

Botulinum Toxin Injection for Treatment of Scleroderma-Related Anterior Neck Sclerosis

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PRACTICE POINTS

- Scleroderma is a chronic autoimmune connective tissue disease that results in excessive collagen deposition in the skin and other organs throughout the body.
- Although there is no curative treatment for scleroderma, there are options to slow disease progression and improve quality of life.
- Botulinum toxin injection may be a preferred treatment option in patients with features of sclerosis or fibrosis related to scleroderma, particularly in the neck region.

To the Editor:

Scleroderma is a chronic autoimmune connective tissue disease that results in excessive collagen deposition in the skin and other organs throughout the body. On its own or in the setting of mixed connective tissue disease, scleroderma can result in systemic or localized symptoms that can limit patients' functional capabilities, cause pain and discomfort, and reduce self-esteem—all negatively impacting patients' quality of life.^{1,2} Neck sclerosis is a common manifestation of scleroderma. There is no curative treatment for scleroderma; thus, therapy is focused on slowing disease progression and improving quality of life. We present a case of neck sclerosis in a 44-year-old woman with scleroderma that was successfully treated with botulinum toxin (BTX) type A injection, resulting in improved skin laxity and appearance with high patient

satisfaction. Our case demonstrates the potential positive effects of BTX treatment in patients with features of sclerosis or fibrosis, particularly in the neck region.

A 44-year-old woman presented to the dermatology clinic for treatment of thickened neck skin with stiffness and tightness that had been present for months to years. She had a history of mixed connective tissue disease (MCTD) (positive anti-ribonucleoprotein, anti-Sjögren syndrome-related antigen, and anti-Smith antibodies) with features of scleroderma and polyarthritis. The patient currently was taking sulfasalazine for the polyarthritis; she previously had taken hydroxychloroquine but discontinued treatment due to ineffectiveness. She was not taking any topical or systemic medications for scleroderma. On physical examination, the skin on the anterior neck appeared thickened with shiny patches (Figure 1). Pinching the skin in the affected area demonstrated sclerosis with high tension.

The dermatologist (J.J.) discussed potential treatment options to help relax the tension in the skin of the anterior neck, including BTX injections. After receiving counsel on adverse effects, alternative treatments, and postprocedural care, the patient decided to proceed with the procedure. The anterior neck was cleansed with an alcohol swab and 37 units (range, 25–50 units) of incobotulinum-toxinA (reconstituted using 2.5-mL bacteriostatic normal saline per 100 units) was injected transdermally using a 9-point injection technique, with each injection placed approximately 1 cm apart. The approximate treatment area included the space between the sternocleidomastoid

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FIGURE 1. At the initial presentation, the skin of the anterior neck appeared thickened, shiny, and tense.

anterior edges and below the hyoid bone up to the cricothyroid membrane (anatomic zone II).

When the patient returned for follow-up 3 weeks later, she reported considerable improvement in the stiffness and appearance of the skin on the anterior neck. On physical examination, the skin of the neck appeared softened, and improved laxity was seen on pinching the skin compared to the initial presentation (Figure 2). The patient expressed satisfaction with the results and denied any adverse events following the procedure.

Mixed connective tissue disease manifests with a combination of features from various disorders—mainly lupus, scleroderma, polymyositis, and rheumatoid arthritis. It is most prevalent in females and often is diagnosed

in the third decade of life.³ It is associated with positive antinuclear antibodies and human leukocyte antigen (HLA) II alleles (HLA-DR4, HLA-DR1, and HLA-DR2). Raynaud phenomenon (RP), one of the most common skin manifestations in both scleroderma and MCTD, is present in 75% to 90% of patients with MCTD.³

Scleroderma is a chronic connective tissue disorder that results in excessive collagen deposition in the skin and other organs throughout the body.⁴ Although the etiology is unknown, scleroderma develops when overactivation of the immune system leads to CD4⁺ T-lymphocyte infiltration in the skin, along with the release of profibrotic interleukins and growth factors, resulting in fibrosis.⁴ Subtypes include localized scleroderma (morphea), limited cutaneous systemic sclerosis (formerly known as CREST [calcinosis, RP, esophageal dysmotility, sclerodactyly, and telangiectasia] syndrome), diffuse cutaneous systemic sclerosis, and systemic sclerosis sine scleroderma.⁵ Scleroderma is associated with positive antinuclear antibodies and HLA II alleles (HLA-DR2 and HLA-DR5).

