GAVIN PUBLISHERS

Plastic Surgery and Modern Techniques

Brooks K, et al. Plast Surg Mod Tech 3: 134.

DOI: 10.29011/2577-1701.100034

Mini Review

Scleroderma and the Role of Plastic Surgery Intervention

Kenneth Brooks[1], Shelley S. Noland[2], Raman C. Mahabir[2*]

[1]University of Arizona- Tucson, Arizona, USA

[2]Mayo Clinic Arizona, Phoenix, Arizona, USA

[*]**Corresponding author:** Raman C. Mahabir, Chair, Mayo Clinic Arizona, Chair, Division of Plastic, Reconstructive Surgery and Hand Surgery, Department of Surgery, Phoenix, Arizona, USA. Tel: +14803421379; Email: Mahabir.raman@mayo.edu

Citation: Brooks K, Noland SS, Mahabir RC (2018) Scleroderma and the Role of Plastic Surgery Intervention. Plast Surg Mod Tech 3: 134. DOI: 10.29011/2577-1701.100034

Received Date: 16 January, 2018; **Accepted Date:** 02 February, 2018; **Published Date:** 12 February, 2018

Abstract

Scleroderma is a rare autoimmune condition of uncertain etiology that affects approximately 1 in 40,000 people in the United States and is characterized by excessive collagen deposition in all organ systems including the skin [1]. Common symptoms of scleroderma include Calcinosis, Raynaud phenomenon, Esophageal dysmotility, Sclerodactyly, and Telangiectasia (CREST syndrome) as well as vascular, pulmonary and cardiac pathology [2]. Symptoms are often debilitating and lead to functional and aesthetic compromise. Plastic surgical intervention may be a viable option for a subset of patients to ameliorate functional and / or aesthetic symptomatology depending on the subtype of scleroderma, the magnitude of disease extension and the operative setting.

What is Scleroderma?

Scleroderma is a rare autoimmune disease characterized by abnormal function of the immune system resulting in excess deposition of collagen in tissues [3]. This aberrant activity leads to a range of pathologies predominantly affecting the skin, vasculature, and GI tract. Skin thickening is one of the earliest clinical features and typically affects the fingers, hands and wrists, although the face is also commonly involved as well [4]. The additional skin findings include pruritus, edema, and telangiectasia [4,5] which are often difficult to conceal and can be an aesthetic concern for patients. Early functional losses may include flexion contracture of the digits, destruction of sweat glands and esophageal dysmotility [5]. Functional losses may lead to generalized weakness and contribute to muscle and joint pain. The magnitude of anatomic involvement varies depending on scleroderma subtype (diffuse vs. localized) and is an important clinical tool in determining treatment options for affected patients.

Biochemical Pathogenesis

Although the inciting etiology of scleroderma remains unknown, it is apparent that the biochemical pathogenesis is multifactorial and includes abnormal interactions of growth factors, immunologic cytokines, lymphocytes and macrophages. Examples of signaling molecules thought to contribute to pathogenesis include TGF-Beta and Platelet Derived Growth Factor [6,7]. Tubo, Tamaki, et al. identified elevated levels of transforming growth factor beta (TGF-B1) mRNA transcripts in the skin samples of select patients with the localized scleroderma subtype [6]. Excess activity of TGF-B1 is thought to lead to the increased production of collagen via aberrant secondary fibroblast activation, which could explain excess collagen deposition characteristic of the disease. Similarly, Jones, Gay, et al. evaluated skin biopsies from 8 patients with known scleroderma and through immunohistochemistry found a large abundance of PDGF in the macrophages of capillaries in affected tissues [7].

Numerous other immunologic mediators have been implicated in the pathogenesis of scleroderma, including high titers of immunologic markers such as anti-centromere autoantibodies. These have been found in abundance in patients with the limited systemic scleroderma subtype [8]. These markers have not only been important for initial diagnosis, but have also contributed to distinguishing the various subtypes of scleroderma. Regardless of the inciting biochemical pathway, eventual aberrant fibroblast activation and extracellular matrix deposition contributes to the fibrosis of peripheral and central organ systems leading to significant morbidity and mortality. Understanding the precise etiology of scleroderma will be important in identifying opportunities where medical therapy may halt future disease progression.

