POSTINFLAMMATORY ELASTOLYSIS AND CUTIS LAXA

A REPORT ON A NEW VARIETY OF THIS PHENOMENON AND A DISCUSSION OF SOME SYNDROMES CHARACTERIZED BY ELASTOLYSIS

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Loosening of the skin to such an extent that it seems too large for the surface it covers is a rare phenomenon which occurs as the main or a subsidiary feature in a number of unrelated diseases. When large areas are involved the appearances are striking if not spectacular, and in the days when doctors still enjoyed the advantages of a classical education they were irresistible to neologists. Few writers in the past deigned to use the nomenclature of a predecessor in reporting a new case with loose skin.

Most of the terms are synonymous, but they might be used simply to describe the cutaneous changes or be applied to the disease of which they are part; some served in both capacities. To make matters worse they were, and still are, sometimes misused for diseases such as cutis hyperelastica in which the skin is not loose at all, or for conditions like Von Recklinghausen's disease in which loose skin may be an incidental finding.

The terms oftenest used these days are 'cutis laxa' and 'anetoderma'. Although synonymous they describe, respectively, extensive and circumscribed areas of loose skin; but they are also used for some relatively well-defined syndromes. Unhappily, nobody is quite sure where 'circumscribed' ends and 'extensive' begins, and one man's anetoderma is the other's cutis laxa.

In an earlier communication[1] concerning a patient with cutis laxa and emphysema we suggested that certain syndromes might be rescued from the confusion. These syndromes have two factors in common, loose but normal-looking skin and elastolysis, and we classified them into 2 groups under the general heading of primary elastolysis: (1) generalized cutaneous elastolysis (cutis laxa, congenital or acquired, with or without systemic manifestations) and (2) localized cutaneous elastolysis (blepharochalasis and the primary anetodermas).

We were then aware of the few cases described in the literature in which cutis laxa followed some inflammatory episode, but underestimated their significance. The observation of a series of cases in which cutis laxa followed a curious chronic annular erythematous eruption has led us to broaden our classification and make provision for the possibility that systemic elastolysis may exist without skin lesions (Table I).

TABLE I. CLASSIFICATION OF ELASTOLYSIS

Generalized Cutaneous Elastolysis (cutis laxa)

Congenital (*a*) Apparently restricted to skin
(*b*) With systemic lesions

Acquired (*a*) Insidious onset { (i) apparently restricted to skin; (ii) with systemic lesions
(*b*) Postinflammatory

Circumscribed Cutaneous Elastolysis

Blepharochalasis
Anetoderma (cryptogenic)

Systemic Elastolysis

An open category to cover the possibility that elastolysis may not always involve the skin.

THE NEW DISEASE

The disease begins in infancy or early childhood and presents an eruptive phase lasting several months to several years which is succeeded by a permanent state of cutis laxa.

Five cases have been seen. We have followed 3 patients from the onset of the disease for from 6 months to 6 years, and have had access to 2 others, one of whom was in the burnt-out phase.

None of the patients was older than 3 years at the onset of symptoms. Four patients were girls, one a boy; all were Coloured (Afro-European) and were born and live in the Cape Province of South Africa. The cutaneous picture is so stereotyped that the following description covers all the cases:

The primary lesion is a juicy, bright red papule which quickly begins to extend peripherally and become dark bluish-red in the centre. Enlargement continues over several days to a week or two and the final lesion is a round or oval plaque, 2 - 10 cm. in diameter, with a bright red cord-like margin up to 1 cm. wide. The central area subsides to skin level and becomes wrinkled and hyperpigmented. Within the lesion a collarette of scaling is usually visible, running parallel to the margin and a few millimetres to a few centimetres from it. Confluence of plaques may produce large lesions with circinate margins.

