Scleroderma in Children

Pediatric patients with localized forms of scleroderma significantly outnumber pediatric patients with systemic sclerosis. In fact, information on systemic sclerosis in this age group has generally been gleaned from small-case series. A recent international survey on pediatric systemic sclerosis reported 135 patients from 46 centers.[1] The mean age at onset was 8.8 ± 3.3 years (range 1.5-15.8 years) and the disease duration was 5.0 ± 3.3 years (range 0.3-21 years). Eight patients in this study died, with a median disease duration until death of two years (range 1-8 years). Causes of death were as follows: cardiovascular in five patients; renal in one; sepsis in one and unknown in one. In general, it appears that systemic sclerosis is similar in children and adults, although the outcome may be better in children.

Because of its rarity in children, it will be extremely difficult to conduct randomized controlled trials in children and adolescents with systemic sclerosis. Therefore, it is recommended that the approach to treatment be similar to that of adults with systemic sclerosis, combining organ-specific treatments with an immunosuppressant regime, and paying careful attention to rehabilitation and psychosocial issues. Recently, three children were described who underwent autologous stem cell transplantation for severe systemic sclerosis;[2] two of the children improved, and in one there was improvement in the pulmonary fibrosis.

Localized forms of scleroderma outnumber systemic disease by approximately 10 to one in childhood. These disorders are primarily limited to the skin and subcutaneous tissue. The skin pathology in both the localized and systemic forms of scleroderma is identical, and they likely form two ends of a spectrum of disease, with skin fibrosis being the link. Evolution from localized to systemic disease, however, is considered extremely unusual.

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Many authors have proposed that the word "scleroderma" be dropped, and that all cases be called "localized morphea." One classification scheme has been proposed by authors from the Mayo Clinic of Rochester, Minnesota (Table 1).[3]

Incidence figures from 1960 to 1993 in Olmsted County, Minnesota, suggest that the disease is on the rise.[4] This suggestion may reflect the true picture, better recognition, or inclusion of an expanded classification scheme. Localized forms of scleroderma are more common in females by approximately two to one, and the frequency increases with increasing age. The mean age of onset is approximately eight years, although it may occur at any age.

CLINICAL PICTURE

Morphea. Patients with plaque morphea generally present with an indurated plaque of skin, most commonly on the trunk and upper extremity. Typically, there is an ivory-colored, waxy central area of the plaque, forming a circular or oval shape, and surrounded by an erythematous or violaceous halo. Such plaques may itch, burn and/or tingle, but are usually asymptomatic. The natural history of these lesions is to soften with time, leaving residual hyperpigmentation with or without atrophy. Deeper morphea lesions extend into the panniculus and fascia, and include disabling pansclerotic morphea of childhood[5] and eosinophilic fasciitis. In childhood, a number of cases of eosinophilic fasciitis have evolved to morphea.[6]

Linear Morphea. These lesions typically present as firm and band-like lesions; they usually involve an extremity. If they cross joint lines, these lesions can lead to rapid and significant loss of range of motion in that joint. Atrophy is frequent, and can involve soft tissues and muscle. Occasionally, the bone itself may be affected, resulting in deformities and limb shortening.

En Coup de Sabre. Morphea lesions may present on the face in a linear band. These lesions usually involve the forehead, and extend upward to the scalp. These lesions appear in a form similar to a

depression caused by the cut of a sword, and are thus called "en coup de sabre." These lesions leave depressed areas, which may involve the skull. Additional abnormalities can include changes in dental and palatal growth, loss of eyebrows and eyelashes, ptosis and uveitis. Occasionally, seizures may occur. Structural changes have been noted on magnetic resonance imaging (MRI). The significance of the MRI changes is not clear, and MRI is therefore not recommended if the child is otherwise asymptomatic.

Parry Romberg Syndrome (progressive hemifacial atrophy). This syndrome is marked by a lack of superficial change and a progressive loss of tissue under the skin, resulting in severe cosmetic as well as structural facial deformity. These deformities do not involve the forehead. Frequent coexistence with linear bands of sclerosis on the face and elsewhere have been observed, and therefore it is believed that Parry Romberg Syndrome is truly a part of the morphea spectrum.

