CASE REPORT

INTESTINAL PSEUDO-OBSTRUCTION AS AN INITIAL PRESENTATION OF SYSTEMIC SCLEROSIS IN TWO CHILDREN

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SUMMARY

Two children are reported in whom intestinal pseudo-obstruction was the initial manifestation of systemic sclerosis. Gastrointestinal symptoms and skin changes resolved or improved in both children following treatment with prednisone and penicillamine (case 1) or methotrexate (case 2), although radiological changes of the gastrointestinal tract persisted at 3 and 2 yr of follow-up, respectively.

KEY WORDS: Systemic sclerosis, Intestinal pseudo-obstruction, Methotrexate, Penicillamine, Prednisone, Treatment, Outcome.

Systemic sclerosis (SSc) is a chronic multisystem connective tissue disease characterized by sclerodermatous skin changes and fibrous degenerative changes of the viscera [1]. Onset during childhood is very uncommon, and fewer than 100 cases have been reported in the literature [2]. The most common clinical presentations for SSc in children, in order of frequency, are skin tightening, Raynaud’s phenomenon and soft-tissue contractures [3–5]. Occasionally, children may present with fatigue, muscle weakness, failure to gain weight, dysphagia, exertional dyspnoea or cutaneous calcifications [3–5].

Gastrointestinal (GI) involvement in adults frequently includes oesophageal dysfunction, which may antedate cutaneous manifestations by years [6]. Small and large bowel involvement manifesting with abdominal cramps, bloating, and with alternating constipation and diarrhoea, may develop in adult and paediatric patients during the disease course, but these symptoms have not been reported as presenting manifestations of SSc in children.

We present two children in whom intestinal pseudo-obstruction (IPO) was the initial presentation of SSc. These patients were successfully treated with corticosteroids plus penicillamine or methotrexate. There has been a complete remission of GI symptoms, although radiographic abnormalities have persisted.

CASE 1

AB, a 2½-yr-old Caucasian girl, was first seen in the rheumatology clinic at British Columbia’s Children’s Hospital (BCCH) 3 months after the onset of generalized aching, muscle weakness and recurrent vomiting, followed by marked abdominal distension and increased frequency of grey-coloured stools. Two months prior to presentation, she developed cold-induced Raynaud’s phenomenon with ischaemic necrosis and scarring of her fingertips. Just prior to presentation, she developed a rash around her mouth and nose. AB’s paternal grandmother and aunt had died of systemic lupus erythematosus.

Physical examination showed a well-grown and well-nourished child (height and weight on the 90th percentile). Skin changes included numerous erythematous papules < 5 mm in diameter clustered around her mouth and nostrils, palmar erythema, diffuse swelling and erythema of the distal parts of the fingers with some pitting scars of the fingertips, and similar but milder changes on her toes. There were mild telangiectatic capillary changes of the periangual skin. There were no sclerodermatous changes of the skin proximal to the metacarpophalangeal joints. The blood pressure was slightly elevated (100/56 mmHg), but the cardiovascular examination was otherwise normal. Muscle strength was reduced so that she had difficulty rising from a sitting position. The abdomen was grossly distended, and tympanic, with visible peristalsis, but there was no hepatosplenomegaly.

The results of the following investigations were negative or normal: complete blood count, ESR, CK, anti-Sm, -RNP, -Scl 70, -SSA, -SSB and -dsDNA. The serum LDH level was normal (1338 U/l, normal up to 730); as was AST (81 U/l, normal up to 40). Faecal fat excretion was 45 mmol/day (normal 7–21 mmol/day). Upper GI contrast studies showed decreased motility and delayed emptying of the distal oesophagus without reflux, marked dilatation of the small bowel with closely stacked mucosal folds, particularly in the proximal loops, and decreased motility (Fig. 1). Upper GI endoscopy and duodenal biopsy were normal, although there was overgrowth of Escherichia coli in the duodenal aspirate.

