REVIEW ARTICLE

MANAGEMENT OF SYSTEMIC SCLEROSIS - A REVIEW

S C Ng, P J Clements, H E Paulus

ABSTRACT

Establishing a correct diagnosis is the first step in the management of this condition. The ARA (American Rheumatism Association) diagnostic criteria is a useful guideline. Next, a multisystem evaluation is needed to define the extent of visceral involvement. Patient education is important to enable them to understand and participate in the management of their disease. Skin care and protection from trauma and cold and physiotherapy to retard contractures are taught. Raynaud's phenomenon may be helped by topical nitrates, ketanserin, nifedepine and vasodilatory prostaglandins.

D-penicillamine may be tried for patients with generalised scleroderma of less than 3 years' duration. Colchicine may help but other drugs like N-acetylcystein and chlorambucil have tested and found ineffective. Cyclosporin seems promising.

Finally, all visceral complications should be managed accordingly.

Keywords: Systemic sclerosis, therapy

SINGAPORE MED J 1990; Vol 31: 269 - 272

INTRODUCTION

Systemic sclerosis is a generalised disorder of the connective tissue characterised by fibrosis and degenerative changes in the skin (scleroderma), synovium, muscles and certain internal organs, notably the gastrointestinal tract, lung, heart and kidney(1). In the USA, the estimated prevalence is 10/100,000 and an annual incidence is 10/1,000,000(2). The prevalence in Singapore is not known. Though uncommon, it is an important condition because of the morbidity from multisystem involvement and increased mortality. Survival at 5 years is 60% (range from 34 to 80%) and at 10 years is 47% (range from 35 to 74%) (3).

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MANAGEMENT OF SYSTEMIC SCLEROSIS

The principles of management will be discussed as follows:-

(1) Establish diagnosis: Exclude other conditions which resemble scleroderma. The ARA criteria for diagnosis of systemic sclerosis is a useful guide.
(2) A multisystem evaluation should be done to quantify the extent and severity of the condition.
(3) Patient education.
(4) General management – Skin care and physiotherapy to prevent contractures should be stressed.
(5) Management of Raynaud's phenomenon.
(6) Consider the use of drugs to arrest/improve the disease.
(7) Management of complications of disease.

(1) Establish Diagnosis

As there are many conditions which mimic scleroderma, it is important to think of them before making a diagnosis of systemic sclerosis. Primary skin conditions (like scleredema, porphyria cutanea tarda) or primary systemic disease with skin thickening (eg. Graft verse Host disease, carcinoid syndrome) and scleroderma-like conditions induced by chemicals (like vinyl chloride, rapeseed oil, silicone implant) have different outcomes and should be managed differently. Hence a complete history including occupational exposure to vinyl chloride, drug history, family history, a history of breast implant, ingestion of rapeseed oil etc. is important. In general, the absence of Raynaud's phenomenon should make one rethink the diagnosis.

The diagnostic criteria set up by the American Rheumatism Association is a useful guideline.

Scleroderma proximal to the metacarpal phalangeal joint and metatarsal phalangeal joint is considered a major criterion with a sensitivity of 91% and specificity of over 99%. The three minor criteria are sclerodactyly, digital pitting scars on fingertips and pulmonary fibrosis at both lung bases and in the absence of the major criteria, presence of 2 of these 3 is adequate for diagnosing systemic scleroderma(4).

(2) Multisystem Evaluation

It is important to do a multisystem evaluation to determine the extent and severity of the disease. This includes careful examination of the skin. The skin score(5) is determined by clinical palpitation of the skin over 10 body surface areas (face, back, chest, abdomen, upper arms, forearms, hands-including fingers, thighs, leg and feet). We use a 0-3 scale (0 for normal, 1 for mild tethering, 2 for moderate tethering and 3 for severe tethering). In each area, the score recorded is that of the most severely tethered locale within a given body area bilaterally - forearm, thigh etc. The total skin score is the sum of the individual scores from all 10 areas. The maximum score would be 30. A high total skin score is associated with a poor prognosis. Digital ulcers are difficult to heal(6). The following investigations are useful - esophageal manometry, Barium studies to look at the esophagus, stomach, duodenum, small bowel and colon, chest X-ray, pulmonary function tests (including DLCO), ECG, echocardiogram, Holter monitoring (if arrhythmias are suspected), renal function, urinalysis, urea, electrolytes, full blood counts, stools for fat, d-xylose absorption, other tests for malabsorption (if indicated), and muscle enzymes (if myositis is suspected).

Patients with renal involvement have a lower cumulative survival rate, followed by patients with cardiac involvement and patients with pulmonary involvement as compared with patients without these organ involvements(7).

(3) Patient Education

The patient should be told the diagnosis and the systemic nature of the disease. Though there is no miracle drug that is guaranteed to make her look normal and cure her illness, much can be done to treat the complications of this disease and make her feel better. Patient education material from the Arthritis Foundation of USA(8) and Universal Scleroderma Foundation(9) are useful aids for patient education. Psychosocial problems arising from this chronic illness should be discussed and managed accordingly.

(4) General Management of skin and joints

The scleroderma skin is dry and often itchy. The patient should be advised to avoid rough, occlusive and irritative clothes. Lanolin and oil baths are helpful as are mild soaps and the use of moisturing creams, and ointment to soften the skin.

Any digital ulcer should be meticulously cleaned with hydrogen peroxide and Eusol lotion. Antibiotics like erythromycin are helpful for infected ulcers. Keeping the limb warm and treatment of Raynaud's phenomenon hasten healing. Intractable gangrenous lesions often auto-amputate.