LABORATORY MEASURES

A number of laboratory abnormalities occur with varying frequency in patients with morphea. It has been suggested that elevations in the erythrocyte sedimentation rate (ESR), serum levels of immunoglobulin G and the presence of eosinophilia predict more active and severe disease. Serum levels of soluble interleukin-2 (IL-2) receptor may be an indicator of disease activity. Both rheumatoid factor and antinuclear antibodies (ANA) are frequently present, but do not seem to predict type, severity, or degree of activity. ANAs include antibodies to histones and single-stranded deoxyribonucleic acid (DNA).

MANAGEMENT

Many pharmacologic agents have been recommended for pediatric morphea patients based on single cases or small-case series. Only two placebo-controlled trials have been performed on this age group, and both were limited by small numbers. Nevertheless, these studies showed that neither gamma-interferon[7] nor vitamin D_3[8] was effective. Ultraviolet A in high and low doses, with and without psoralens, has been reported to be effective.

In the program at Toronto's Hospital for Sick Children, systemic treatment is recommended for the following indications:

1) lesions that are expanding or multiple additional lesions;
2) lesions across joint lines that impair function; and
3) lesions that may be cosmetically disfiguring.

The treatment regime at the Hospital for Sick Children combines corticosteroids and methotrexate.[9]

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Table 1
CLASSIFICATION OF MORPHEA

Plaque morphea

- Morphea en plaque
- Guttate morphea
- Atrophoderma of Pasini and Pierini
- Keloid morphea (nodular morphea)
- [Lichen sclerosus et atrophicus]*

Generalized morphea

- Bullous morphea
- Linear morphea
- Linear morphea (linear scleroderma)
- Coup de sabre scleroderma
- Progressive hemifacial atrophy

Deep morphea

- Subcutaneous morphea
- Eosinophilic fasciitis
- Morphea profunda
- Disabling pansclerotic morphea of children

**The entry in brackets is not universally accepted.*

From: Peterson LS, Nelson AM, Su WP. Classification of morphea (localized scleroderma). Mayo Clin Proc 1995; 70(11):1068-76.

CRA News

ILAR 2001

The 20th Congress of the International League of Associations for Rheumatology (ILAR), entitled "Therapy for the 21st Century," was held in Edmonton, Alberta from August 26-30, 2001. The Winter issue of the *CRAJ* (scheduled to mail in December 2001) will comprise select coverage of this event.

ANNUAL ACR/ARHP SCIENTIFIC MEETING 2001

The 65th Annual Scientific Meeting of the American College of Rheumatology (ACR) and the 36th Annual Scientific Meeting of the Association of Rheumatology Health Professionals (ARHP) will be held from Sunday, November 11 to Thursday, November 15, 2001 at the Moscone Convention Center in San Francisco, California. Pre-meeting courses begin Saturday, November 10.

The Annual Scientific Meeting is planned to promote research in rheumatology that directly relates to the mission of the ACR and to provide a forum for the exchange of ideas about research, education, patient care and socioeconomic issues.

ANNUAL CRA MEETING 2002

The Annual Meeting of the Canadian Rheumatology Association (CRA) will be held in Lake Louise, Alberta from February 20-23, 2002. Mark your calendars and make your plans now!

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Methylprednisolone is begun at 30 mg/kg/day for three days, and is given once a month for three months, together with methotrexate 10-15 mg/m^2. This dose is increased up to a maximum of 30 mg if tolerated. If the dose of methotrexate is increased above 15 mg, the dose is administered subcutaneously, again weekly. Folic acid is used concomitantly, and ongoing hematologic and hepatic monitoring is performed as recommended for patients with arthritis.[10] In patients with rapidly spreading disease that impairs functioning, daily oral prednisone 1 mg/kg/day also is prescribed, and is tapered over approximately six months. This author believes the natural history of the disease has been altered with this treatment. Once a patient's morphea has been inactive for about one year, the dose of methotrexate is tapered.

SUMMARY

Localized forms of scleroderma are much more common than systemic disease in the pediatric age group. Although localized disease is primarily limited to the skin and subcutaneous tissue, severe functional and cosmetic deformities may arise. Therefore, systemic treatment is frequently necessary. Well-conducted clinical trials are required to determine the best treatment. Currently, methotrexate seems to be the preferred treatment for patients in whom systemic therapy is required.

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