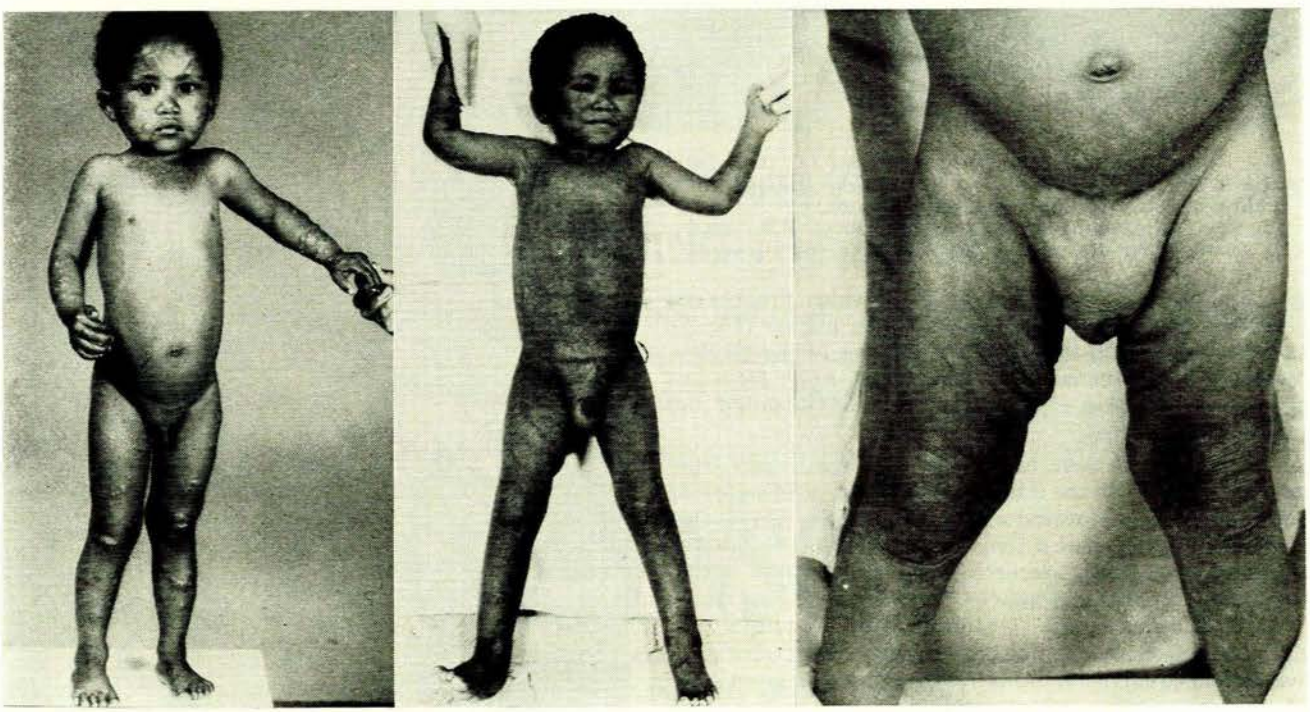

Fig. 1 *Fig. 2* *Fig. 3*

Fig. 1. Postinflammatory elastolysis. Patient D.S. at the onset of disease. *Fig. 2.* Patient D.S. when disease had been in progress for 6 months. *Fig. 3.* Patient D.S. in arrested phase 18 months after onset of disease.

At any given time there may be anything between a few and scores of lesions at varying stages of development. The plaques are a little reminiscent of those of erythema annulare centrifugum (Darier) or of erythema chronicum migrans (Lipschütz). Any part of the body may be affected except for the palms and soles, but the face, ears and neck are invariably involved at some time in the attack (Figs. 1, 2 and 3).

In 4 cases lesions continued to erupt in new areas or in previously affected skin for 6 - 12 months before finally subsiding, and in the fifth, after an original attack lasting about a year, the patient was still sporadically producing crops of lesions 3 years after onset (Fig. 4).

Laxity of the skin is apparent as soon as lesions have subsided and worsens for a few months. Thereafter it may remain constant or improve a little. Only skin affected by the eruption becomes lax. The phenomenon is always pre-

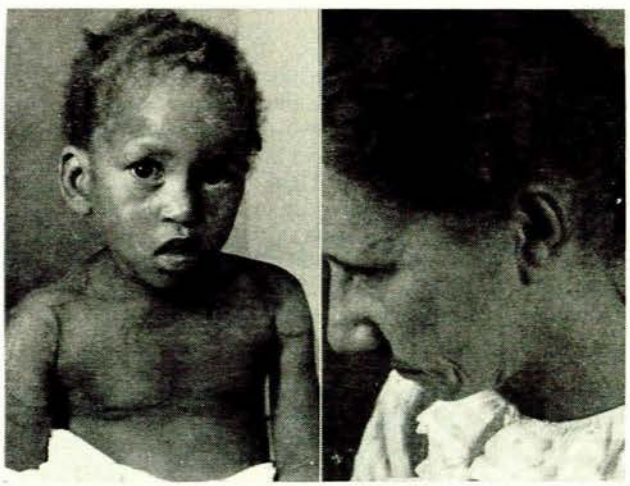

Fig. 4 *Fig. 5*

Fig. 4. Postinflammatory elastolysis. Patient J.C. The disease is still active 3 years after onset. Note collarette of scaling in active lesions and sagging earlobe.
Fig. 5. Postinflammatory elastolysis. Patient P.B., aged 15 years, when disease had been inactive for 10 years.

