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CALCINOSIS IN GENERALIZED SCLERODERMA

Aksel Otkjær Nielsen, Birgitte Brun and Lena Secher

Departments of Dermatology and Radiology, University Hospital, Copenhagen, Denmark

Abstract. 20 cases of generalized scleroderma with calcinosis, i.e. Thibierge-Weissenbach syndrome, were reviewed concerning the clinical and radiological findings. 60% of the patients complained of esophageal dysfunction, and in 85% radiological abnormalities of the esophagus were found. Gastro-intestinal complaints, with or without radiological changes, were found in accordance with other reports. Decreased pulmonary function was a frequent feature, but only half of these cases showed pulmonary fibrosis on chest X-ray. Calcinosis primarily affects areas of sclerosis, but can be found elsewhere. Six of our patients had intervertebral calcifications in the thoracic and/or lumbar spine. This seems to be a new observation in patients with scleroderma.

Key words: Systemic scleroderma; Calcinosis cutis; Intervertebral calcifications

Calcinosis in association with scleroderma was first described in 1911 by Thibierge & Weissenbach (16). Sporadic cases have been reported since then, and in 1964 Winterbauer introduced the CRST syndrome with the associated findings of calcinosis, Raynaud's phenomenon, sclerodactyly, and teleangiectasia (18). The calcinosis, consisting of calcium apatite crystals (13), is limited to the dermal and subcutaneous tissues. It is found primarily, but not exclusively, in the areas affected by sclerodactyly and is not associated with abnormalities of the calcium metabolism (11). The sclerodactyly is morphologically identical with that seen in classical acrosclerotic scleroderma. The teleangiectasies are similar to those seen in the Rendu-Osler-Weber syndrome.

This is a report on the clinical and radiological findings in 20 cases of circumscribed calcinosis in patients with systemic scleroderma.

MATERIAL AND METHODS

The records of 170 patients with systemic scleroderma were reviewed. In 18 females and 2 males calcinosis was diagnosed clinically and by X-ray examination. All of them were suffering from acrosclerosis which was subdivided into moderate or severe cases, according to the severity of Raynaud's phenomenon and the extent of the sclerosis. The mean age at onset of skin symptoms was 40.2 years. At the time of investigation it was 57.8 years. The condition of the patients was reviewed especially concerning the degree and location of calcinosis. Clinical and radiological evidence of visceral involvement was noted, and so was the development of diseases other than scleroderma within the observation period. Laboratory investigations included the serum concentrations of calcium and phosphorus, examination of the hepato-renal function, and tests for rheumatoid factor, LE cell reaction and antinuclear antibodies.

RESULTS

Clinical findings

All 20 patients were suffering from acrosclerosis; 16 to a moderate and 4 to a severe degree. Sclerosis of the hands was present in all patients; location of the sclerosis is indicated in Table 1. Raynaud's phenomenon was a prominent feature in 18 patients; of these, 16 also had teleangiectasia, primarily localized to the face. Fifteen of 20 patients gave a history of recurrent ulcerations on hands and feet.

Twelve patients (60%) were troubled by esophageal dysfunction, making this the most common manifestation of visceral involvement. Retrosternal burn was a symptom in 7 patients, nausea and vomiting occurred in 3 cases. Exertional dyspnea was a prominent symptom in 10 (50%) of the patients. Testing the pulmonary function, lowering of the diffusion capacities was demonstrated in 12 patients. In 5 patients it was found normal, 3 were not tested.

