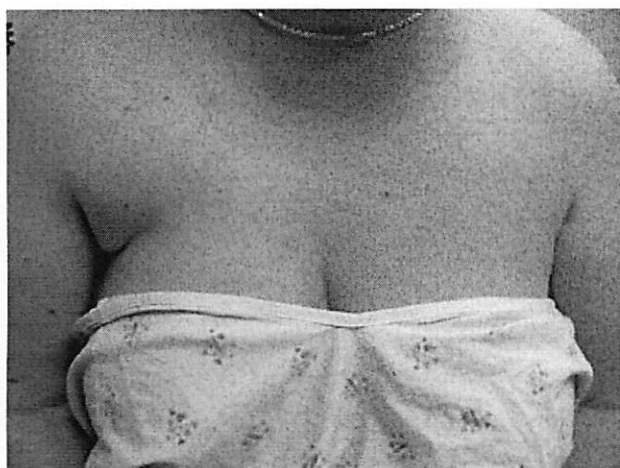
Submitted for publication August 27, 2009; accepted in revised form November 2, 2009.

## Case Report

The patient, a 40-year-old woman with a history of localized scleroderma, asthma, and migraine headaches, presented to our institution in August 2005 with right arm discomfort. The patient first noticed changes in her skin at age 7 years and was subsequently diagnosed with linear scleroderma at an outside institution. As a child, she underwent treatment with methotrexate and unknown antibiotic therapy without improvement, and subsequently discontinued all medical therapy during her adolescence. She noted that her lesions waxed and waned throughout the years; however, more recently she started to experience debilitating discomfort of her right upper extremity. She described a chronic tight aching sensation with periodic sharp pain that followed the ulnar nerve distribution on the right. However, most worrisome was a numb sensation affecting her right shoulder girdle and arm that occurred when she lifted her right arm.

Physical examination revealed subcutaneous thickening and skin dimpling on the right forearm extending to the upper arm. There was indurated skin thickening of the right shoulder girdle and right pectoralis region that wrapped around the right lateral side to involve the right infrascapular area, as evidenced by an indentation of the pectoralis region across the right upper breast (Figures 1A and B). Another thickened linear lesion was noted on the left flank that wrapped around the rib cage to involve the left inframamillary fold. A friction rub was appreciated on the right forearm on full extension of the fingers, and a positive Tinel's sign was present at the right elbow. Opening and closing of the hands while the arms were abducted and the elbows flexed at 90 degrees provoked numbness and tingling in her right hand. Pressure on the right supraclavicular area provoked numbness in her right hand and arm. Her peripheral pulses remained strong in the neutral position; however, with abduction of her right arm, the right radial pulse disappeared and right hand pallor was noted.

Duplex sonography of her right subclavian artery revealed a decrease in the peak systolic velocity from 151 cm/second to 53 cm/second with right arm abduction, as



A



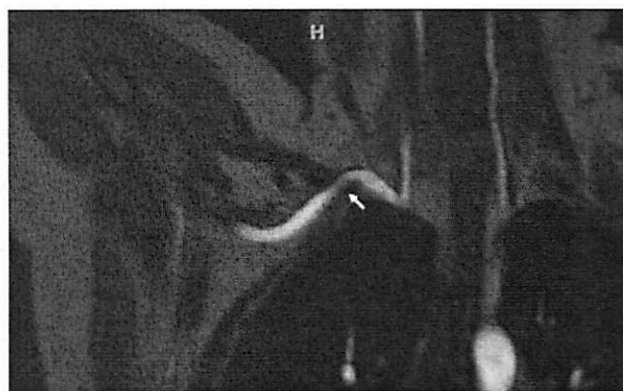
B

**Figure 1.** A, Asymmetric right upper breast and pectoralis region indentation related to dermal and fascial tethering from localized scleroderma. B, Skin indentation of the right infrascapular region extending toward the right lateral side due to dermis to fascia tethering of localized scleroderma.