sent and most outspoken in the face which droops and gives the child a lugubrious appearance of old age (Fig. 5). In other areas, with the possible exception of the genitals, the laxity is of little cosmetic importance. Apart from loss of elasticity the skin is unchanged; colour, sensation and sweating are normal.

In 3 cases there were no signs or symptoms apart from those in the skin. In the 2 others concurrent or intercurrent pneumonia was discovered during the eruptive phase. One girl, aged 3 years, had a long stay in hospital because of migrating pneumonia, recurrent attacks of otitis media, keratoconjunctivitis and attacks of diarrhoea during which fresh blood was passed. Treatment with broad-spectrum antibiotics produced no improvement. Because of a positive second-strength Mantoux reaction she was given antituberculous therapy and promptly produced a shower of papules which at first resembled papulonecrotic tuberculides but proved, by their progress and histological appearance, to be the same as her original lesions.

Lung-function tests performed on 2 patients showed no evidence of emphysema; cardiac catheterization studies were normal in one of the two. Repeated investigations for infective agents (including rickettsiae) were negative in the 3 cases studied in the active phase. All showed a moderate degree of anaemia, the erythrocyte sedimentation rate was raised, and fractionation of the serum proteins showed lowered albumin and raised globulin values. Serum copper values were normal in 2 cases, and in one case there was no evidence of any increase of elastase activity.

The oldest patient, now aged 15 years, is emotionally disturbed because of her ancient appearance, but is alert and intelligent. She is normally developed for her age in all other respects.

We have found no specific treatment. Systemic steroids controlled the eruption well in one case, partially in another; a late relapse in a third case subsided untreated. Antibiotics were of no avail.

Although we have, as yet, discovered no evidence of systemic involvement, the occurrence of pneumonia in 2 cases makes us unwilling to be dogmatic on this subject and further detailed studies will be published later.

HISTOLOGY

Acute Phase

The epidermis appears normal. There is subepidermal oedema, capillary hyperaemia and slight neutrophilic infiltration. The oedema is often severe and extends into the middle third of the corium where the inflammatory infiltration is

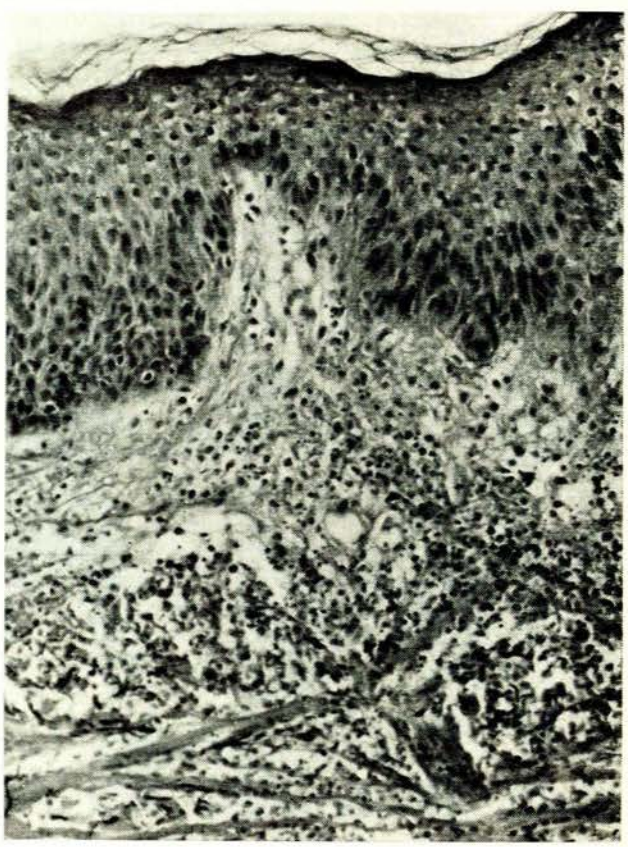

Fig. 6. Postinflammatory elastolysis. Acute phase. Oedema and mild inflammatory infiltrate in upper dermis; denser infiltrate with nuclear debris in deep dermis (H & E x 400).

much denser than in the subepidermal layer. Dense neutrophilic infiltrations are found particularly around blood-vessels and epidermal appendages. There are a few eosinophil leucocytes and occasionally some nuclear debris in the infiltrations (Fig. 6).