Radiological findings (Table II)

The esophagus was examined in all 20 patients. In 17 of the examinations a decreased peristaltic activity was seen, and in 11 cases the esophagus was dilated as well (Fig. 1). Three of these patients had a short,

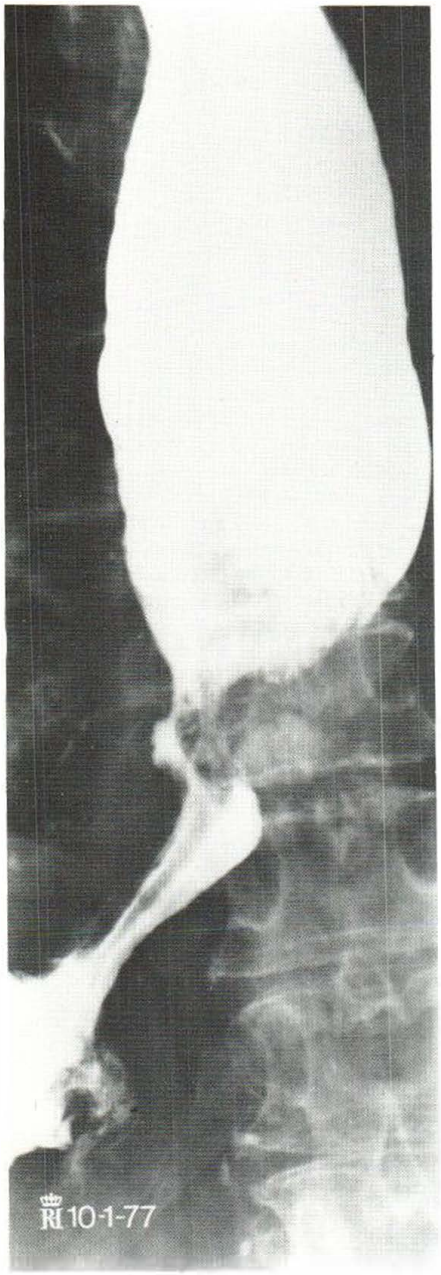

Fig. 1. Dilated esophagus with a short, distal stenosis and a sliding hiatus hernia.

distal stenosis. Nineteen of the 20 patients underwent examination of the stomach. In 3 cases a small sliding hiatus hernia was demonstrated, but the stomach itself was otherwise normal in all cases. Two patients showed evidence of doudenal ulcer; one of them had only a deformation of the duodenal bulb, the other had an ulcer which healed during the observation period. In 2 cases there was a marked dilatation of the descending and horizontal duodenum (Fig. 2). Radiological studies on the small intestine showed pathological changes in 6 of the 15 patients examined. In all 6 cases there was a dilatation of segments of the small intestine, but in spite of this, the valvulae conniventes were clearly seen and appeared close together (Fig. 2). In 1 patient signs of intussusception was noted. The transit time was normal in all cases, and no sacculations or pseudoverticula were found. A barium enema of the colon was performed in 6 patients. Three of the examinations showed severe constipation. One patient had characteristic pseudodiverticula with faeculiths, and in one case there was a marked dehaustration. Pulmonary fibrosis was found in only 6 cases; in 2 patients the changes developed during the observation period.

Table I

Location of sclerosis	No. of patients
Hands	20
Feet	15
Arms	11
Legs	10
Face	14
Chest	2

The location of calcinosis is shown in Table III. Hands were involved in all cases (Fig. 3). In patients examined more than once, changes in severity were observed. Thus, in one patient calcifications diminshed, in 6 they increased, and in 4 there were fluctuations. In 16 patients there was evidence of absorption of the distal phalanx of one or more fingers. Three patients of 8 examined had calcinosis of the forearms. Shoulders were involved in 7 cases (Fig. 4), elbows in only 4. None had calcifications of

Table II. *Radiological changes in the gastro-intestinal tract*

	No. of patients	Abnormal findings	
		No.	%
Esophagus	20	17	85
Stomach	19	3	16
Duodenum	19	4	21
Small intestine	15	6	40
Colon	6	4	67