On its own or in the setting of MCTD, scleroderma can result in systemic or localized symptoms. Overall, the most common symptom is RP.⁵ Localized scleroderma and limited cutaneous systemic sclerosis manifest with symptoms of the skin and underlying tissues. Diffuse cutaneous systemic sclerosis involves cutaneous and visceral symptoms, including lung, esophageal, and vascular involvement.⁶ Similar to MCTD, scleroderma is most prevalent in middle-aged females,⁷ though it occurs at a higher rate and with a more severe disease course in Black patients.⁸

A highly sensitive and specific test for scleroderma that can aid in diagnosis is the neck sign—tightening of the skin of the neck when the head extends.^{9,10} In one study, the neck sign was positive in more than 90% of patients with scleroderma and negative for control patients and those with primary RP.⁹ Thus, neck sclerosis is a common manifestation of scleroderma for which patients may seek treatment.

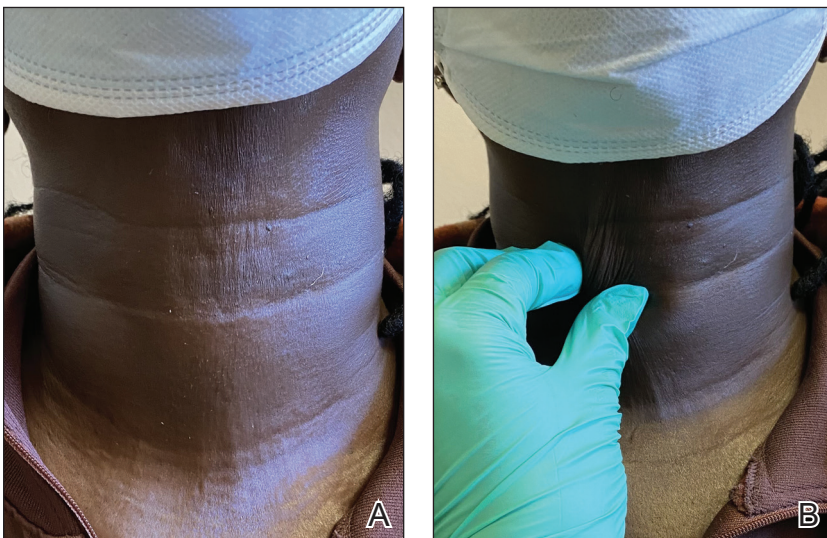


FIGURE 2. A and B, 3 weeks after treatment with incobotulinumtoxinA transdermal injection, the skin appeared softer and had improved vertical skin laxity compared to the initial presentation.

While there is no curative treatment for scleroderma, skin manifestations can be treated with mycophenolate mofetil or methotrexate.⁵ Systemic treatments may be recommended if the patient has additional symptoms, such as azathioprine for myositis/arthritis and cyclophosphamide for interstitial lung disease.⁵ However, it is important to note that these medications are associated with risk for gastrointestinal upset, mouth sores, fatigue, or other complications.

Botulinum toxin is a bacterial protein toxin and neuromodulator that inhibits neurotransmitter release by cleaving SNARE proteins at peripheral nerve terminal junctions.¹¹ It has been used in a variety of dermatologic and nondermatologic conditions, including migraines, hyperhidrosis, contractures, scars, and overactive bladder. It also has been used in aesthetics for facial rejuvenation and minimization of wrinkle appearance. Dermatologists and rheumatologists have successfully used BTX to treat primary and secondary RP—the most common symptom of scleroderma—due to its vasodilatation properties.¹² Although our patient did not have RP, use of BTX to treat other features of scleroderma, including en coup de sabre, thoracic outlet syndrome, dyspareunia, gastroparesis, pterygium inversum unguis, and dysphagia has been documented.¹³⁻¹⁸ An in vivo mouse study that examined the possible mechanism for BTX as a treatment in scleroderma found that BTX injections significantly decreased dermal thickness and inflammation in fibrosis ($P < .05$). An analysis of oxidative stress and mRNA expression showed that BTX may treat fibrosis by suppressing oxidative stress and inflammatory cells, resulting in decreased apoptosis and oxidant-induced intracellular accumulation of reactive oxygen species.¹⁹ Another animal study demonstrated the positive effects of BTX treatment for fibrosis of the bladder in rats.²⁰ In one case report, a female patient with scleroderma and facial fibrosis received perioral BTX injections for cosmetic purposes but also observed improvement in mouth constriction, demonstrating the potential efficacy of BTX for facial fibrosis.²¹

Our case demonstrates the potential positive effects of BTX treatment in patients with features of sclerosis or fibrosis, particularly in the neck region. We recommend assessing the efficacy of the initial BTX treatment after 2 to 3 weeks, with additional injections as needed to achieve the patient's desired level of comfort and appearance at approximately 3-month intervals (aligning with the expected duration of efficacy of BTX).²² Our patient experienced considerable relief and high satisfaction with BTX treatment. Given the limitations of sclerosis treatments and the unwanted adverse-effect profile of systemic treatments, BTX injections may be a preferable treatment option for cutaneous manifestations of scleroderma among patients. Future studies with larger patient populations and a control group are warranted to further explore the use of BTX for the dermatologic treatment of scleroderma.

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