Treatment of Systemic Sclerosis with Shark Cartilage Extract

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Introduction

Systemic sclerosis (SSc, scleroderma) is a disease characterized by an increase in synthesis and deposition of extracellular matrix, resulting in fibrosis and microvascular injury of the skin and internal organs. Two subtypes which define the degree of disease involvement are recognized: diffuse cutaneous and limited cutaneous.[1] The disease spares children and increases in prevalence with age, occurring most frequently in women of childbearing age,[2] and most frequently and severely in black women.[3] Cardiac,[4] pulmonary[5] and renal[6] involvement are among the most severe complications of the diffuse form of the disease. Individuals with scleroderma have a significant decrease in lifespan, with a ten-year survival from diagnosis of <50%.[7] Pharmacologic treatment of scleroderma includes 5-fluorouracil, D-penicillamine, dipyridamole, and para-aminobenzoic acid,[8] in addition to pharmaceuticals aimed at controlling the symptoms of organ involvement.[9] Disease progression leads to a decrease in dermal pliability with a resultant loss of range of motion in the joints. Progressive fibrosis results in a progressive reduction in pulmonary function and failure of the internal organs occurs with time. The pathogenesis of scleroderma is poorly understood; however, a disruption in the immune system, the fibroblast cells and the vasculature have all been identified.[10]

Inflammatory Process

Increased numbers of mast cells are found in the serum of patients with scleroderma, and through their influence on endothelial cells and fibroblasts cause fibrosis.[11] In addition, abnormalities in cytokine production resulting in abnormal binding of T-lymphocytes to fibroblasts may be a factor in the pathogenesis of scleroderma.[12]

Autoimmune Mechanism

Studies of scleroderma implicate autoimmune mechanisms in the pathogenesis of the disease. Eighty-five percent of patients demonstrate increased titers of antinuclear antibodies (ANA), RNA polymerases, anti-topoisomerase and anticentromere antibodies.[13] Measuring autoantibodies may be useful in predicting disease progression. Autoantibodies directed against topoisomerase are associated with rapid and diffuse disease progression whereas antibodies to centromere proteins are more predictive of slow and limited progression of disease.[14]

Cellular Changes

The fibroblasts in patients with scleroderma have been found to produce excessive amounts of collagen (due to upregulation of collagen-gene expression)[15] and other connective-tissue macromolecules.[16] Overproduction of collagen by the fibroblasts results in fibrosis, the hallmark of scleroderma.

Cartilage Extract Therapy

Prudden reported beneficial effects in the treatment of psoriasis, colitis, osteoarthritis and rheumatoid arthritis and scleroderma utilizing bovine (tracheal) cartilage extract, administered by intramuscular injection (IM) and topical formulations.[17-18] It is believed that anti-inflammatory and wound-healing effects were demonstrated.[19] Since this initial report on the treatment of scleroderma with bovine cartilage, Dr. Prudden has reported verbally but not documented in the literature, further

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benefit in 13/14 cases of scleroderma with subcutaneous injections of cartilage (bovine), following similar protocols to those in the aforementioned studies.[20]

In an open trial, four patients have ingested shark cartilage extract (Car-T-Cell®). It is a frozen extract of shark cartilage prepared without preservatives, and is packaged in 7cc vials. Suggested use is one vial sublingually on an empty stomach daily. Although it is not clear whether the active principles can be absorbed by the oral route, this study utilized an oral sublingual form of cartilage (shark).

Case Studies

The following patients were given shark cartilage extract (one 7cc vial daily, sublingually), on an empty stomach for a period of one year. Patients signed an informed consent prior to initiating therapy due to the experimental nature of the trial.

Patient #1 is a 63 year old female, diagnosed with scleroderma in 1974 by skin biopsy and positive ANA (nucleolar and speckled). In addition she suffers from Raynaud's phenomenon, Hashimoto's thyroiditis and fibromyalgia.

Initial medications included omeprazole, cisapride, potassium citrate, diltiazem, fluoxetine, conjugated estrogen, medroxyprogesterone, clonazepam, amitriptyline hydrochloride, hydrocodone, acetaminophen, vitamin E, calcium, and fundamental sulfur. Modifications to her medications occurred as deemed appropriate by her rheumatologist (PBH).