Scattered necrotic foci may be seen in the dermal connective tissue, but this is not a constant finding. Special staining shows breaking up and granular degeneration of elastic fibres even in the early phases of acute lesions. Changes in the collagen are less marked, but some fibres stain irregularly with the Van Gieson method.

Subacute and Late Phases

The epidermis is normal in contrast to the dermis which appears atrophic. Slight to moderately dense predominantly perivascular infiltrations of lymphocytes and a few histiocytes are found: they diminish with ageing of the lesions. Elastic fibres are almost totally absent in the upper two-thirds of the dermis. The remnants of elastic fibres still present are thinner than normal and frequently granular and fragmented (Fig. 7). The collagen fibres show a yellow core with Van Gieson staining and appear atrophic. The degeneration and atrophy are most obvious in the upper two-thirds of the dermis, but may extend to some degree into the deep dermis next to the subcutaneous tissue. The epidermal appendages are unaltered, but lie much more superficially than normal because of the atrophy of the upper parts of the dermal connective tissue.

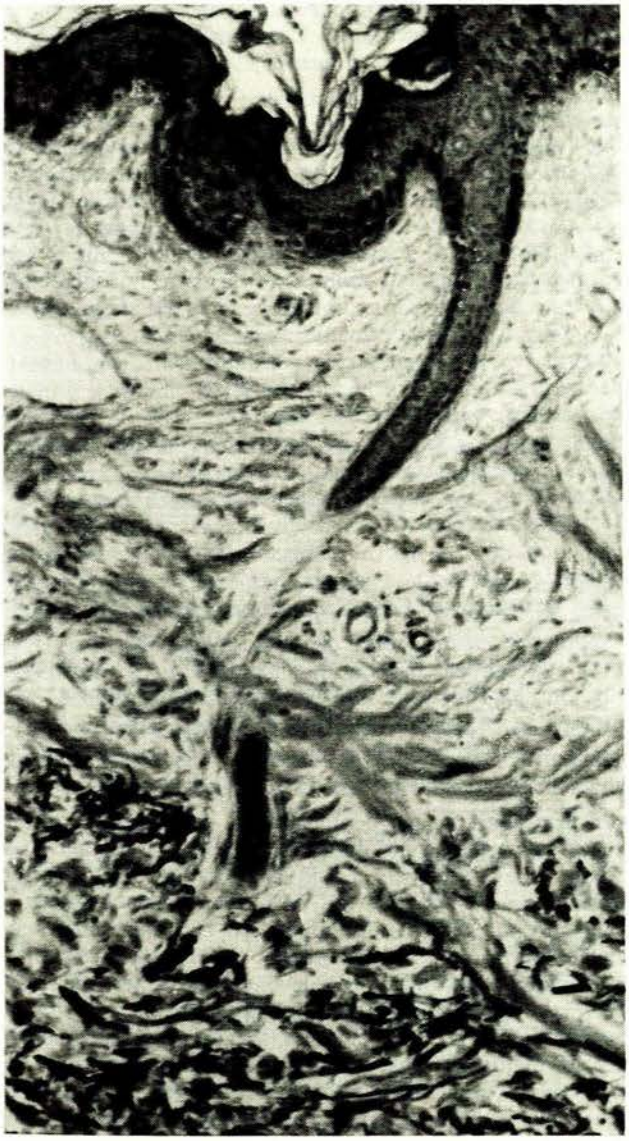

Fig. 7. Postinflammatory elastolysis. Final phase. Disappearance of elastic from upper dermis and fragmentation of what remains (Verhoeff x 400).

DEFINITION OF TERMS

Cutis laxa is defined in the *Nouvelle Pratique Dermatologique*[2] as 'a rare disease that is most often congenital but sometimes acquired. Lesions may be regional, extensive or generalized, and the skin tends to hang in flaccid folds.' Among the synonyms for cutis laxa we find loose skin, lax skin, *Schlaffhaut*, dermatolysis, cutis pedula, cutis pensilis, cutis lapsus, cutis rugositas, dermatochalasis, dermatomegaly, chalodermie and chalazoderma; and there are many others.