well as a change in the wave form from triphasic to monophasic. She was initiated on conservative therapy for TOS with pregabalin and physical therapy; however, there was only a minimal symptomatic response. Magnetic resonance imaging with angiogram revealed a focally stenosed right subclavian artery when the patient's right arm was elevated (Figure 2A). No masses or anomalous ribs were noted; however, there was evidence of tissue fibrosis extending from the area of localized scleroderma overlying the brachial plexus and subclavian vessels (Figure 2B). A repeat duplex sonogram showed a chronic occlusive thrombosis within the right subclavian, brachial, and basilic veins. Before considering surgical management, the patient underwent a computed tomography (CT)-guided anterior scalene block with 1 cc of 0.25% bupivacaine, which produced more than 50% relief of her symptoms. Approximately 1 month later, she underwent a botulinum toxin injection (20 units) in the same muscle under CT

guidance. The Short-Form McGill Pain Questionnaire noted a 100% decrease in the patient's sensory, affective, and pain intensity scores after the third month following the initial botulinum injection (5). The patient described some dysphagia and phonation disturbances immediately after the initial injection, but no adverse effects after the second or third months.

Throughout the entire followup period at our institution, the patient did not show any progression or improvement of her skin. The patient has undergone 4 botulinum injections in the right anterior scalene muscle. She reported a remarkable decrease in pain in her right arm, allowing stoppage of all pain medications (ibuprofen and pregabalin) and complete ability to do full activities after each injection lasting 3–4 months before requiring repeat treatment. However, a fifth botulinum injection did not produce the same degree of symptomatic improvement as her previous 4 treatments. Palpation of the right anterior scalene muscle at that time revealed a focal indurated area; therefore, the botulinum therapy was stopped and conservative management was reinitiated with the goal of in-



A



B

**Figure 2.** A, Coronal postcontrast T1-weighted arterial phase magnetic resonance angiogram image demonstrating focal extrinsic stenosis (from 6 mm to 4 mm) and kinking of right subclavian artery (arrow). B, Coronal postcontrast T1-weighted magnetic resonance angiogram image showing focal fibrosis (arrowhead) in the region of the right subclavian vein (curved arrow) and cords and divisions of the brachial plexus (arrow). H = head; designates cephalic direction.

creasing the interval between successive botulinum treatments and avoiding surgery.

## Discussion

The main lesson of this case is that presumed deep tissue fibrosis of localized scleroderma can impinge on the brachial plexus and subclavian vessels, causing TOS. In addition, it demonstrates that botulinum toxin injection can provide dramatic relief, allowing avoidance of invasive surgery in TOS secondary to localized scleroderma.

TOS results from compression of the neurovascular structures traversing the thoracocervical region. It can be classified into 3 groups based on the anatomical structures involved and the resultant clinical symptoms. Arterial TOS is the least common type (1%) and is associated with pain, paresthesias, coldness, and color changes (6). It is caused by subclavian artery stenosis or aneurysm that is most commonly due to a cervical rib or an anomalous first rib (6). Two to three percent of patients with TOS have venous TOS, which can present as arm swelling, cyanosis, aching, and mild paresthesias (6). It is due to an obstruction of the subclavian vein, such as an anatomical narrowing or thrombosis of the vein (6). The most common type of TOS is neurogenic (>95%), wherein patients experience pain, paresthesias, and weakness, most notably in the ulnar nerve distribution along the forearm and to the fourth/fifth fingers (6). Patients can also experience neck, head, and shoulder pain, and tenderness (7). It is most commonly associated with trauma, such as hyperextension of the neck seen in a whiplash injury, or repetitive stress at work (6).

Treatment of TOS is catered toward the anatomical structure involved. Neurogenic TOS typically begins with a trial of conservative therapy involving physical therapy and pain management with nonsteroidal antiinflammatory agents and muscle relaxants (6,7). Scalene block and fluoroscopically guided botulinum toxin injections have been successfully used either as an adjunct to physical therapy or as a bridge to surgery (8). Surgery, either transaxillary first rib resection or supraclavicular anterior scalenectomy, is used to decompress the brachial plexus if there is a lack of symptomatic improvement with less invasive measures (6). Arterial and venous TOS are treated with rib resection and anterior scalenectomy, with and without therapeutic anticoagulation, respectively (7).

