Emphysema and cutis laxa

L TURNER-STOKES, C TURTON, FM POPE, M GREEN

From the Brompton Hospital, London; and the Dermatology Research Group, Medical Research Council Clinical Research Centre, Northwick Park Hospital, Harrow

We describe two teenage patients with severe, generalised emphysema, occurring in association with cutis laxa, a heritable disorder of elastin. Emphysema is described in infants with the recessive form of cutis laxa, but our patients are unusual in that emphysema was not apparent until adolescence.

Case reports

CASE 1

A 14 year old boy, the child of unrelated Caucasian parents, had suffered from infantile eczema, and wheezed in the presence of cats. There was a strong history of atopy on his father's side. When he was 6 grommets were inserted for otitis media, but he was otherwise well; and he showed a remarkable talent for football until the age of 11, when his wheezy cough became more troublesome. A year later an attack of severe breathlessness led to hospital admission.

On examination, in addition to signs of airflow obstruction, he was found to have a supraumbilical hernia and skin laxity, with infraorbital sagging and loose skin around the eyelids and ear lobes (fig 1). Earlier photographs showed normal facial appearances until he was 10, when infraorbital haloes started to appear.

Routine investigations gave normal results apart from transient leucocytosis and raised immunoglobulin fractions compatible with an infective exacerbation. Serum copper, caeruloplasmin, and alpha₁-antitrypsin concentrations were all normal. Responses to skin prick test for common allergens were positive.

The chest radiograph showed severe bilateral basal emphysema with absence of peripheral vessels. Lung function tests showed a severe obstructive defect (FEV₁, 520 ml, 22% predicted), increased residual volume (RV, 435% predicted) and reduced gas transfer factor (TLCO, 70% predicted). Mid-range compliance of the lungs was considerably increased at 260 ml/cm water (247% predicted), while aortic compliance was reduced at 68% predicted. Skin biopsy samples showed short, thick elastic fibres with fragmentation, characteristic of cutis laxa.

Lung function improved only slightly despite bronchodilator treatment in hospital and an extended trial of high dose prednisolone. Over the subsequent three years dyspnoea has worsened and lung function deteriorated despite growth.

Address for reprint requests: Dr M Green, Brompton Hospital, London SW3 6HP.

Accepted 19 April 1983

Fig 1 Characteristic facial appearance of cutis laxa (case 1), with loose skin under the eyes and around the eyelids and ear lobes.

CASE 2

This girl was the normal, healthy child of unrelated parents. There was a family history of asthma on her mother's side. She had two healthy brothers. She enjoyed sports but at 10 years she began to develop progressive dyspnoea (without cough or sputum) and she lost weight. By the age of 13 she could barely climb one flight of stairs, and was referred to hospital.

On examination she was thin and breathless, with pendulous ear lobes and lax skin on her prepubertal genitalia. Her height was on the 10th centile, but her weight was under the third. There was slight joint hyperextensibility. The chest appeared overinflated; breath sounds were quiet and there were signs of pulmonary hypertension.

Fig 2 Chest radiograph (case 2) showing severe bullous emphysema.

Routine haematological and biochemical investigations yielded normal results. Concentrations of serum immunoglobulins, copper and caeruloplasmin, alpha₁-antitrypsin, sweat sodium, and urinary hydroxyproline were also normal. Responses to skin prick tests for house dust and *Alternaria* were positive.

The chest radiograph showed severe bullous emphysema in both lung bases, extending into the upper lobe on the left (fig 2). Lung function tests showed a severe obstructive pattern (FEV₁ 420 ml, 23% predicted) with hyperinflation (total lung capacity 6.8 litres, RV 6.1 l) and very low TLCO (24% predicted). A small skin biopsy specimen showed no fragmentation of elastin.

There was no response to bronchodilator or corticosteroid treatment. Her disease progressed and she died of respiratory failure at the age of 14.