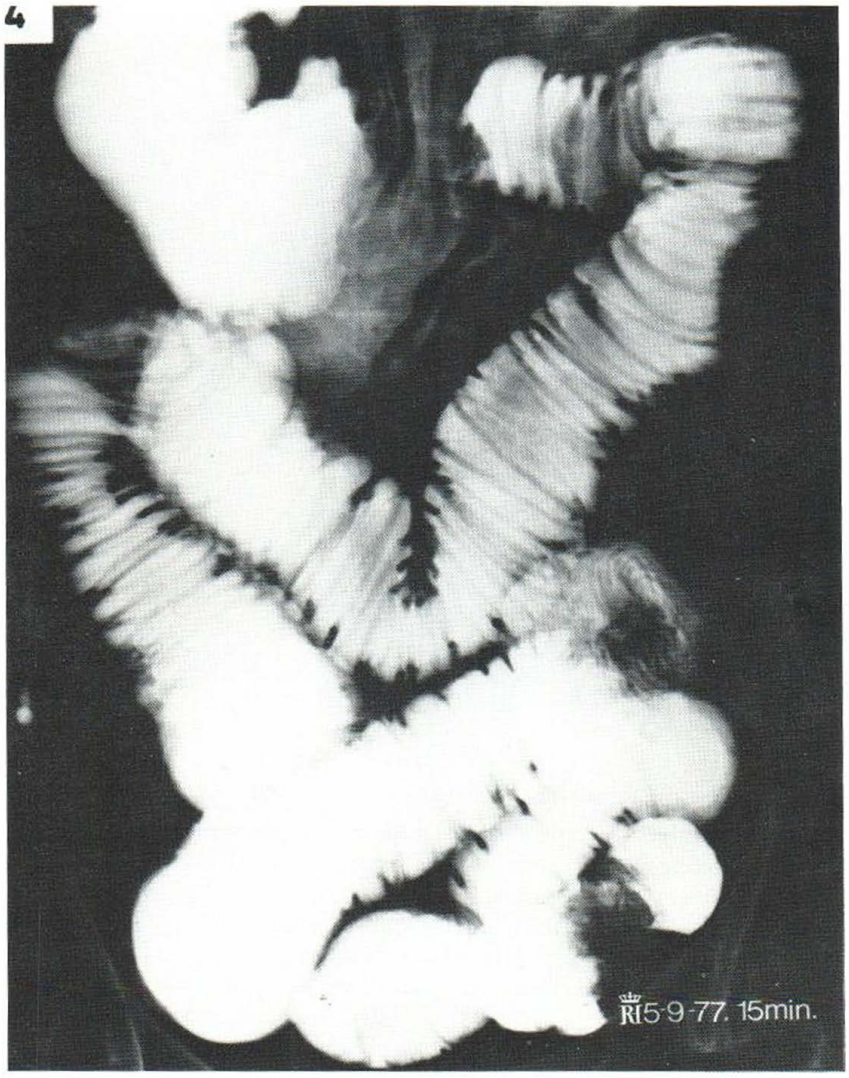

Fig. 2. Barium examination of the small intestine shows dilatation of the duodenum. In the jejunum there is a slight dilatation and a tightly packed fold pattern with a decreased distance between the mucosal folds.

the upper arms. Calcinosis of the hips was demonstrated in 5 patients. The thigh was involved in one case, the lower leg in 5 cases. Five patients had calcifications confined to the knees; one improved during observation. Calcification of the soft tissues of the neck was found in one case. Only 3 patients of 12 examined had calcinosis of the feet; there was no change in the observation period. Halisteresis of the feet was present in 8 patients.

The thoracic and lumbar spine was examined in 8 cases. Five of these patients had peripheral intervertebral calcifications. The calcifications were found more frequently in the thoracic than in the lumbar spine and appeared with a pronounced bulging on the anterior side of the spine, presumably in the annulus fibrosus. Similar calcifications were seen on a chest film of another patient, whose spine was not examined separately (Fig. 5).