Our patient showed a clinical picture most consistent with neurogenic TOS that was successfully treated with single, CT-guided botulinum toxin injections in the anterior scalene muscle over an extended period of approximately 13 months. She also showed evidence of asymptomatic venous and arterial TOS, as indicated by the chronic venous occlusion, and a marked decrease in arterial peak systolic velocity on duplex. This case incorporates a novel technique of a diagnostic local anesthetic block followed by botulinum injection in the anterior scalene muscle under CT guidance. The botulinum toxin likely works by relaxing the muscle tension that is exacerbating the fibrosing entrapment of the neurovascular bundle, and thus helping to release the compression and improving symptoms. The complications of the continual

use of botulinum injections for the treatment of TOS remains unknown, but there has been a concern that repeated treatments can lead to scarring of the muscle and surrounding tissue (7). However, studies show no evidence for the development of tissue fibrosis with repeat botulinum injections. For example, repeated botulinum injections in the detrusor muscle of patients with neurogenic detrusor overactivity and neurogenic bladder dysfunction did not increase the risk of bladder fibrosis (9,10). Furthermore, it has been reported that the use of botulinum can improve urethral wound healing in rat urethral muscle by reducing tensile muscle forces that can lead to scarring (11). In this case, surgery remains an unattractive option for her, given the surgical complexity of releasing the fibrosing entrapment and the unknown risk for scleroderma disease reactivation. Although there was consideration of treatment with antiinflammatory or immunosuppressive medications, there was no clinical, radiographic, or laboratory evidence of active inflammation that would suggest ongoing scleroderma disease activity. The patient reinitiated pregabalin and physical therapy to relax the right anterior scalene muscle in an attempt to reduce the frequency and potential local complications of repeated botulinum injections. Reinjection of botulinum will be considered after a rest period of several months.

Neurologic complications are commonly seen in patients with localized scleroderma, particularly with the linear subtype involving the face and head, which is referred to as "en coup de sabre." However, these complications, manifesting as seizures, focal neurologic deficits, and migraines, have a different mechanism whereby the symptoms are a result of direct involvement of the neurologic structures (4,12). The symptoms of the patient described above are more consistent with an entrapment neuropathy, wherein the tissue fibrosis affects the area surrounding the neurovascular bundle. There have been only a few reported cases of neuropathies caused by compression due to collagen deposition of localized scleroderma, such as carpal tunnel syndrome (13), dystonia (14), and hemimasticatory spasm (15). Analogous to the treatment approach in this case, Kim et al successfully treated hemimasticatory spasm of a localized scleroderma patient with local botulinum injection of the masseter muscle (15).

The extracutaneous manifestations of localized scleroderma are mostly associated with the linear subtype, where there is involvement of the deeper underlying structures (4). It has been found to entrap joints, peripheral nerves, and arterial/venous vasculature (3,4). Therefore, it is not surprising that the linear scleroderma surrounding the arm, pectoral region, and axilla of this patient resulted in the entrapment of the brachial plexus and subclavian vessels. Entrapment neuropathies are a rare complication of skin sclerosis, and to our knowledge, we are the first to report that TOS is another noncutaneous complication of localized scleroderma. Treatment of these neuropathies is often aimed at resolving the sclerosis; however, this case shows that injection of botulinum toxin in the anterior scalene muscle may be a potential alleviant for the disabling discomfort and functional impairment.

### AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Wigley had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study conception and design.** Le, Freischlag, Christo, Wigley.