Subtypes of Scleroderma

The classification of scleroderma as either localized or diffuse plays a significant role in identifying potential downstream complications. Patients with localized limited cutaneous scleroderma typically present with a series of symptoms that fall within the clinical acronym "CREST". CREST is an acronym for Calcinosis cutis, Raynaud's phenomenon, Esophageal dysmotility, Sclerodactyly, and Telangiectasia [9]. Complications linked to CREST syndrome are often debilitating and increase the probability of joint dysfunction and digital ischemia. There is also an increased risk of malignancy, such as esophageal adenocarcinoma [10]. One common clinical presentation in patients with limited sclerosis is reactive color changes in the digits as seen in Raynaud's phenomenon which is an arterial vasoconstriction of the distal phalanges triggered by stress or changes in temperature [11]. The vessel response is present in a litany of conditions and is reversible in most patients when the causative factors are removed. However, chronic vasoconstriction is a clinical concern amongst scleroderma patients. Chronic vasoconstriction increases the probability of digital ischemia and ulceration, which may lead to amputation [12] which can be incapacitating for affected patients and dramatically affects their quality of life.

The diffuse form of systemic sclerosis is characterized by disseminated disease that contributes to potentially lethal multi-system organ failure. Complications of diffuse scleroderma include skin sclerosis, esophageal hypo-motility (with increased risk for Barrett's esophagus), pulmonary interstitial lung disease, pulmonary vascular disease, lung cancer, and renal cancer [10,13,14]. Relative to the localized subtype of scleroderma, the diffuse subtype is significantly direr, with five-year and 10-year survival rates of 70% and 55% respectively [2].

Plastic Surgical Intervention: Hand

When hand defects are present, hand surgery plays an important role in the management of scleroderma. Treatment is aimed at limiting ischemia to the distal phalanges, removing calcified nodules, and improving the function of the phalanges by repositioning the fingers from a hyperflexed position to a more functional orientation. Procedures including sympathectomy and micro-surgical revascularization of the distal phalanges are just two examples of surgical techniques that have been shown to be effective in a number of patients with scleroderma associated hand pathology [12]. Gilbart and Bogoch evaluated the efficacy of joint excision arthroplasties as well as interphalangeal joint fusions in 10 patients with systemic sclerosis. Interphalangeal joint fusions were successful in all 7 patients who returned post operatively for follow up, however nearly all had wound healing issues [3,7]. Three of the seven patients required additional surgery to alleviate complications from the tension band wires [15].

As previously described, Raynaud's phenomenon is a feature of the CREST variant of scleroderma. The pathogenesis of Raynaud's phenomenon was initially thought to occur via aberrant sympathetic activation of peripheral vessels in the presence of cold temperatures or stress, leading to reduced tissue perfusion [16]. The pathogenesis of Raynaud's phenomenon has subsequently become better elucidated with research implicating serum Endothelin-1 concentrations as a contributing factor [17]. Surgical intervention to reduce sympathetic induced vasospasm of palmar and digital arteries through sympathectomy may reverse aberrant sympathetic vasoconstriction of palmar arteries, thus preventing chronic vasoconstriction, digital tissue ischemia and necrosis [16].

Jones, Raynor, Medsger's, et al. evaluated two scleroderma patients who underwent microsurgical reconstruction of the radial and ulnar artery inflow tract using interposition vein grafts to provide adequate perfusion to the hand and superficial palmar arch [18]. Initially, both patients had inadequate flow to the distal phalanges as well as proximal narrowing of the radial and ulnar arteries, which acted as a target for microsurgical intervention. The postop pulsatile flow of blood to the fingers was noted to be enhanced relative to pre-treatment values in both patients suggesting that select patients with more proximal vascular pathology may be good candidates for revascularization [18].

Digital ulcers are present in roughly 50% of systemic sclerosis patients and are associated with reduced digital tip tissue perfusion, leading to digital tip ulceration and eventual gangrene [19]. Another proposed treatment option is the use of autologous fat grafting for affected digital ulcers. Del Bene, Bonomi et al., found that the vast majority of disease induced ulcers successfully healed following fat grafting [19]. Specifically, 15 ulcers were treated over 9 total patients with systemic sclerosis whereby fat was injected at the borders of the ulcers. 10 of 15 ulcers were identified as completely healed 8-12 weeks' post-op, with follow up ranging from 6 months to 2 years [19]. While this demonstrates fat grafting as a potentially exciting treatment option for distal ulcer management it was more successful in patients who were treated early in their disease process and diminished with advanced ulcer formation and prolonged ischemia prior to intervention [19]. Hand surgery for both aesthetic and functional enhancement in affected patients is possible and requires further evaluation.

Plastic Surgical Intervention: Face

Tightening of the facial skin is frequently present in scleroderma patients and is associated with significant aesthetic facial disfigurement and functional losses. Facial abnormalities include skin contraction, leading to the loss of naso-labial fold and forehead wrinkling, which are often difficult to conceal and are a frequently reported concern amongst patients. Treatments aimed at alleviating facial disfigurement represent a quintessential area

for Plastic Surgical intervention. Asjoe, Khan and Frame described the use of a free dermal graft and fat injection to the upper lip of a patient with scleroderma whose upper lip had retracted secondary to the disease process [20]. In that case report, the authors illustrate how their dermal-fat graft, harvested from right infra mammary fold proved effective for the upper lip tightening. Likewise, the authors noted that following the initial procedure; the patient approved of the aesthetic result and requested a lower lip graft using the same technique.