Laboratory investigations

Results of studies of serum calcium and phosphorus were normal in all patients. No patients suffered from severe renal involvement. Serum creatinine was normal in all but one case, in which it was slightly raised; proteinuria was present to a slight degree in 2 patients only. No signs of abnormal liver function were found in any patient.

LE cell reactions were negative in all cases, while

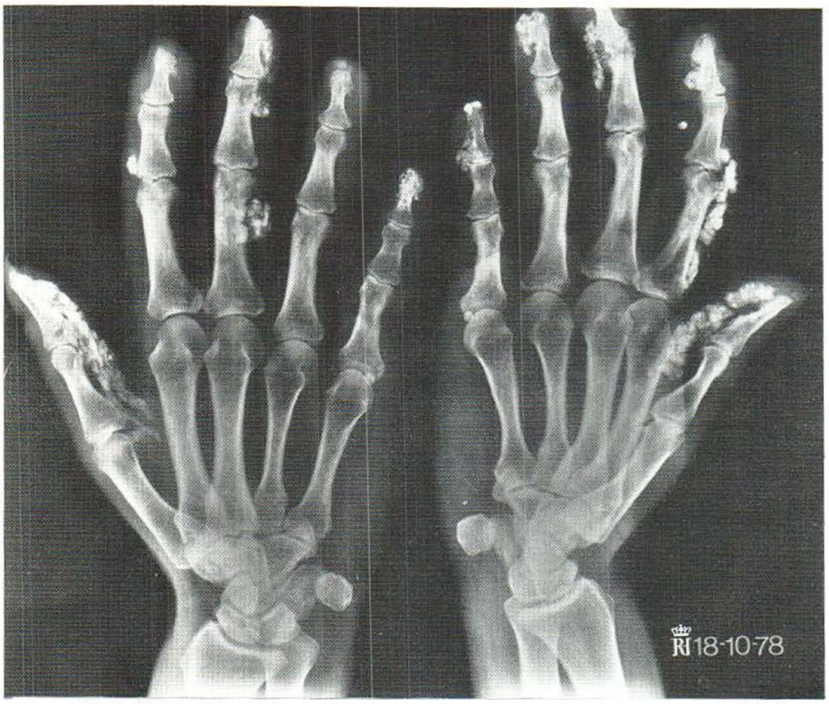

Fig. 3. Extensive soft tissue calcifications of the hands in a 45-years-old female.

antinuclear antibodies were demonstrated in 13 of 19 patients. One patient had a positive test for rheumatoid factor; she was suffering from rheumatoid arthritis as well as scleroderma. Other collagen diseases were represented by 2 cases of Sjögren's syndrome.

Three patients in our series developed malignancies: 2 cancers of the breast and one of the vulva.

DISCUSSION

A series of 170 cases of systemic scleroderma included 20 cases of the Thibierge-Weissenbach syndrome, i.e. the combination of scleroderma and calcinosis. This is a somewhat higher incidence than reported by others (17). With 18 females and 2 males, giving a ratio of 9:1, our series is in complete agreement with other reports (17).

It is also a confirmation of the observation made by others, that calcinosis occurs in combination with acrosclerosis. Sixteen of our patients also had Raynaud's phenomenon and teleangiectasia, thus qualifying as examples of the CRST syndrome. Regarding the degree and extent of sclerosis, calcinosis and visceral involvement, they did not differ from the other 4 patients in our series, possibly indicating calcinosis as the more important feature. In systemic scleroderma the changes in the gastrointestinal tract are caused by fibrosis of the submucosa and muscularis, resulting in hypomobility and dilatation (9, 12). The esophagus is most frequently involved, but pathological changes can be found in the stomach and in the intestines as well (4, 7, 12).