**Acquisition of data.** Le, Freischlag, Christo, Chhabra, Wigley.

**Analysis and interpretation of data.** Le, Freischlag, Christo, Chhabra, Wigley.

### REFERENCES

- Peterson LS, Nelson AM, Su WP. Classification of morphea (localized scleroderma). *Mayo Clin Proc* 1995;70:1068–76.
- Zulian F, Athreya BH, Laxer R, Nelson AM, Feitosa de Oliveira SK, Panaro MG, et al. Juvenile localized scleroderma: clinical and epidemiological features in 750 children. An international study. *Rheumatology (Oxford)* 2006;45:614–20.
- Bielsa I, Ariza A. Deep morphea. *Semin Cutan Med Surg* 2007;26:90–5.
- Zulian F, Vallongo C, Woo P, Russo R, Ruperto N, Harper J, et al, for the Juvenile Scleroderma Working Group of the Pediatric Rheumatology European Society (PRES). Localized scleroderma in childhood is not just a skin disease. *Arthritis Rheum* 2005;52:2873–81.
- Melzack R. The short-form McGill Pain Questionnaire. *Pain* 1987;30:191–7.
- Sanders RJ, Hammond SL, Rao NM. Thoracic outlet syndrome: a review. *Neurologist* 2008;14:365–73.
- Fugate MW, Rotellini-Coltvet L, Freischlag JA. Current management of thoracic outlet syndrome. *Curr Treat Options Cardiovasc Med* 2009;11:176–83.
- Jordan SE, Ahn SS, Freischlag JA, Gelabert HA, Machleder HI. Selective botulinum chemodenervation of the scalene muscles for treatment of neurogenic thoracic outlet syndrome. *Ann Vasc Surg* 2000;14:365–9.
- Da Silva CM, Cruz F. Has botulinum toxin therapy come of age: what do we know, what do we need to know, and should we use it? *Curr Opin Urol* 2009;19:347–52.
- Akbar M, Abel R, Seyler TM, Bedke J, Haferkamp A, Gerner HJ, et al. Repeated botulinum-A toxin injections in the treatment of myelodysplastic children and patients with spinal cord injuries with neurogenic bladder dysfunction. *BJU Int* 2007;100:639–45.
- Sahinkanat T, Ozkan KU, Ciralik H, Ozturk S, Resim S. Botulinum toxin-A to improve urethral wound healing: an experimental study in a rat model. *Urology* 2009;73:405–9.
- Kister I, Inglese M, Laxer RM, Herbert J. Neurological manifestations of localized scleroderma: a case report and literature review. *Neurology* 2008;71:1538–45.
- Winkelmann RK, Connolly SM, Doyle JA. Carpal tunnel syndrome in cutaneous connective tissue disease: generalized morphea, lichen sclerosus, fasciitis, discoid lupus erythematosus, and lupus panniculitis. *J Am Acad Dermatol* 1982;7:94–9.
- Zivkovic SA, Lacomis D, Medsger TA Jr. Muscle cramps associated with localized scleroderma skin lesions: focal dystonia, neuromyotonia, or nerve entrapment? [letter]. *J Rheumatol* 2006;33:2549.
- Kim HJ, Jeon BS, Lee KW. Hemimasticatory spasm associated with localized scleroderma and facial hemiatrophy. *Arch Neurol* 2000;57:576–80.

DOI 10.1002/acr.20135

### Submissions Invited for Themed Issue of *Arthritis Care & Research*: Vascular Comorbidity in the Rheumatic Diseases

*Arthritis Care & Research* is soliciting manuscripts for a themed issue addressing vascular comorbidity in the rheumatic diseases. Manuscripts covering a broad range of topics related to the major theme are invited, for example: common pathways in rheumatic and vascular disease, risk factors for onset of cardiovascular disease among persons with rheumatic conditions, and adverse outcomes when comorbid cardiovascular disease is present in rheumatic conditions. Submissions from a range of disciplines relevant to vascular aspects of rheumatic disease are welcome, and we will entertain both original research articles and review articles.

The issue will include regular submissions as well, but a certain number of pages will be reserved for manuscripts accepted in response to this solicitation. Manuscripts will be subject to the usual review process.

The deadline for submission is July 1, 2010. For further information, contact the editors, Edward H. Yelin, PhD (Ed.Yelin@ucsf.edu) or Patricia P. Katz, PhD (Patti.Katz@ucsf.edu).