In the earlier literature the condition oftenest described under the title of cutis laxa is neurofibromatosis (Von Recklinghausen's disease) with pendulous tumours. Neurofibromatosis can stand on its own feet, and we feel that the term cutis laxa should be abandoned in describing or classifying it. The use of cutis laxa as a synonym for cutis hyperelastica is equally unwarranted, and the term should be abandoned or carefully qualified in describing cases of pseudoxanthoma elasticum, subsiding haemangioma or other dermatoses of known origin in which there may be areas of pendulous skin. We suggest that cutis laxa (unqualified) be used to describe only those cases in which large areas of skin or the whole integument become loose and pendulous and where elastolysis is the most prominent histological feature.

Anetoderma is defined in the *Nouvelle Pratique Dermatologique*[3] as a 'circumscribed atrophoderma of slow, chronic progression characterized by little erythematous plaques, evolving under the influence of a state of inflammation that is microscopic rather than clinical'.

For clarity we suggest that anetoderma be used to describe small (up to 5 cm. diameter) discrete patches of loose skin resulting from elastolysis of unknown cause. In other words, we would reserve the term for the primary cryptogenic anetodermas. As Degos[4] points out, these anetodermas may begin in different ways, but the final picture is the same in all. The little herniations of skin in terminal anetoderma are easily distinguishable from lesions caused by cicatricial atrophy. When small patches of loose or atrophic skin succeed the lesions of some known disease or occur *de novo* in patients with some systemic disorder, we prefer the term 'macular atrophy', suitably qualified, e g. syphilitic macular atrophy.

THE VARIETIES OF ELASTOLYSIS

Congenital Elastolysis

Cutis laxa may be evident at birth or appear soon afterwards, and it has even been reported in a 6-month-old foetus (Houel, cited by Petges and Lecoulant[2]). The whole integument is generally affected, and the skin sags so far that the child presents a mournful appearance of advanced old age (Fig. 8). Facial changes are so stereotyped that affected children look almost identical. This *Shangri-la* phenomenon is not confined to congenital elastolysis; it occurs in acquired elastolysis of insidious onset,

and may appear very rapidly in cases of postinflammatory elastolysis in children or adults.

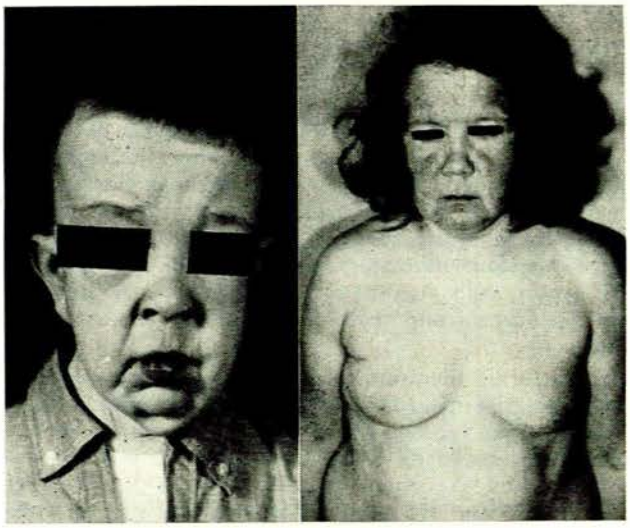

Fig. 8 *Fig. 9*

Fig. 8. Congenital elastolysis in a boy aged 7 years (Goltz's case).
Fig. 9. Sarcoidosis as a cause of lax skin in a girl aged 14 years (Degos' case of infantile geroderma).

The cutaneous changes of congenital cutis laxa are not likely to be confused with those of progeria where the ancient-looking child has an atrophic, wizened skin that does not sag appreciably. Dwarfism is a characteristic of progeria ; growth is normal in congenital cutis laxa.

