EARLY ASSESSMENT OF PULMONARY INVOLVEMENT IN LIMITED SCLERODERMA*

A Case Report

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Limited scleroderma is typified by insidious progression of skin involvement. The onset of internal organ involvement is delayed until the second decade, the lungs being the most important from the prognostic point of view. Early detection of pulmonary lesions is of paramount importance. This paper presents a 16-year-old male patient with a history of Raynaud's phenomenon followed by progressive tightening of skin over the fingers, hands and face. He had early pulmonary involvement detected by high resolution computed tomography (HRCT) and proven by histopathologic examination as usual interstitial pneumonia; even the chest x-ray and pulmonary function tests were normal. A combination of prednisolone and D-penicillamine was planned for treatment because of his having both pulmonary and gastrointestinal system involvement. 99m technetium diethylenetriamine pentaacetate (99m Tc-DTPA) test is very sensitive for pulmonary lesions and it has shown a rapid clearance in the early stage. This method is also useful for following up the therapeutic trial. *Key words: limited scleroderma, high resolution computed tomography, 99m Tc-DTPA.*

Systemic sclerosis is a remarkably heterogeneous disorder with diverse initial presentations and a variable disease course, including wide differences in pace, extent and severity of any of its clinical manifestations[1]. It has an estimated annual incidence of 4.5-12 per million. Childhood onset is very uncommon and accounts for only a small proportion of patients; there are a number of case reports totalling less than 1000 patients[2]. It can be classified into several subtypes, based on the degree of skin and internal organ involvement. Limited scleroderma (CREST syndrome) is a subgroup which has a more benign course than the systemic disease. Skin thickening is less prominent and remains limited to the distal extremities, face and neck. Internal organ involvement occurs only

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after many years of the disease. The most frequent visceral manifestations are pulmonary and esophageal involvement. Esophageal dysmotility is the most common internal organ manifestation and occurs in the majority of children. Fibrosis of the lower two-thirds of the esophagus results in poor propulsive activity, and it leads to reflux[3]. Early detection of pulmonary lesions, especially at the inflammation phase, is of paramount importance, enables one to give early adequate treatment and increases the survival rate[4]. This paper presents a case of limited scleroderma with early pulmonary involvement, describes the diagnostic approach, and discusses the treatment strategy and monitoring.

Case Report

A 16-year-old male patient was referred to the Pediatric Rheumatology Department with a two-year history of his fingers turning blue, especially in winter. He had developed puffy fingers and then had progressive tightening of the skin over the fingers, hands and face in the following months. On careful questioning, it was learned that he did not have shortness of breath or mid-chest pain. On physical examination, he weighed 41 kg (under 3rd percentile), and his height was 159 cm (between 10th and 25th percentiles). The skin over the face was thickened and tightened; the natural creases of his forehead had disappeared. Oral aperture was reduced and radial furrowing was present around the lips. There was a significant change as compared to an earlier age (Fig. 1). The hands appeared shiny and taut with flexion contractions of the finger (Fig. 2). The skin was normal on the other parts of the body. Cardiovascular and

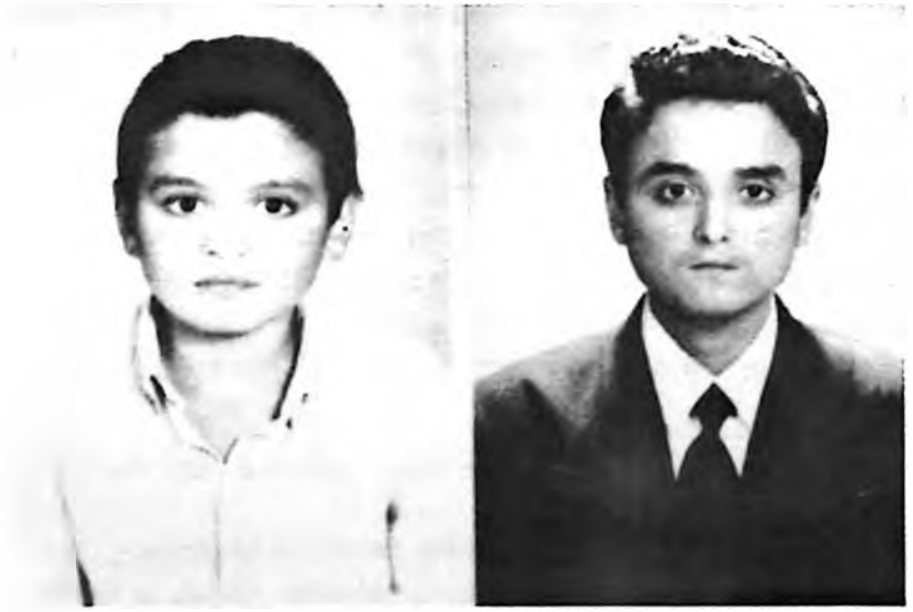

Fig 1. The patient's appearance at 12 and 16 years of age, respectively. Note especially the definite narrowing of the lips and radial furrowing.