Based on the presence of muscle weakness, Raynaud’s phenomenon, and abdominal distension associated with characteristic abnormalities in the upper GI contrast studies, the diagnosis of SSc was made. Treatment was initiated with prednisone (2 mg/kg/day), penicillamine (3 mg/kg/day), cisapride and amoxicillin. Three weeks later, all GI symptoms disappeared and have not recurred in the 3 yr since initial presentation. Eight weeks after beginning treatment, the prednisone dose was tapered; penicillamine was discontinued after 6 months, and cisapride after 17 months of therapy. Skin abnormalities around her mouth and nostrils cleared after 2 months of treatment, and nail-fold capillary loop

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abnormalities normalized 1\frac{1}{2} yr later. The Raynaud’s phenomenon improved gradually, and she has not had an episode in the last 2 yr. Abdominal distension was no longer evident after 1 yr of follow-up. Growth has remained normal. An upper GI contrast study 3 yr after initial presentation showed persistence of the small bowel abnormalities.

**CASE 2**

LH, a previously well 12 yr and 10 month old Caucasian girl, presented to the gastroenterology clinic at BCCH 2 months after the onset of intermittent fever, nausea, vomiting and diarrhoea, and a 9 kg weight loss. She had abdominal distension and discomfort, and her stools were pale and foul smelling. Abdominal radiographs showed distension of large and small bowel with multiple persistent air fluid levels. Upper GI and follow-through studies, and barium enema, demonstrated small bowel dilatation and minor bowel wall thickening, without evidence of an obstructive lesion. Based on these findings, a diagnosis of IPO was made. Biopsies of large and small bowel obtained 2 months after her initial presentation showed an inflammatory visceral myopathy.

Other investigations, including complete blood count, ESR, ANA, anti-DNA, anti-Sm, anti-RNP, anti-SSA,
anti-SSB, anti-Scl 70, and anti-neutrophil cytoplasmic antibodies, were normal or negative.

The patient was managed with total parenteral nutrition for 4 months and later a gastrostomy tube was placed through which she was given elemental feeds. Recurrent episodes of fever, malaise, abdominal bloating with vomiting and diarrhoea were thought to be secondary to bacterial overgrowth, but responded only partially to treatment with tetracycline and metronidazole. Because of persisting GI complaints 8 months after initial presentation, she was treated with prednisone 20 mg/day and within days there was a rapid and dramatic improvement in her symptoms.

One year after onset of GI symptoms, when prednisone had been tapered to 20 mg on alternate days and her abdominal complaints had resolved, she developed multiple firm nodules on her legs, and noticed that her skin had become tender and tight. Over the next few weeks, the tightness of her skin became widespread, she complained of generalized aching not localized to the joints, and she was referred to the paediatric rheumatology service. She denied the use of L-tryptophan or other naturopathic medications, and there was no history of blood transfusion, no known contact with potentially toxic agents such as pentazocine, or bleomycin, and no insertion of prostheses.

On examination, she was thin, weight 42.5 kg (between 5th and 10th percentile) and height 163.5 cm (between 50th and 75th percentile). There was marked, diffuse, ‘bound-down’ induration of the skin on her trunk, limbs and neck, with sparing of the hands, fingers and distal feet. There was less severe involvement of the lower face with mild restriction when she opened her mouth. She had angular cheilitis, but no oral mucous membrane changes. Firm, flesh-coloured nodules measuring <5 mm in diameter were present within areas of induration on the lower limbs (Fig. 2A).

Telangiectasia was noted on the face. Patchy telangiectasia and hyperpigmentation were also observed in sclerodematous areas on the trunk (Fig. 2B) and limbs. The skin was generally very dry with an ‘eczema craquele’ appearance. She had minimal nail-fold erythema, but no definitive capillary loop changes. There was no evidence of arthritis and muscle strength was normal.

Histological examination of a skin biopsy showed dense collagenization of the deeper dermis; in the mid-dermis, the fibroblasts appear activated and there were a few foci of perivascular lymphocytes. These findings were consistent with the diagnosis of scleroderma.

She was treated with high-dose prednisone (2 mg/kg/day) and methotrexate (12.5 mg/m²/week). Her clinical course showed a slow but steady softening of her skin, first noticed 6 months after treatment with methotrexate combined with prednisone was initiated. There was no exacerbation of her skin changes or of her GI symptoms during gradual prednisone reduction. One and a half years later, while still on methotrexate, and on low-dose prednisone (5 mg daily), she had only minimal tightness of the skin over her arms, shins and trunk. Residual skin changes also included telangiectasia, patches of mottled erythema, pigmented changes and a prominent vascular pattern on the trunk and lower limbs. She has had no recurrence of the GI symptoms, although GI contrast studies remain abnormal.