Elastolysis may seem to be confined to the skin as in the case reported by Robinson and Ellis[5] or there may be signs of lung involvement as well.[6-8] In several cases inguinal or ventral hernias and diverticulosis have been discovered,[9] and osseous dystrophies and laxness of the ligaments of the fingers and toes accompanied cutis laxa in a case described by Debré *et al.*[10]

Congenital elastolysis has occurred in siblings and evidence of parental consanguinity has been discovered.[9,11-14] Patients may die in infancy or early childhood as a result of the disease, or they may live the normal span. Postmortem studies have shown degenerative changes in the elastic tissue throughout the body.[9]

Acquired Elastolysis of Insidious Onset

Elastolysis may manifest itself insidiously in childhood or adult life. Signs of disease may apparently be confined to the skin, there may be emphysema as well,[1] or there may be total elastolysis as in Bettman's case.[15]

The clinical and histological pictures in congenital elastolysis and in acquired elastolysis of insidious onset are superposable, and it seems likely that we are dealing with early and late-developing varieties of the same disease.

Familial acquired cutis laxa is noted by Graf (quoted by Steiner[16]). A man, one of his sons and a daughter, and one of his grandchildren sired by a normal son, all developed the disorder in the fifth decade. In another family a man who had begun to show signs of cutis laxa at the age of 16 years had a son in whom the disorder was present at birth.[17,18]

We are not alone in speculating about the possibility of the discovery of cases of generalized elastolysis in which cutaneous changes are absent or minimal (Table I). Goltz *et al.*[9] suggest that those cases in which emphysema, diverticulosis and hernias are present at birth or appear soon afterwards, might conceivably be examples of a similar or related connective-tissue defect.

We would note, in passing, that the case of cutis laxa associated with systemic abnormalities reported by McCarthy *et al.*[19] presents neither the clinical nor the histological characteristics of elastolysis.

Postinflammatory Cutis Laxa

Cutis laxa may develop after some inflammatory disease of the skin or other organs. Pneumonia preceded the skin changes in a boy seen by Haushalter,[20] and Goth[21] described a case in a young woman where loss of weight and articular rheumatism were the first symptoms. Petges and Lecoulant[2] cite Radcliffe Crocker's case where scarlatina was followed after a year by cutis laxa.

The case oftenest quoted is that of the girl, Armandine Schlesser. At the age of 10 years, after a few days of fever, headache and abdominal pain, she developed a generalized rash of non-pruriginous urticaria-like papules. Within a few weeks the skin became loose and her facial appearance grossly altered. The eruption seems to have persisted or recurred over at least 6 months, but it had subsided when, aged 13 years, she was seen by Dubreuihl[22] who described her as a case of generalized dermatolysis. Souques and Charcot[23] saw her again when she was 21 and called her condition cutaneous geromorphism;[24] her appearance in the illustration recalls that seen in those varieties of elastolysis previously discussed.

A similar case is illustrated by Degos[4] in his *Dermatologie*. A girl aged 16 developed a generalized, constantly recurring eruption of urticated elevations which itched only slightly. At 22 years she had the facial appearance of a woman of 60. She had circumscribed atrophic lesions on the arms, and Degos classifies her case as one of anetoderma of Pellizzari with chalazoderma of the face.

Schuppli[25] has reported on a man aged 20 years who developed red patches on the face and neck. Elastolysis and loosening of the skin subsequently developed, and Schuppli's title for the condition is 'dermatochalasis'.

In none of these cases is there any suggestion that elastolysis had occurred in any organ other than the skin.

A case apart is one demonstrated by Degos[26] as infantile geroderma in a girl with sarcoidosis. At the age of 9 months she developed a diffuse micropapular eruption which persisted until the age of 4 years when it was succeeded by an oedematous infiltration accompanied by articular pains and iridocyclitis. A biopsy had shown a tuberculoid appearance in the skin, but tuberculin reactions were persistently negative. Radiological examination showed bone and lung changes suggestive of sarcoidosis. Steroid therapy reversed the changes in the skin, bones and lungs without affecting the iridocyclitis. Now aged 14 years, she presents a facial picture of old age and cutis laxa (Fig. 9). There is degeneration of the dermal elastic tissue, though not to the extent seen in cases of cutis laxa of unknown origin.

Blepharochalasis

Blepharochalasis, which generally makes its appearance in young people, may be inherited as a dominant trait. The histological appearances are comparable to those seen in cutis laxa. It is possible that blepharochalasis may represent a *forme fruste* of the disorder which manifests itself fully in congenital elastolysis or acquired elastolysis of insidious onset.