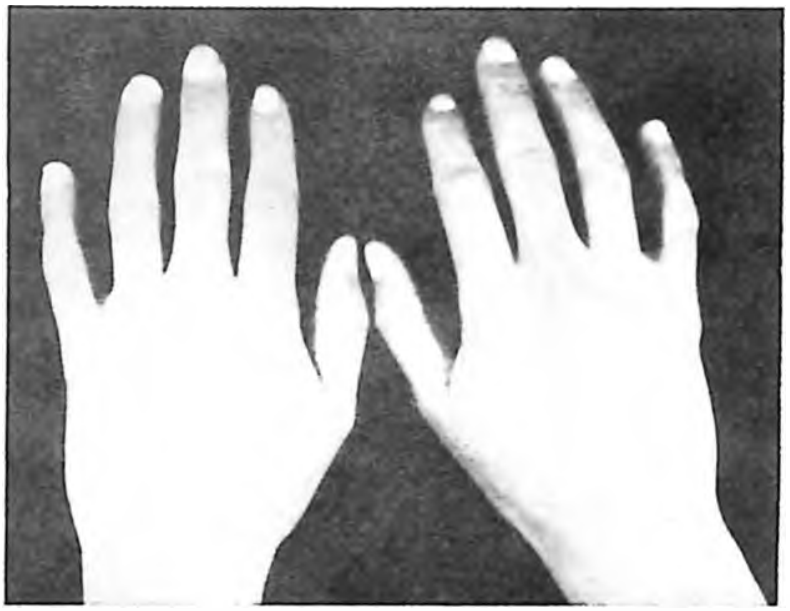

Fig. 2: Sclerodactyly and shiny appearance of the hands with flexion contractions.

respiratory system examinations revealed no pathological signs. He was diagnosed with limited scleroderma. Screenings for renal functions by routine tests and for cardiac functions, including echocardiography and thallium scintigraphy, were normal. The stool examination showed no signs of malabsorption. Gastroesophageal reflux scintigraphy was performed with the indications of pyrosis for the previous two months, and revealed reflux and delayed esophageal movements (Fig. 3). Despite a lack of signs or symptoms

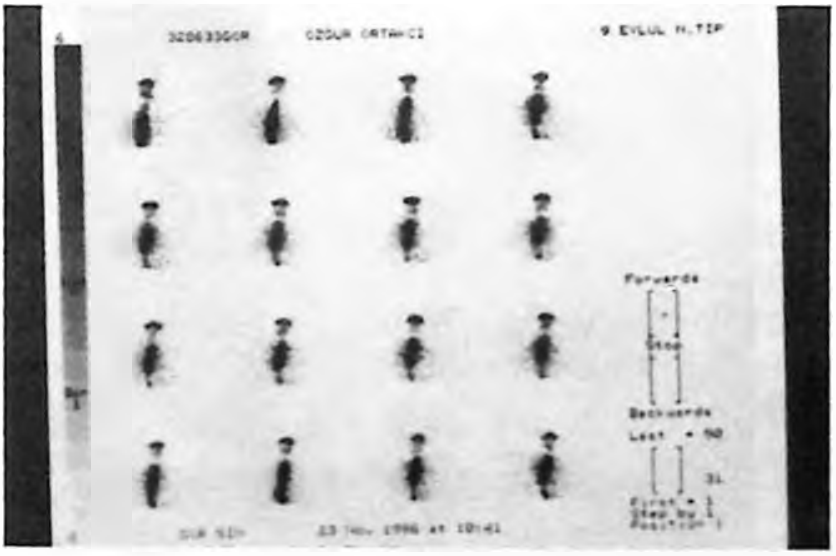

Fig. 3: There is a marked delay in esophageal movements and reflux in series taken during scintigraphy.

of lung involvement and presence of a normal chest x-ray with respiratory function tests, we wanted to evaluate the patient further considering the ominous effects of pulmonary fibrosis on morbidity and mortality. High resolution computed tomography (HRCT) of the lungs revealed small reticular patterns in the lower lobes related with fibrosis (Fig. 4). The hazy appearance of the lung parenchyma suggested an active inflammatory process. The patient underwent bronchoalveolar lavage (BAL), which was normal (90% pulmonary alveolar macrophages, 8% lymphocytes and 2% neutrophils), but histopathologic examination of the biopsy material revealed usual interstitial pneumonia (Fig. 5). 99m technetium scintigraphy was done to determine the degree of involvement as well as to make a comparison between initial findings and the progress (Fig. 6). The clearance rate was increased (t 1/2:30 min, normal value: t 1/2:80 min). Prednisolone (1 mg/kg/d) and D-penicillamine (5 mg/kg/d) therapy was planned for the early multisystemic involvement.

