

SCLEROEDEMA

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Although scleroedema is uncommon it is probably much less rare than the relatively small number of recorded cases (about 125) would imply, as many of the authors who have become interested in the condition have been able to collect several cases within quite short periods. As our knowledge of the collagen diseases has increased, scleroderma has attracted the attention of physicians in many specialities and now usually receives consideration as a diagnostic possibility. This wider recognition of scleroderma lends greater importance to scleroedema with which in its early stages it is so easily confused and from which it differs in course and prognosis.

Historical

Although Buschke (1902) gave the first adequate description of the condition and proposed the name of scleroedema adutorum, Henry G. Piffard (1876) of New York in his 'Elementary Treatise on Diseases of the Skin' described 'scleriosis' in a blacksmith, aged 49, and differentiated it from scleroderma. He noted 'apparent spontaneous recovery and absence of appreciable histological change' (Saffron, 1943).

Touraine *et al.* (1936) in an exhaustive review of the literature have discovered at least ten other case reports antedating Buschke, the earliest being that of Curzio (1752). In the last half century many further examples have been reported and a very comprehensive study of all the cases then published was undertaken by Touraine and Golé (1937). Until 1932, when Epstein recorded two cases in the United States, the majority of cases had been recognized in Continental Europe. Since 1932, however, many further American cases have been reported (Sweitzer and Laymon, 1938; Michelson and Laymon, 1937; O'Leary *et al.*, 1940; Vallee, 1946; Madison, 1950).

Scleroedema has received very little attention in Great Britain. Gordon (1936) described a single case, but no other reference has been discovered in the English literature.

Clinical Features

Sex

Females are affected approximately twice as frequently as males.

Age

Children and young adults are usually affected. The majority of reported cases occurred in the first three decades and the disease has been recognized in early infancy. Cases over 50 are very uncommon but the oldest patient reported was 68 (Audry and Gadrat, 1930).

Familial Incidence

A brother and sister who were simultaneously affected were reported by Jagtman (1948). In both children the scleroedema developed after whooping-cough and first involved the buttocks.

Race

The distribution of case reports throughout the world literature does not suggest any racial predisposition. No reports from tropical countries have been discovered, but this may be due to the relative inadequacy of diagnostic facilities in some tropical regions or to climatic factors.

Seasonal Incidence

O'Leary *et al.* (1940) drew attention to the frequency with which their cases began in the colder months of the year. Three of Vallee's (1946) four cases began in the winter or early spring and most other reported cases in which the month of onset is stated show the same seasonal incidence, but cases have been reported beginning at all seasons.

Mode of Onset

In the majority of cases a febrile illness has preceded the onset of the cutaneous changes. Scarlet fever, rheumatic fever, tonsillitis, nephritis, otitis media, dental and wound infections have been most often recorded. Influenza and ill-defined fevers, especially respiratory infections, are next in fre-

quency. Measles, mumps and typhus have occasionally been observed. Arnold's (1938) case was possibly related to a tuberculous cervical adenitis. Between 5 per cent. and 10 per cent. of cases have apparently not been preceded by any infection.

After the initial infection there is an asymptomatic period usually of two to four weeks' duration but sometimes as short as two or three days or as long as three months. At the end of this latent period the skin changes are usually the first to attract attention but a few cases develop mild fever, joint or muscle pains and malaise. If these symptoms are present they are seldom severe.

Occasionally a transitory erythema, roseolar, urticarial or annular, may precede the appearance of the scleroedematous changes (Touraine *et al.*, 1937). The skin changes usually begin in the neck whence they extend by continuity to involve the face, the upper trunk and the upper arms. In most cases the process remains limited to these sites but in some the buttocks, abdomen and thighs are also affected and occasionally the process may be generalized sparing only the hands and feet. Scleroedema may first develop in other sites, particularly the face and the abdominal wall, but extension is almost always by continuity. Extension usually takes place rapidly and is complete in two to fourteen days. More rarely, it may continue for two or three months. The rarity of involvement of the hands has been emphasized by most writers, but it may occasionally occur and was indeed present in Buschke's original case. Maschkilleison and Abramowitsch (1935), Darier *et al.* (1919) and Arnold (1938) have also recorded cases with involvement of the hands. In such cases the palms and fingers escape or are only affected in the slightest degree and there is no succeeding sclerodactyly.