**DISCUSSION**

SSc is a rare disease in childhood. The largest series of childhood-onset disease report features similar to those described for adult-onset disease [1–5]. Cutaneous abnormalities are by far the most prominent manifestations in SSc and form the basis for classification [7, 8] into limited or diffuse cutaneous forms. Both of our patients fulfil the ACR classification criteria for SSc [7], with the first patient meeting minor criteria for that designation with sclerodactyly and digital pitting scars. This patient could probably be described as having ‘limited’ cutaneous SSc which includes the CREST variant. Skin involvement is
usually limited to the hands, feet, face and forearms. Unlike this patient, however, GI involvement in the limited form tends to occur only in the oesophagus and late in the course of the disease [6–8]. The second patient, although fulfilling ACR classification criteria, had a very unusual pattern of disease, with the cutaneous thickening sparing the distal limbs, no Raynaud’s phenomenon and a persistently negative test for ANA. However, visceral involvement in the diffuse form of SSc is often severe, can occur early [6] and may even precede the skin involvement [8–10], as occurred in the second patient’s case. Despite the atypical disease pattern in both children, we believe that SSc is the term that best defines their conditions.

While the course of the skin disease is difficult to predict [11, 12] in the generalized form, there may be progressive skin thickening with more proximal involvement for the first 5 yr, after which the cutaneous changes often stabilize, and may even regress. Both of our patients have had a much briefer time course with dramatic improvement within several months of treatment, which has been sustained at 2 and 3 yr of follow-up.

The oesophagus is the most common site of GI involvement in both categories of SSc; as many as 75–90% of adults with SSc have abnormalities of motility when tested [6, 9, 10]. IPO of varying severity occurs in as many as 40% [8, 9] of patients, but has only been reported in 12 cases as a presenting manifestation of SSc; only one had onset in childhood and SSc was diagnosed at autopsy [13].

Manometric findings in patients with IPO early in the course of SSc have been suggestive of a neuropathic disorder, whereas IPO developing late in the course of SSc has been thought to be due to a myopathic disorder [6]. In case 2, the GI histological findings demonstrated myopathic changes of the smooth muscle early in her disease course.

Visceral myopathy [14, 15], a major cause of IPO, may be histologically indistinguishable from the intestinal changes of SSc. However, by definition, it is not associated with systemic disease. The first patient presented with systemic features in addition to IPO, so the diagnosis was not considered. The second patient presented with isolated GI symptoms, and the histological evidence from the gut supported a diagnosis of visceral myopathy. It was only with evolution of her disease and development of sclerodermatous skin changes that the intestinal disease could be ascribed to SSc.

In SSc, GI involvement may be progressive with the development of oesophageal strictures, malabsorption, pseudo-obstruction and faecal incontinence [11]. In adults with SSc, treatment of the GI disease is usually symptomatic with general measures such as elevation of the head on the bed, multiple small meals, avoidance of recumbency after meals and cessation of smoking. Drug treatment aimed at treating the complications of SSc includes the use of H2 blockers, omeprazole (a proton-pump inhibitor), and prokinetic drugs such as cisapride [6, 10]. We are not aware of any reports of treatment that specifically reverses or arrests the GI disease. Both our patients appeared to respond rapidly to treatment. In patient 2, the resolution of the skin manifestations following the institution of methotrexate was particularly impressive. Symptomatically, the intestinal disease was rapidly arrested in both patients. The persisting GI radiological abnormalities may indicate some permanent post-inflammatory fibrosis; radiographically, it is difficult to distinguish this from active disease. However, there has been no progression on successive radiological studies, and the overall clinical picture is suggestive of inflammatory arrest. The long-term prognosis in both these children remains uncertain.

These two patients demonstrate that intestinal pseudo-obstruction in childhood may be the initial manifestation of systemic sclerosis. In childhood-onset SSc, treatment with disease-modifying agents such as penicillamine or methotrexate may be successful in arresting or reversing cutaneous and visceral manifestations.

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REFERENCES