Recently, there has been a growing interest in the use of autologous adipose derived stem cells to improve characteristic facial involvement seen in systemic sclerosis. Grifiin, Butler et al., studied the use of adipose derived stem cells of patients with systemic sclerosis and compared them to the adipose derivatives of healthy patients [21]. Their interest was in identifying a difference in the phenotype, surface antigen expression as well as invasion capacity of adipose derived stem cells from affected patients relative to unaffected patients, in an attempt to evaluate the safety of using autologous adipose derived samples from affected patients. The surface antigen expression was equivalent in the normal adipose derived stem cells compared to the pathologic sample. This is intriguing in that it suggests that ex-vivo expansion of autologous adipose derived stem cells from affected patients should behave similarly to patients without pathology, allowing for use during reconstruction. Autologous fat grafting would reduce the probability of potential graft rejection, allowing for potentially long-term post surgical success. Beyond aesthetic concerns, autologous fat grafting has also been employed as a potential therapy for functional losses attributable to skin tightening. Specifically, fat grafting has been suggested to benefit patients with disease-induced microstomia, suggesting that both aesthetic and functional losses resulting from the disease may be alleviated through the procedure [22]. Although preliminary, the research is promising and may provide an option to patients with facial disfigurement [21].

Surgical Considerations

Scleroderma is classified as an autoimmune condition and as such, treatment commonly includes systemic corticosteroids in order to diminish the patient's overactive immune system, reduce symptoms and potentially slow disease progression [10]. While systemic corticosteroids may provide therapeutic benefit in patients, a weakened immune system may increase the probability of postoperative wound infection [23]. This too must be factored into the decision for surgical intervention and contributes to concerns that operating on patients with scleroderma may be further complicated based upon suspected "slow wound healing and poor post-operative range of motion" [4]. Additionally, disease associated changes in soft tissue vascularity highlighted previously, describe a common concern amongst the surgical community, that reduced tissue perfusion as a consequence of consistent digital artery vasoconstriction may increase the chances of intra-operative and post-operative wound complications. However, the use of vasodilators and local wound care to ensure soft tissues perfusion prior to surgery has been effective, and offers a pre-operative method of preventing post-surgical complications [12]. Judicious surgical intervention has provided therapeutic benefit in select patients without increased post-operative wound complications [4].

When multi-organ involvement is present, an additional concern amongst the surgical community includes potential operative complications; particularly when organ sites are affected that may compromise intraoperative organ perfusion and respiratory function. The process of evaluating the risk to benefit ratio of surgery for patients who desire correction of functional or aesthetic disfigurement is elaborate and often patient specific. Given that the etiology of scleroderma remains elusive, treatment for scleroderma is a multilayered approach including both medical and surgical interventions. Medications to improve peripheral blood circulation, reduce peripheral cytokine synthesis and release, is central to limiting disease progression. Likewise, immunosuppressant therapy to inhibit fibroblast activity, and thus collagen deposition, is vital for patient care [24].

When surgical intervention is planned electively for scleroderma patients, efforts can be taken to improve the chance of success and minimize complications. The emergent setting does not offer the same peri-operative optimization and plays a role in the probability of postoperative complications. When possible, multi-disciplinary coordinated care is fundamental to improving outcomes in scleroderma patients who present in an emergency setting. Safe surgical intervention in patients with scleroderma is clearly a complex issue that requires thorough evaluation of the risks and benefits to the patient.

Summary

Scleroderma is a debilitating condition that produces substantial defects in both the form and function of the patient. The exact etiology of scleroderma remains unknown and a topic of interest amongst the research community. Scleroderma has two subtypes, both of which have specific organ distributions and potential downstream complications. As such, surgical intervention is patient dependent, and the goals, risks and benefits of the procedures must be discussed prior to operating. Surgeons continue to pursue opportunities to safely operate on affected patients in order to improve the function of affected limbs and reduce aesthetic compromise that are a consequence of the disease. After careful evaluation of the patient, preoperative optimization and disclosure of the inherent risks, plastic surgery can play a meaningful role in scleroderma management.

Financial Disclosure and Products

The authors have no relevant financial interests or commercial associations to disclose.

Statement of institutional review board approval.

This study is exempt from IRB review.