Most patients complain only of stiffness and tightness of the involved skin. The rigidity may, however, be sufficiently constricting to cause dyspnoea and a sensation of tightness across the chest on exertion. Tancredi's (1951) patient was unable to walk up or downstairs and the movements of her neck were also greatly restricted. Dysphagia and hoarseness have been present in some cases and involvement of the tongue may also cause dysarthria.

The affected areas may show no gross changes on casual inspection. The skin is usually pale but the waxy or ivory-like appearance of scleroderma is absent. Obliteration of the skin folds may transform the face into a rigid mask. The eyelids may be swollen but are more often merely puffy or are unaffected. Palpation reveals a resistant induration which will not pit on pressure. The skin cannot be pinched up and will not move freely

over the subcutaneous tissues. At the borders of the affected regions the abnormal skin merges gradually into the normal.

Until recently most reports have drawn attention to the rarity of systemic involvement and the scleroedematous process was often considered to be localized to the skin, although weakness of the muscles underlying the involved skin had been fairly frequently noted; the muscles sometimes seem swollen and infiltrated and weakness may be quite marked. However, recent case reports indicate that scleroedema involves a wide variety of tissues. Vallee (1946) discovered a pleural effusion in two of four cases he reported and a pericardial effusion in a third. Hydrarthrosis was reported by Voss (1938), Schnitzer (1941) and O'Leary (1940). Madison's (1950) patient showed striking bilateral parotid enlargement and a probable pericardial effusion. Vallee's patient showed low voltage electrocardiograms. These other lesions regress at the same time as the skin lesions.

No constant alteration of the blood chemistry has been recorded. There is usually no leucocytosis and the erythrocyte sedimentation rate is either normal or only slightly elevated. Kircher's (1951) patient had persistent eosinophilia. There are no constant urinary abnormalities.

Course and Prognosis

In the majority of cases complete resolution takes place. This is neither so universal nor so rapid as many textbook accounts of the condition imply. Regression of the cutaneous changes usually begins in those areas which were last involved. Resolution may be complete in three or four weeks but most commonly takes six months or rather longer. Residual areas of scleroedema may persist for many years and the eyelids were still oedematous after 20 years in one case (Adler, 1926). More rarely extensive involvement may persist for long periods, e.g. over 15 years (Hoffman, 1927).

In the great majority of cases the prognosis for life is excellent and complete restoration of function follows resolution of the oedema. The skin is restored completely to normal and there is no atrophy, sclerosis or pigmentary change. Leinwand (1951) has recorded the only case in which death was apparently the direct consequence of the scleroedema. The first skin changes were detected at the age of 57 and the patient died about six years later.

Recurrences after complete recovery are not uncommon and run the same course as the initial attack, being likewise usually preceded by an infective episode. The interval between attacks has varied from one to twenty years.

Pathology

The histopathology of the skin in scleroedema has been carefully studied by Freund (1930). The epidermis is usually unaffected although there may be some flattening of the basal layer. The upper third of the dermis shows only some perivascular infiltration with lymphocytes and occasional histiocytes and plasma cells. The cellular infiltrate may be more marked in the lower dermis in which the characteristic connective tissue changes are present. The collagen bundles are swollen and are separated by interstitial oedema which may form spaces (fenestration), which in sections stained with haemotoxylin and eosin may appear empty. This oedema fluid was shown by Freund to stain bright red with cresyl violet. Some investigators have failed to obtain this staining reaction. Vallee partially obtained it in one of his cases and not at all in the other. Madison (1950) suggests that the presence of the staining reaction and the type and extent of the cellular infiltrate may depend on the stage of the disease at which the biopsy is performed. Recently Braun-Falco (1952) on the basis of histochemical studies claims that there is an increase of dermal hyaluronic acid in scleroedema and that this substance fills the characteristic spaces between the connective tissue bundles. He suggests that this would also explain the metachromasia.

Since the diagnosis in Stenbeck's (1940) autopsied case is uncertain and was probably scleroderma

only one autopsy report is so far available. Leinwand's (1951) patient died of pneumonia, but her death was attributed to the scleroedema since her respiratory movements had been grossly restricted by extensive involvement of the thoracic wall and the rigidity of her abdominal wall limited her consumption of food. On macroscopic examination the oedema and rubbery consistency of the tissues were obvious and held them apart after section. In addition to the skin the subcutaneous tissues, the voluntary muscles and the walls of the ventricles also showed this rigidity. Hydrothorax and hydropericardium were present. Microscopy showed a widespread increase in the size of collagen bundles and the presence of a mucinous substance in their interstices. The muscle bundles of the rectus muscle were reduced in number and separated by lobules of adipose tissue in which were moderate amounts of pale staining eosinophilic intracellular material. The muscle cells and nuclei of the heart showed no significant changes but there was widening of the spaces between small muscle bundles and between groups of bundles. Neither the lungs nor gastrointestinal tract showed the changes encountered in scleroderma.