Radiological changes of the esophagus are found in 50–88% of patients in other series (2, 7, 14, 17). In this study, changes in the esophagus were found in 17 of the 20 patients (85%) corresponding to the

Table III

Location of calcifications	No. of patients
Neck	1
Spine	6
Shoulders	4
Upper arms	–
Elbows	4
Forearms	3
Hands	20
Hip joint	5
Thighs	1
Knees	5
Lower legs	5
Feet	3

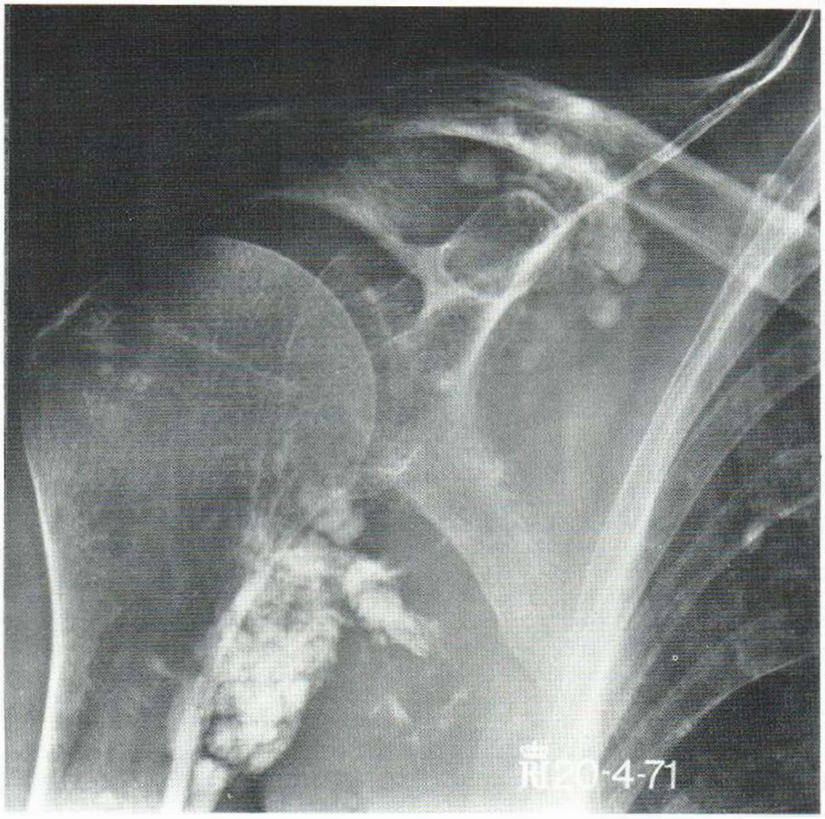

Fig. 4. Calcifications of the shoulder region in a 52-year-old female.

highest incidence in other materials (2, 7). The most frequent abnormality was hypomobility and a smooth mucosa devoid of folds, but a high incidence of dilatation was found as well. The occurrence of an esophageal stricture and a sliding hiatus hernia has sometimes been considered characteristic in systemic scleroderma (3), while others have discussed this point (4, 14). In the present series, 3 patients had a short stenosis in the distal esophagus, one in association with a hiatus hernia. Two other patients had a hiatus hernia without stenosis.

The stomach as such is usually not involved, but dilatation and diminished peristalsis with delayed emptying has been described (7, 9). The occurrence of duodenal ulcer during the course of the disease has been observed (17), but our material, with evidence of duodenal ulcer in 2 of 19 examinations, is too small to verify the significance of this finding.

Changes in the small intestine in systemic scleroderma are often marked. The second and the third part of the duodenum, to the midportion of the horizontal limb can be considerably dilated (4, 5, 6, 14), and compression from the superior mesenteric artery has been suggested as the cause (10, 15). In our material only 2 patients showed this abnormality.

As in the duodenum, dilatation is the prominent feature in the rest of the small intestine (4, 9, 14). The valvulae conniventes are clearly seen, and the intervalvular distance may be reduced (6, 10). Hypomobility of the small intestine can lead to pseudo-obstruction (4, 9) and to the formation of pseudodiverticula. None of these were found in the present study, and no delay in the transit time was observed.