Calcinosis is very difficult to treat and fortunately rarely seen in Singapore. Various treatments include probenecid, intralesional steroids, EDTA, diphosphonates and aluminium hydroxide. A low calcium and high phosphate diet have been tried without much effect. Surgical excision can be done but the patient should be warned of poor healing and possible recurrence.

Contractures from periarticular fibrosis often occur, resulting in inability to flex and extend the fingers. Early physical and occupational therapy should be started to teach patients exercises to improve range of motion and strengthen the muscles.

(5) Management of Raynaud's Phenomenon

Raynaud's phenomenon is present in about 95% of patients. The typical description of a triphasic colour change of pallor to cyanosis to flushed hyperemia is very rarely described by patients in Singapore. Nevertheless our patients do complain of severe cold and numbness of fingers followed by some flushing on entry into airconditioned rooms. Raynaud's phenomenon occurs not just in the skin but has also been demonstrated in the pulmonary vessels and renal vessels. The abnormal vessels are thought to be pathogenic in the development of scleroderma.

Treatment of Raynaud's phenomenon should be started early.

In mild disease, simple advice to keep extremities warm, to stop smoking and to avoid drugs like cafergot is all that is needed. Biofeedback techniques have been reported by some to be useful and free from side effects.

Vasodilators eg. intra arterial reserpine (for acute attack) oral methyldopa and phenoxybenzamine have been tried but hypotension is a major problem. Calcium channel blockers like nifedipine and diltiazem are more useful for primary Raynaud's phenomenon and less so for Raynaud's associated with systemic sclerosis. When using nifedipine in these patients, the side effect of decreasing the lower esophageal sphincter pressure should be kept in mind as this will aggravate reflux esophagitis.

The serotonin antagonist ketanserin was found useful in 83% (15 out of 18 patients) scleroderma patients and 33% of other patients with Raynaud's (4 out of 12 patients)(10). The dose has to be 80mg or more a day. Vasodilatory prostaglandins PGE_1 and PGI_2 are useful and may hasten healing of refractory ulcers.

Other interesting treatments are antiplatelet agents (eg. aspirin) and drugs that reduce viscosity (eg. dextran) but they are not found to be effective.

Surgery may be tried. However, sympathectomy – preganglionic or superselective, is difficult to do well and relapses are common.

6) Consider the Use of Agents which may Arrest/ Reverse the disease process

Patients who have generalised sclerosis and high total skin scores, particularly within their first three years of disease may benefit from the use of agents which may arrest or reverse the disease process.

D-penicillamine is one of the most commonly used drugs for scleroderma. It acts to inhibit collagen cross-linkage. The major paper supporting its use is a study of 73 patients who were given D-penicillamine compared with 45 patients who were not. The follow-up period was about 38 months. Sixteen percent of patients on D-

penicillamine developed new organ involvement while 33% of those not on D-penicillamine did so. The 5 years survival was 88% for those on D-penicillamine and 66% for those not on the drug(11). Unfortunately this is a retrospective study and not a prospective study.

Colchicine is another drug used for systemic sclerosis. It deploymerises microtubules and inhibits secretion of collagen molecules. Patients whose disease was less than 5 years duration, and who took a total dose of 1438mg did better(12).

N-acetylcysteine has been tested in a one year double blind placebo controlled trial but was not shown to be effective(13).

Chlorambucil has been meticulously studied in a 3 years double blind placebo controlled fashion. This drug is no better than placebo(14).

POTABA (Potassium para-aminobenzoate) is anti-serotonin and antifibrosis. It has been shown useful in other fibrotic conditions and a controlled trial is in progress.

Cyclosporin A seems promising in case reports and small open studies(15). Other agents of interest are recombinant gamma interferon (which inhibits collagen production) and tissue plasminogen activator. These were recently reported at the 53rd American College of Rheumatology 1989.

As these drugs listed above have not been proven to be effective in a large controlled, prospective study, we sometimes chose not to use any of them when side-effects outweigh the benefits. The newer agents should be used cautiously in a research environment. Much more research is needed to find an effective drug for systemic sclerosis.

(7) Management of Complications

Upper gastrointestinal problems like dysphagia and reflux esophagitis can be treated with H_2 blockers - cimetidine and ranitidine. Practical measures like avoiding a heavy meal before bedtime and elevating the head of the bed are useful. Motility may improve with metoclopramide. Sucralfate is useful for mucosal protection.

Small bowel disease with malabsorption syndrome may be treated with cyclical antibiotics. Venting enterostomy and alimental diet can be used. When all else fails, central venous hyperalimentation(16) can provide nutrition to the patient without causing severe abdominal pain and pseudoobstruction.

Constipation from large bowel involvement can be relieved by high fibre and bulk agents. Rupture of pneumatosis coli will result in an acute abdomen. This can sometimes be managed conservatively but surgery is required if there is spillage of colonic contents with peritonitis.

Interstitial pulmonary fibrosis may be treated with D-penicillamine as it has been reported to improve the diffusion capacity. Pulmonary hypertension may respond to nifedipine and hydralazine. All super imposed infection should be treated aggressively with the appropriate antibiotics.

Renal crisis had been a significant cause of death in the past. However, with the use of angiotensin converting enzyme inhibitors like captopril, control of hypertension is effective with prevention of progressive renal disease.

Cardiac involvement is treated with conventional therapy for arrhythmias or heart failure.

All patients should be followed up regularly looking for hypertension and any visceral involvement. Complications should be treated early. As in the management of all chronic illness, a good doctor-patient relationship is very important and the same doctor should preferably follow-up the patient.

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