Aetiology

Although many hypotheses have been advanced the cause of scleroedema remains unknown. The frequency with which both initial attacks and re-

	Scleroedema	Scleroderma
Preceding infection.	In almost all cases. Usually streptococcal. Latent period one to six weeks.	Rare—no constant relationship.
Prodromal symptoms	Usually absent. Brief when present: malaise, myalgia, low fever.	Common. Often prolonged. Pain, swelling, stiffening of joints. Raynaud-like syndrome extremities.
Cutaneous changes.	Develop rapidly, reaching maximum extent in a few weeks. Initial involvement usually neck or trunk. Hands and feet very rarely involved. Involved areas pale but not dead white. Complete restitution. No atrophy, pigmentation or telangiectasis. No irreversible changes.	Progressive extension over many years. Earliest changes often in hands. Hands and feet involved at onset or early in disease. White or ivory colour. Waxy sheen. Atrophy, telangiectasis, pigmentation. Sclerosis.
Systemic involvement	Hydrarthrosis, hydrothorax, hydropericardium. No irreversible changes. Lungs and oesophagus not involved.	Oesophageal and pulmonary lesions most in evidence.
Course	Complete recovery in 6 to 18 months in majority of cases. Occasionally longer course. Death exceptional.	Progressive atrophy and sclerosis. Permanent loss of function. Spontaneous remission very rare. Prolonged progressive course. Eventually fatal in many cases.
Pathology	No epidermal change. Swelling of collagen fibres. Fenestration by mucin-like substance. No endarteritis.	Atrophy of epidermis. Homogenization of collagen leading to sclerosis. Endarteritis.

currences have followed an infection, particularly a streptococcal infection, suggests a possible causal relationship which is further emphasized by the occasional onset of the scleroedema around the site of the pre-existing infective process.

Differential Diagnosis

Scleroedema is most frequently confused with generalized scleroderma. The distinctive differences between the two conditions are illustrated in the previous table (modified from Madison).

In the early oedematous stage some cases of diffuse scleroderma may be difficult to distinguish from scleroedema, but the diagnosis is usually soon apparent from the course of the condition.

O'Leary (1938) has drawn attention to the difficulty sometimes experienced in differentiating dermatomyositis and scleroedema and states that it may sometimes be necessary to reserve judgment until the patient has been observed for some time. O'Leary and Waisman (1940) obtained a history of a preceding acute infection in 11 of 40 cases of dermatomyositis. Skin rashes, absent or transitory in scleroedema, were present in 38 of these cases of dermatomyositis. The skin lesions were the presenting symptoms in 60 per cent. of Sheard's (1952) 25 cases; the remainder presented with muscle weakness or stiffness. Cutaneous oedema is a feature of both conditions and in both the periorbital skin is frequently involved, but whereas in scleroedema the neck and shoulders seldom escape, in dermatomyositis the extremities, especially hands, wrist and forearms are more often affected and neck and trunk are spared. In scleroedema the skin lesions regress completely, but in many cases of dermatomyositis atrophy, pigmentation, telangiectasis, calcification or scleroderma persist indefinitely. Scleroedema is usually afebrile; fever, a raised erythrocyte sedimentation rate, and a slight or moderate leucocytosis are common in dermatomyositis. Death is quite exceptional in scleroedema, but the mortality of dermatomyositis is approximately 50 per cent. Although the histological changes in skin or muscle may be non-specific in both conditions in the early stages, in most cases characteristic changes eventually develop. The histological changes of dermatomyositis have been well described by Pagel *et al.* (1949) and by Wainger and Lever (1949). Focal degenerative changes in voluntary and cardiac muscles, widespread fibrinoid degeneration in arteriolar walls and homogenization and fibrinoid degeneration of connective tissue are quite unlike the reversible connective tissue oedema of scleroedema.

Trichiniasis and myxoedema could theoretically

be confused with scleroedema but in practice no difficulty should arise.