The colon is considered less frequently involved than the small intestine by some authors (14), while others find pathological changes to be more common (4, 7). The occurrence of wide-neck pseudodiverticula, best shown on post-evacuation films, is a characteristic finding (4, 7). A dilatation which can be so marked that it may simulate Hirschsprung's disease, is another typical feature (7, 9).

Pulmonary involvement is a frequent feature of

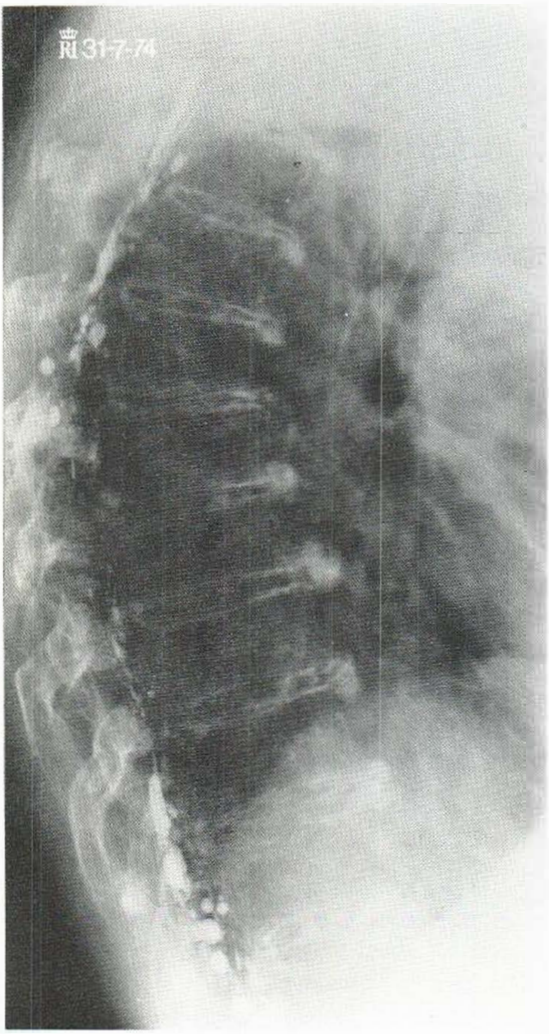

Fig. 5. Intervertebral calcifications of the thoracic spine in a 59-year-old female. The calcifications are located in the periphery of the discs, presumably in the annulus fibrosus. The anterior extensions of the calcifications are well marked. Traces of contrast material are seen in the spinal canal.

systemic scleroderma (17); our series includes 12 cases of impaired lung function and is thus no exception. The location of calcifications in our patients corresponded closely to other cases of the Thibierge-Weissenbach syndrome, as well as to other cases of the CRST syndrome. However, the intervertebral calcifications seem to be remarkable. Involvement of the spine in collagen diseases is rare apart from rheumatoid arthritis and ankylosing spondylitis. Although soft tissue calcifications close to the spine have been observed, real intervertebral calcifications have not previously been mentioned in connection with scleroderma. Distinction of these calcifications from osteophytes and syndesmophytes presented no problem. Annulus fibrosus calcifications are usually symptomless (1), and none of our patients had complaints from their backs. The fact that 2 of our patients developed carcinoma of the breast is suggestive. A few cases of this combination have been recorded in the literature (8). Our series includes a total of 3 malignancies.

At the time of this study, our group of patients had been ill for almost 20 years on average. It is also well known from other reports (11, 17) that calcinosis takes several years to develop.

Patients with the Thibierge-Weissenbach variant of scleroderma thus represent a selected group with a disease of great chronicity. This probably accounts for their relatively good survival prospects, as pointed out by some authors (11, 18).

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A. Otkjær Nielsen, M.D.
Department of Dermatology
Rigshospitalet
Blegdamsvej 9
DK-2100 Copenhagen
Denmark