The patient used 1 vial/day of shark cartilage extract sublingually, which was started in May 1997. A few months passed before an improvement in health was noticed, and it appears that she had reached a plateau in her improvement, at the time of this article.

Computed tomography (CT) scans and pulmonary function tests (PFT) have been performed consistently over the past three years, and have demonstrated an obstructive defect, and a progression of pulmonary disease. The patient experiences dyspnea and fatigue with walking. There has been no change in these symptoms in the past year since shark cartilage therapy has been initiated.

The patient has been diagnosed with reflux esophagitis, and has suffered from dysphagia and constipation for many years. A video fluoroscopy performed in October 1996 revealed marked narrowing of the esophagogastric junction. After the patient began shark cartilage therapy in May 1997, a repeat video fluoroscopy performed in October 1997 revealed a dilated atonic esophagus, poor peristalsis, hiatal hernia and no significant improvement when compared with the previous fluoroscopy. Another fluoroscopy in April 1998 (11 months into shark cartilage treatment) revealed mild dilation of the esophagus but no overt sign of significant stricture. The radiologist at this time did not indicate signs of atony, dysfunctional peristalsis or hiatal hernia. The patient takes omeprazole and cisapride regularly; the cisapride dose was doubled to 20 mg QID one year ago. She now reports some relief in the symptoms of dyspepsia, dysphaga and constipation.

The patient reports a general improvement in mobility over the last six months since the introduction of shark cartilage therapy to her previous therapeutic regimen. This is demonstrated by her improvement in symptoms of pain. Her hands are currently tender; however, according to medical records the tenderness and edema has decreased and manual dexterity have improved in the last year. In addition there has been an improvement in manual dexterity over the last year. For the first time the patient is now able to fully close her fists, which was not possible until shark cartilage therapy was initiated.

The patient reports that her skin is more supple, that she can smile better and wrinkle her forehead, which were not possible in the past. Incisor distance measured

by her rheumatologist, (PBH), were: 7/97 (30 mm), 8/97 (31 mm), 2/98 (34-35 mm) and 3/98 (37mm). She has a history of temporo-mandibular joint disease (TMJ), and has suffered numerous infections in her salivary glands, which have not occurred since the introduction of shark cartilage therapy. She finds that eating is easier, and has no difficulty with salivary dribble, or symptoms of Sjogren's disease. During the winter of 1997 the patient reported frequent infections and operations due to calcinosis, however, during the winter of 1998 there were no episodes of calcinosis or consequent infections or surgery.

An Activities and Lifestyle Index (ALI) was documented throughout the trial, and showed a trend toward improvement. Additionally, the 36-Item Short Form Health Survey (SF36) was completed during the trial, which demonstrated no appreciable change. Her pain fluctuates daily, her energy has improved overall in the past year, and her fibromyalgia has greatly improved, allowing her to decrease her dose of clonazepam, and amitriptyline hydrochloride. In the past year she has doubled her fluoxetine dose (to 40 mg daily) and is consistently attending support-group meetings (for alcoholism). Avoiding alcohol, and attending meetings for alcoholism are both significant lifestyle changes, which may contribute to her reports of an improvement in quality of life.

Patient #2 is a 45 year old female. She first developed symptoms in 1988, postpartum and was diagnosed with scleroderma in 1992 by positive ANA (nucleolar pattern). She currently uses no medications, and has used shark cartilage extract one vial daily for one year. She noticed benefits in her facial skin after three weeks of therapy and an improvement in her pulmonary symptoms after four months. Her energy improved steadily over six weeks, and continued to do so over the course of the year. She has made significant lifestyle changes in the last year, most importantly she has discontinued her employment as a blackjack dealer in a casino, which resulted in sleep deprivation and continuous exposure to second-hand smoke.