Discussion

Emphysema presenting in teenagers is unusual, even in homozygous alpha₁-antitrypsin deficiency. In the cases presented here it was associated with a clinical diagnosis of cutis laxa, a skin condition characterised by abnormal elastic tissue. Classically patients with cutis laxa have loose skin which recovers only slowly after stretching. The ear lobes are large, pendulous and striated, and the eyes are baggy with infraorbital sagging and loose skin around the eyelids. The nose is hooked with long columella and everted nostrils.¹ Skin biopsy may reveal short, thick, fragmented elastic fibres, with normal collagen.²

Cutis laxa is generally an inherited condition. The mode of inheritance varies, recessive inheritance being associated with the severest clinical manifestations. Children with the disease (often with consanguineous parents) have obviously loose skin at birth, and most die during infancy from cardiopulmonary complications, although many sys-

tems may be affected. Emphysema frequently occurs, leading to cor pulmonale.¹⁻⁴ In contrast, autosomal dominant inheritance is associated with a mild condition without systemic abnormalities.¹ The biochemical defect has not been identified; but reduced copper availability, on which some enzymes responsible for cross linking of connective tissue depend, may play a part.⁵

A third type of "cutis laxa" appears to be transmitted by X linked inheritance.⁶ Affected males have the characteristic appearance but only mild skin laxity, associated with structural abnormalities of the urinary tract, skeletal malformations, and joint laxity. Joint laxity is not associated with classical cutis laxa, but is a prominent feature of Ehlers-Danlos syndrome, with which it is often confused. In this the skin may be stretched unduly far, but is not lax and springs back immediately on release.² Histological examination of skin in both Ehlers-Danlos syndrome and X-linked cutis laxa shows disruption and irregularity of collagen fibres rather than elastin.⁶

The two patients described here had clinical cutis laxa. The first had the skin features together with diagnostic histological appearances. The second patient was less typical; she had florid skin changes, though skin biopsy was not helpful. She also had joint hyperextensibility. Nevertheless, her dermatological features were sufficiently characteristic to justify the diagnosis, and her emphysema was exceedingly severe. She had increased lung compliance but reduced aortic compliance. A possible explanation is that, owing to a lack of elastic fibres, the tissues can be stretched easily until maximum dimensions (imposed by non-elastic collagen) are reached. Thus, measured in the mid-range, the lung is more compliant while, at full stretch, the aorta is less so.

Emphysema was first described in conjunction with cutis laxa by Christeans *et al*⁴ in a patient who died of respiratory failure at the age of 10 months. In later case reports the patients developed respiratory distress and died between the ages of six months and two years.^{3, 6} Our two patients not only survived into adolescence but, to judge by their sporting activities, were fit during childhood. There are very few reports of similar cases; Reed *et al*⁷ write of a 17 year old boy with cutis laxa and emphysema diagnosed after he had presented with an urticarial eruption. Merten and Rooney⁸ described radiographic emphysema in a 12 year old with cutis laxa but few clinical details are given. It is not clear whether these cases represent a distinct group of cutis laxa, mild expression of the severe form, or the effect of an external stimulus on a predisposed individual. One of our patients had atopic eczema and both had a family history of atopy, so perhaps chronic asthma with hyperinflation, in the presence of abnormal connective tissue, contributed to the development of destructive emphysema.

Cutis laxa should be considered in young patients with emphysema and possibly in older non-smokers who have normal alpha₁-antitrypsin levels.

References

- 1 Beighton P. The dominant and recessive forms of cutis laxa. *J Med Genet* 1972;9:216-21.

- ² McKusik, VA. *Heritable disorders of connective tissue*. 4th ed. St Louis: CV Mosby Company, 1975:372-83.
- ³ Mehregan AH, Lee SC, Nabai H. Cutis laxa (generalised elastolysis). A report of 4 cases with autopsy findings. *J Cutan Pathol* 1978;**5**:116-26.
- ⁴ Christeans L, Marchant-Alphant A, Foret A. Emphyseme congenital et cutis laxa. *Presse Méd* 1954;**62**:1799-801.
- ⁵ Linares A, Zarranz JJ, Rodriguez-Alarcon J, Diaz-Perez JL. Reversible cutis laxa due to internal D-penicillamine treatment. *Lancet* 1979;ii:43.
- ⁶ Byers PH, Siegel RC, Holbrook KA, Narayenen AS, Bornstein P, Hall JG. X-linked cutis laxa. Defective cross-link formation in collagen due to decreased lysyl oxidase activity. *N Eng J Med* 1980;**303**:61-5.
- ⁷ Reed WB, Horowitz RE, Beighton P. Acquired cutis laxa. *Arch Dermatol* 1971;**103**:661-9.
- ⁸ Merten DF, Rooney R. Progressive pulmonary emphysema associated with congenital generalised elastolysis. *Radiology* 1974;**113**:691-2.