In the infant scleroedema has to be differentiated from sclerema neonatorum, subcutaneous fat necrosis, the generalized oedema of erythroblastosis and the localized oedema of orbital skin, feet and lower legs sometimes observed in the newborn, particularly in the premature infant and possibly due to water retention from renal immaturity (Potter, 1952).

Case Report

Mrs. E. G., housewife, age 55. The patient has had no serious illnesses. She has three children alive and well; two children died of meningitis. Her general health was good until 1938 when she spent about six months in bed with an illness which was febrile in its early stages and which was then diagnosed as rheumatic fever. She experienced considerable pain in the larger joints, the pain moving from joint to joint, and she remembers severe and persistent sweating. She was not admitted to hospital. Ever since this attack she has been short of energy but this symptom has been really troublesome only in the last eight years, during which time she has suffered from giddiness and palpitation on exertion and headaches, usually occipital, most severe in the mornings.

In October 1950 she first noticed thickening of the skin of the neck and chest and this gradually became more marked and involved an increasingly large area of the neck, upper arms, upper trunk and face. During the next year she noticed an increasing sensation of tightness in the skin, particularly across the chest on exertion.

She was first admitted to hospital in December 1950. She was found to have limitation of neck movements in all directions except forwards and a diffuse firm non-pitting oedema involved the face, neck, trunk and upper arms. No abnormality was discovered on systemic examination other than a blood pressure of $\frac{160}{90}$ and a rough systolic murmur in the mitral region. An X-ray of the chest showed no abnormality of the lung fields but the cardiac outline suggested some left ventricular enlargement. Barium swallow showed no abnormality. The electrocardiogram showed left axis deviation.

Two white blood counts were within normal limits. The haemoglobin was 66 per cent. with 4,000,000 red blood corpuscles.

The patient made some improvement during the next few months but in the summer of 1951 the feeling of tightness in the chest-wall and increasing weakness resulted in her re-admission to hospital. The scleroedema at that time was almost

as extensive as at the time of her previous admission. There was no pigmentation or atrophy in the involved areas. Systemic examination again showed no abnormality other than a blood pressure of $\frac{200}{100}$. A white blood count was within normal limits. Serum proteins, 8.2 g.; albumin, 4.8 g.

Biopsy. The epidermis was not affected. The collagen fibres throughout the section appeared slightly oedematous, but no other abnormality was present.

In July 1952 the patient was re-admitted as there had been no change in her symptoms and re-examination showed the scleroedema to be approximately of the same extent as a year before. She was treated with cortisone from August 7 to August 30. The cortisone was given intramuscularly in divided doses; 25 mg. were given the first day, 50 mg. the second day and 100 mg. daily thereafter for the remainder of the course. There was moderate subjective improvement and possibly some slight objective improvement but this was difficult to assess. There was certainly no extensive or rapid regression of the cutaneous changes. During the year that has elapsed the patient's subjective improvement has been maintained but the extent of the scleroedema remained more or less unchanged until May 1953. During the next two months marked regression was observed and on July 15 the area involved was limited to the neck, shoulders and upper arms, and muscle power had increased.

Discussion

This case of scleroedema illustrates most of the characteristic features of the condition. The prolonged course, contrary to the impression given by many textbook descriptions, is not unusual. The lack of any detectable abnormality in the affected areas after regression of the gross changes observed at the height of the disease was most striking as were the relatively insignificant changes on histological examination by the customary techniques. The lack of response to cortisone was disappointing, but it is possible that the dosage employed was too low.

Vallee has pointed out that since a large proportion of patients with scleroedema are children or adolescents the term 'adulterum' is inappropriate and misleading. Scleroedema without qualification is a satisfactory and non-committal descriptive term.

The concept of the collagen diseases has been useful in directing the attention of clinicians and pathologists to the importance of the connective

tissues in disease, but the prevailing lack of agreement on fundamental issues is demonstrated in the 'Transactions of the First Conference on Connective Tissues' (1950). Scleroedema does not share with the 'collagen diseases' the common denominator, fibrinoid degeneration. However, the essential disease process of scleroedema appears to involve primarily either collagen or ground substance and as an example of a reversible change in connective tissues is worthy of greater attention than it has received.

Summary

The literature on scleroedema is briefly recorded and an account is given of the clinical features, pathological changes and differential diagnosis with special emphasis on the differentiation from scleroderma.

A new case of scleroedema, unsuccessfully treated with cortisone, is reported.

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