Anetoderma

Compared with cutis laxa the lesions of the anetodermas are dull and unspectacular. Deluzenne,[27] in his study of 200 cases in the literature since 1867, suggests a simple classification into primary and secondary types. Primary anetodermas arise in previously normal skin and may be cryptogenic or associated with some dermatosis such as acrodermatitis chronica atrophicans or chronic discoid lupus erythematosus or with a systemic disease such as syphilis or tuberculosis. Secondary anetodermas arise at the sites of the lesions of other diseases. In this group are the anetodermas following syphilides, tuberculides and sarcoidosis.

Craps[25] reported a case of congenital anetoderma with skeletal abnormalities and lesions evocative of the atrophoderma of Pasini and Pierini. Anetoderma is found with osteopsathyrosis and cataract in the Biegvat-Haxthausen syndrome.[29] It was associated with bony abnormalities in a child seen by Grupper and Bonparis,[30] and with dystrophia myotonica in a case reported by Gaté *et al.*[31]

We are here concerned only with the primary cryptogenic anetodermas of which 3 main clinical variants are described. They occur almost always in adults. Lesions vary in number from a few to hundreds; commonly discrete, they may become confluent in places. Sites of election are the trunk and upper arms but any area may be affected. The initial lesions, which are inflammatory, may appear in a single attack or recur *in situ* or in new areas over weeks or months.

The degree of inflammation is variable and may be so slight as to escape recognition in the case of the anetoderma of *Schweninger-Buzzi* where little soft saccular pseudotumoral elevations appear in the skin, with no history of any preceding inflammatory change.

In the anetoderma of *Thibierge-Jadassohn* the primary lesions are round or oval erythematous macules or papules ranging in size from a few millimetres to about 3 cm. After a few weeks to a few months the skin becomes lax and atrophic; some residual erythema may remain for a time around the atrophic centre. There may be only a single crop of lesions, or there may be recurrent attacks.

In the anetoderma of *Pellizzari* (*eritema orticato atrofizzante*) the primary lesions are erythematous and urticaria-like. In Pellizzari's original case the first lesions took 2 months to subside, and the patient suffered recurrent attacks over some years. Deluzenne[27] suggests that the bullous anetoderma of Alexander could safely be integrated with the Pellizzari type.

Despite initial differences the end-result in the cryptogenic anetodermas is the same: little pouches of loose skin which can be pressed into the subcutaneous tissue through gaps in the connective tissue as through a hernial orifice.

The histological changes of mild dermal inflammation followed by degeneration or disappearance of elastic tissue is the same in all. Unhappily, not all cases conform exactly to these classical descriptions and Deluzenne[27] considers that the differences are artificial.

The vast bulk of cases of anetoderma described in the literature are postinflammatory and none, as far as we are aware, has been accompanied by emphysema or other evidence of systemic elastolysis.

Some cases described as anetoderma would, we consider, be more accurately named postinflammatory cutis laxa; Degos'[4] case of anetoderma of Pellizzari, already mentioned, is an example.

It would simplify matters if, pending knowledge of their causes, cases of postinflammatory elastolysis were named according to their final state of atrophy rather than on the initial inflammatory lesions.

DISCUSSION

Elastolysis is a common feature of many dermatoses, but only when it seems to be the solitary or the main final lesion is the cutis laxa-anetoderma phenomenon seen. Elastic tissue has great recuperative power; it may disappear in granuloma annulare and in secondary syphilides, but both these diseases heal without a mark except on the rarest occasions.

Most theories about the causes of elastolysis vary between the improbable and the absurd, but Goltz *et al.*[5] have a plausible suggestion. They discuss the possibility of an *in vivo* balance between elastin, elastase and elastase inhibitor, and argue from their findings in 2 cases that there exists in congenital generalized elastolysis some defect in the normal relationship between serum copper, ceruloplasmin and elastase inhibitor activity of the serum.

Such a mechanism could hardly be invoked to explain the more circumscribed elastolysis of postinflammatory cutis laxa and anetoderma.

It is likely that the classification of cases of elastolysis will be simplified rather than further complicated in the future. We shall probably find that there are two basic groups, congenital generalized elastolysis of early or late expression and postinflammatory elastolysis.

SUMMARY

A series of cases has been observed in which elastolysis and cutis laxa followed a chronic annular erythematous eruption. The diseases characterized by elastolysis and loose skin (cutis laxa; anetoderma) are briefly described, and a scheme for their classification and nomenclature is proposed.

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