Listing of Each Author's Role/Participation

Kenneth Brooks BSc - concept and design, literature search and review, drafting, editing and final approval

Shelley S Noland MD - design, drafting, editing and final approval

Raman C Mahabir MD - concept and design, drafting, editing and final approval

References

1. Mayes MD (2003) Scleroderma epidemiology. Rheum Dis Clin North Am 29: 239-254.
2. Longo D, Fauci A, Kasper D, Hauser S, Jameson J, et al. (2011) Harrison's Principles of Internal Medicine. (18th edition), New York: McGraw-Hill Professional, ISBN 978-0-07174889-6.
3. Katsumoto TR, Whitfield ML, Connolly MK (2011) The pathogenesis of systemic sclerosis. Annual Review of Pathology 6: 509-537.
4. Amin NH, DeLaurier G, O'Neill C, Cerynik D, Johanson N (2011) Hemiarthroplasty in a patient with severe systemic sclerosis. Clinical Rheumatology 30: 735-737.
5. Hajj-ali RA (2013) Systemic Sclerosis. Merck Manual Professional. Merck Sharp & Dohme Corp.
6. Kubo M, Ihn H, Yamane K, Tamaki K (2001) Up-regulated expression of transforming growth factor? Receptors in dermal fibroblasts in skin sections from patients with localized scleroderma. Arthritis Rheum 44: 731-734.
7. Gay S, Jones RE Jr, Huang GQ, Gay RE (1989) Immunohistologic Demonstration of Platelet-derived Growth Factor (PDGF) and sis-Oncogene Expression in Scleroderma. J Invest Dermatol 92: 301-303.
8. Vianna NJ, Davies JNP (1975) Epidemiology of Hodgkin's disease: review and etiologic leads. CRC Crit Rev Clin Lab Sci 5: 245-287.
9. Winterbauer RH (1964) Multiple telangiectasia, Raynaud's phenomenon, sclerodactyly, and subcutaneous calcinosis: a syndrome mimicking hereditary hemorrhagic telangiectasia. Bulletin of the Johns Hopkins Hospital 114: 361-383.
10. Shah AA, Wigley FM (2013) My Approach to the Treatment of Scleroderma. Mayo Clinic proceedings. Mayo Clinic 88: 377-393.
11. Wigley FM (2002) Clinical practice. Raynaud's Phenomenon. N Engl J Med 347: 1001-1008.
12. Jones NF, Imbriglia JE, Steen VD, Medsger TA (1987) Surgery for scleroderma of the hand. J Hand Surg Am 12: 391-400.
13. Marie I, Dominique S, Levesque H, Ducrotté P, Denis P, et al. (2001) Esophageal involvement and pulmonary manifestations in systemic sclerosis. Arthritis & Rheumatism 45: 346-354.
14. Bielefeld P, Meyer P, Caillot D, Dalac S, Camus P, et al. (1996) Systemic scleroderma and cancers: 21 cases and review of the literature. Rev Med Interne 17: 810-813.
15. Gilbart MK, Jolles BM, Lee P, Bogoch ER (2004) Surgery of the Hand in Severe Systemic Sclerosis. Journal of Hand Surgery 29: 599-603.
16. Goddard N (2009) Digital Sympathectomy for Scleroderma. In: Lumley JSP, Hoballah JJ(ed.). Vascular Surgery Springer Surgery Atlas Series. Springer, Berlin, Heidelberg.
17. Zamora MR, O'Brien RF, Rutherford RB, Weil JV (1990) Serum endothelin-1 concentrations and cold provocation in primary Raynaud's phenomenon. Lancet 336: 1144-1147.
18. Jones NF, Raynor SC, Medsger TA (1987) Microsurgical revascularization of the hand in scleroderma. Br J Plast Surg 40: 264-269.
19. Bene MD, Pozzi MR, Rovati L, Mazzola I, Erba G, et al. (2014) Autologous Fat Grafting for Scleroderma-Induced Digital Ulcers. An Effective Technique in Patients with Systemic Sclerosis. Handchir Mikrochir Plast Chir 46: 242-247
20. Ho-Asjoe M, Khan J, Frame JD (1996) Dermal Grafting for a Patient with Scleroderma: Case report. Scand J Plast Reconstr Surg Hand Surg 30: 325-327.
21. Griffin M, Ryan CM, Pathan O, Abraham D, Denton CP, et al. (2017) Characteristics of human adipose derived stem cells in scleroderma in comparison to sex and age matched normal controls: implications for regenerative medicine. Stem Cell Res Ther 8: 23.
22. Del Papa N, Caviggioli F, Sambataro D, Zaccara E, Vinci V, et al. (2015) Autologous fat grafting in the treatment of fibrotic perioral changes in patients with systemic sclerosis. Cell Transplant 24: 63-72.
23. Diethelm AG (1977) Surgical Management of Complications of Steroid Therapy. Annals of Surgery 185: 251-263.
24. Sapadin AN, Fleischmajer R (2002) Treatment of Scleroderma. Arch Dermatol 138: 99-105.