The patient reports having difficulty breathing after climbing one flight of stairs, and suffers from chronic bronchitis. PFTs taken from April 1996 to October 1996 indicated an improvement in static lung volume. The patient started shark cartilage therapy in May 1997. PFTs performed in October 1997 revealed an early restrictive ventilatory defect as documented by a reduction in total lung capacity (TLC) and diffusion capacity. PFTs on April 1998 (eleven months after initiating shark cartilage therapy) revealed an improvement in the following parameters relative to May 1997: TLC (5/97:78%, 4/98:95%), functional residual capacity (FRC) (5/97:68%, 4/98:77%), inspiratory capacity (IC) (5/97:2.19, 4/98:2.92), diffusion capacity (DCO) (5/97:62%, 4/98: 69%). She reports that an improvement in breathing was noticeable three months after shark cartilage therapy was initiated. She is now able to walk one mile daily compared with only a few blocks prior to the shark cartilage trial.

The patient reported pain in the joints of the feet and hands, which improved while utilizing the shark cartilage extract. In addition, within one week of discontinuing the therapy she had a return of these symptoms. This patient also suffers from myalgia and osteo-arthritis, neither of which was altered over the course of the shark cartilage trial. At the onset of therapy this patient had telangectasia on the face, chest, hands and tongue, in addition to discoloration of the normal skin tone. There was evidence of sclerodactyly and facial tightening resulting in a narrowing of the incisor distance. Following shark cartilage therapy the incisor distance had improved and wrinkles now appear on the face.

In the last three months of the trial, the patient suffered periodontal disease and recession of the gingiva. The patient

reported constant exhaustion prior to the initiation of shark cartilage therapy. After utilizing this therapy for eleven months, she was able to return to work full-time and has noticed a continued improvement in overall fatigue.

There were no significant changes or trends demonstrated in the ALI, however the SF-36 demonstrated a trend towards improvement in the following areas: general health, ability to perform daily activities, the ability to perform work, pain, and the ability to participate in social activity.

The following patients began a trial of shark cartilage therapy on their own initiative after learning of the aforementioned cases. They have been in contact with Allergy Research Nutricology to describe the benefit obtained following supplementation with oral shark cartilage.

Patient #3 is a 50 year old female, diagnosed with scleroderma and systemic lupus erythematus (SLE) in 1985. She reports the development of scleroderma following dilantin poisoning. She was using dilantin for ten years for a seizure disorder, which resulted from a previous (1969) motor vehicle accident. Medications currently being used include hydroxychloroquine, hydrochlorothiazide, potassium citrate, phenobarbital, baclofen, sumatriptan succinate, nortryptiline hydrochloride, excedrin and estradiol patches. The patient at this time has completed one 24-day cycle of shark cartilage extract and reports a resolution in her symptoms of low back pain, a decrease in headaches and full days without pain. Within the first twelve days she noticed an increase in energy, which remained stable over the course of the 24-day trial. Nutritional supplements were also used in conjunction with the shark cartilage extract, including *immune-prime*, *perma vite*, symbiotic FOS, vitamin K, aloe vera (topical 2-3 times per day and oral 1/4 cup 2 times per day. The *immune-prime* was started several days prior to initiating treatment with the shark cartilage extract. The patient started shark cartilage treatment in May 1998. She discontinued the shark cartilage in June 1998 and reports a decline in health, a decrease in energy and the return of myalgia and weakness. The patient kept a thorough diary at the time of therapy and reported an improvement in circulation to the hands and a resolution of sores on her hands and feet. Since she has discontinued the therapy, she notes the return of "brain fog," and poor circulation within a few days. The patient is now initiating a second cycle of shark cartilage therapy.

Patient #4: is a 53-year old female diagnosed with scleroderma in 1994. Current medications include shark cartilage extract one vial daily, which was initiated August 96 and has been followed regularly.

The patient reports normal pulmonary function tests, although she describes a history of dyspnea.

A prior history of dyspepsia and gastro-intestinal discomfort is described. These symptoms are currently denied.

The improvement in dermatologic discoloration and thickening are the most significant for this patient in addition to the resultant improved elasticity and joint mobility. The patient reports a steady improvement in dermal compliance over time. In addition, the oral diameter has steadily improved. Recent changes include the growth of body hair in areas previously reported to be fibrotic.