Discussion

Limited scleroderma is typified by insidious progression of skin involvement. Internal organ involvement, other than renal, occurs with frequencies close to that of a diffuse disease, but the onset of involvement is delayed until the second decade. Truly effective and life-extending therapy is available, especially if the diagnosis is made at the beginning of vital organ involvement[1]. The overall mortality rate in scleroderma is 50 percent at seven years, and pulmonary complications are the major cause of death[5]. In the early disease, no signs or

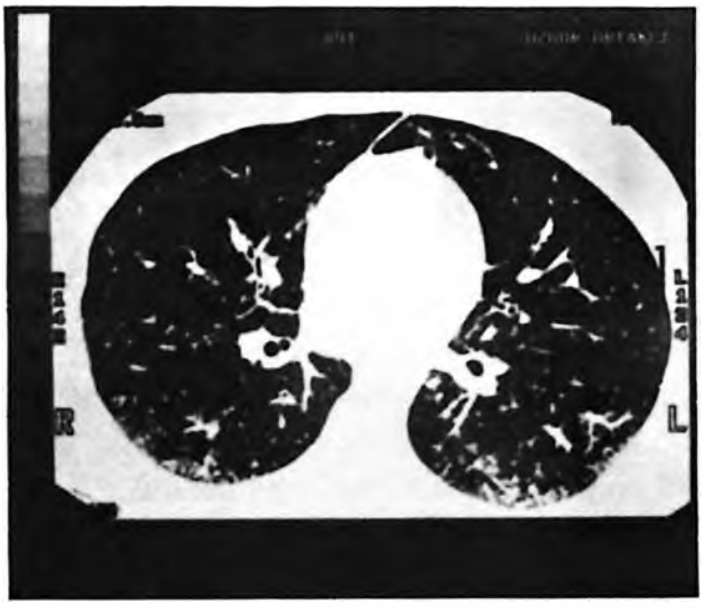

Fig. 4: HRCT findings are definitely seen as small reticular patterns in the lower lobes related with fibrosis.

Fig. 5: A mild degree of alveolar septal thickening caused predominantly by lymphocytes is seen histopathologically (X 40).

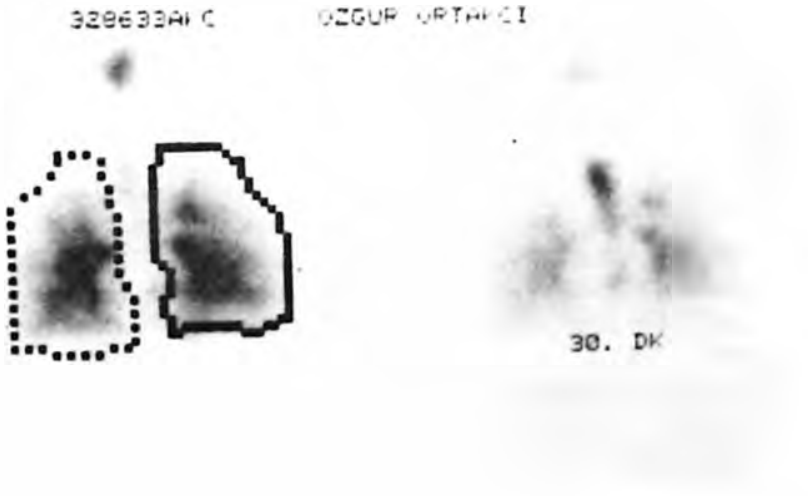

Fig. 6: 99m Tc-DTPA is markedly increased (t 1/2: 30 min).

symptoms of respiratory distress exist and chest radiography may be silent. Only HRCT is able to show early pulmonary involvement at this stage[6]. As we look for the validity of HRCT in diagnosis, we observe that it is highly sensitive in detecting pulmonary lesions (71%) when compared to x-ray films (42%), and pulmonary function tests (42%)[7]. It is also able to classify pulmonary involvement such as "small reticular" and "ground glass" patterns[8]. This patient with limited scleroderma also had normal results including respiratory function tests. Early detection of small reticular lesions in HRCT caused us to examine the lungs in detail. Despite the normal findings in bronchoalveolar lavage (BAL), interstitial pneumonia on histopathologic examination proved the lung involvement.

Regarding the involvement of skin, gastrointestinal and respiratory systems, we planned a combination therapy of prednisolone and D-penicillamine. Prednisolone was successful in treating interstitial pneumonia by delaying the fibrosis, and D-penicillamine had significantly greater effect in improving skin thickening than other disease-modifying agents[1]. Another challenge was to identify a potential marker of progression of the pulmonary disease. We preferred a scintigraphic method, 99m Tc-diethylenetriamine pentaacetate (99m Tc-DTPA). Pulmonary epithelial permeability can be studied by measuring the clearance rate of inhaled 99m Tc-DTPA. This hydrophilic molecule crosses the alveolar-capillary barrier and diffuses from the air space into the vascular space, probably passing through the tight epithelial intercellular junctions. In a recent retrospective study, abnormally rapid clearance of 99m Tc-DTPA at initial measurement was found to identify fibrosing alveolitis patients at higher risk of a decline in functional indices over the subsequent three years[9]. The authors concluded that rapid clearance was likely to reflect both interstitial inflammation and mechanical stretch of the respiratory epithelium due to the lung fibrosis. They pointed out that incomplete control of inflammation in the setting of significant lung fibrosis was an alternative explanation for fixed abnormalities in 99m Tc-DTPA clearance[10-12]. Thus, we were able to reveal both the initial degree of lung involvement, and a method to follow up the patient at regular intervals.

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