Prior to the initiation of shark cartilage therapy the patient describes severe arthritis, significant impairment of mobility, and loss in fine motor dexterity. She now reports a complete reversal of these symptoms, which has taken place gradually with time.

This patient reports a marked improvement in energy, sleep and quality of life. She has gained back much of the weight lost in the initial years of suffering from scleroderma.

Conclusions

Research indicates anti-inflammatory and wound-healing effects of cartilage (bovine) therapy. Case reports have documented improvement in symptoms of psoriasis, rheumatoid arthritis, colitis and scleroderma with the use of cartilage (bovine) by injection. These case reports support prior observations of a benefit of cartilage extract in the treatment of scleroderma. These four patients have experienced both subjective and objective improvement in their symptoms of sceroderma following sublingual administration of shark cartilage extract in addition to previously administered therapies. Controlled trials are necessary due to the relapsing and remitting nature of the disease, and to rule out the placebo effect.

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References

1. Medsger TA Jr: Epidemiology of systemic sclerosis. *Clin Dermatol,* 1994; 2 :207-216.
2. Medsger TA Jr: Epidemiology of systemic sclerosis. *Clin Dermatol,* 1994; 2: 207-216.
3. Steen VD, Medsger TA Jr: Epidemiology and natural history of systemic sclerosis. *Rheum Dis Clin North Am,* 1990; 1: 1-10.
4. Janosik DL, Osborn TG, Moore TL, et al: Heart disease in systemic sclerosis. *Semin Arthritis Rheum,* 1989; 19/3: 191-200.
5. Silver RM, Miller KS: Lung involvement in systemic sclerosis. *Rheum Dis Clin North Am,* 1990; 1:199-216.
6. Steen VD: Systemic sclerosis. *Rheum Dis Clin North Am,* 1990; 3: 641-654.
7. Steen VD, Medsger TA Jr: Epidemiology and natural history of systemic sclerosis. *Rheum Dis Clin North Am,* 1990; 1: 1-10.
8. Torres MA, Furst DE: Treatment of generalized systemic sclerosis. *Rheum Dis Clin North Am,* 1990; 1: 217-241.
9. Mitchell H, Bolster MB, LeRoy EC: Scleroderma and related conditions. *Med Clin North Am,* 1997; 1: 129-149.
10. Furst DE, Clements PJ: Hypothesis for the pathogenesis of systemic sclerosis. *J Rheumatol Suppl,* 1997; 48: 53-57.
11. Mican JM, Metcalfe DD: Arthritis and mast cell activation. *J Allergy Clin Immunol,* 1990; 86(4 Pt 2): 677-683.
12. Needleman BW: Immunologic aspects of scleroderma. *Curr Opin Rheumatol,* 1992; 6: 862-868.
13. Okano Y: Antinuclear antibody in systemic sclerosis (scleroderma). *Rheum Dis Clin North Am,* 1996; 4:709-735.
14. Fritzler MJ: Autoantibodies: diagnostic fingerprints and etiologic perplexities. *Clin Invest Med,* 1997; 1: 50-66.
15. Varga J, Bashey RI: Regulation of connective tissue synthesis in systemic sclerosis. *Int Rev Immunol,* 1995;12/2-4: 187-199.
16. Jimenez SA, Hitraya E, Varga J: Pathogenesis of scleroderma. Collagen. *Rheum Dis Clin North Am,* 1996; 4:647-674.
17. Dupont E, Savard PE, Jourdain C, et al: Anti-angiogenic properties of a novel shark cartilage extract: potential role in the treatment of psoriasis. *J Cutan Med Surg,* 1998; 3:146-152.
18. Prudden JF, Balassa LL: The biological activity of bovine cartilage preparations. Clinical demonstration of their potent anti-inflammatory capacity with supplementary notes on certain relevant fundamental supportive studies. *Semin Arthritis Rheum,* 1974; 3(4): 287-321.
19. Fontenele JB, Araujo GB, de Alencar JW, et al: The analgesic and anti-inflammatory effects of shark cartilage are due to a peptide molecule and are nitric oxide (NO) system dependent. *Biol Pharm Bull,* 1997: 11:1151-1154.
20. Dr. Peter Himmel: personal communication with Prudden JF.