Lipoid Proteinosis: High-resolution Two-dimensional Protein Electrophoresis of Affected and Non-affected Skin

Sir,

Lipoid proteinosis, also known as hyalinosis cutis et mucosae or Urbach-Wiethe's disease, is a rare autosomal recessive disease characterized by depositions of a hyaline, PAS-positive material in the dermis and mucosa of the upper respiratory tract, giving hoarseness, macroglossia and hyperkeratotic exanthema as its main clinical manifestations (1).

The hyaline material has been examined by various techniques, including morphological, histochemical, ultrastructural, immunological and biochemical methods. The chemical nature of the material remains unclear. Some studies suggest that the deposits represent accumulations of defect type IV collagen due to an abnormality in the synthesis of the basal membrane, but other authors favour the view that the hyaline material consists of several non-collagenous proteins (1). Recently, it has been suggested that 2 alterations might coexist in lipoid proteinosis, 1 characterized by impaired normal collagen production and the other related to a metabolic defect that may lead to accumulation of ceramid or more complex lipids (2).

We have had the opportunity to study 3 patients with lipoid proteinosis, all of whom had the typical clinical and histopathological manifestations of the disease (3). The patients were 2 brothers, aged 35 and 28 years, and a 33-year-old unrelated woman. Biopsies were taken from affected as well as non-affected skin of all 3 patients. Specimens from normal skin of 3 volunteers were used as controls. The specimens were analysed by high-resolution 2-dimensional electrophoresis (4), which permits the separation of hundreds of proteins. The skin biopsies were dissolved in 9 mol/l urea containing mercaptoethanol and a detergent. After centrifugation, the supernatants were analysed by 2-dimensional electrophoresis, i.e. separation of the polypeptide chains according to charge in the first dimension, and according to molecular weight in the second dimension. The 2-dimensional protein maps were visualized by a highly sensitive silver staining technique (5). Triplicate analyses of each biopsy specimens were carried out.

The results indicate differences in the protein patterns of involved and uninvolved skin compared with normal skin. Examples of these protein maps are given in Figs 1a–d. Two proteins with molecular weight of less than 11,000 Da were present in trace amounts or not at all in normal skin (Fig. 1a) and in non-affected skin of the patients (Fig. 1b), but were seen in increased amounts in samples taken from skin lesions (Figs. 1c–d). A protein with molecular weight of approximately 14,000 Da was present in moderate amounts in normal skin (Fig. 1a) and increased markedly in the skin lesion samples (Figs. 1c–d). It was, however, barely present in uninvolved skin of the patients (Fig. 1b).

Further studies would be required to elucidate the role of these apparently disease-related proteins.

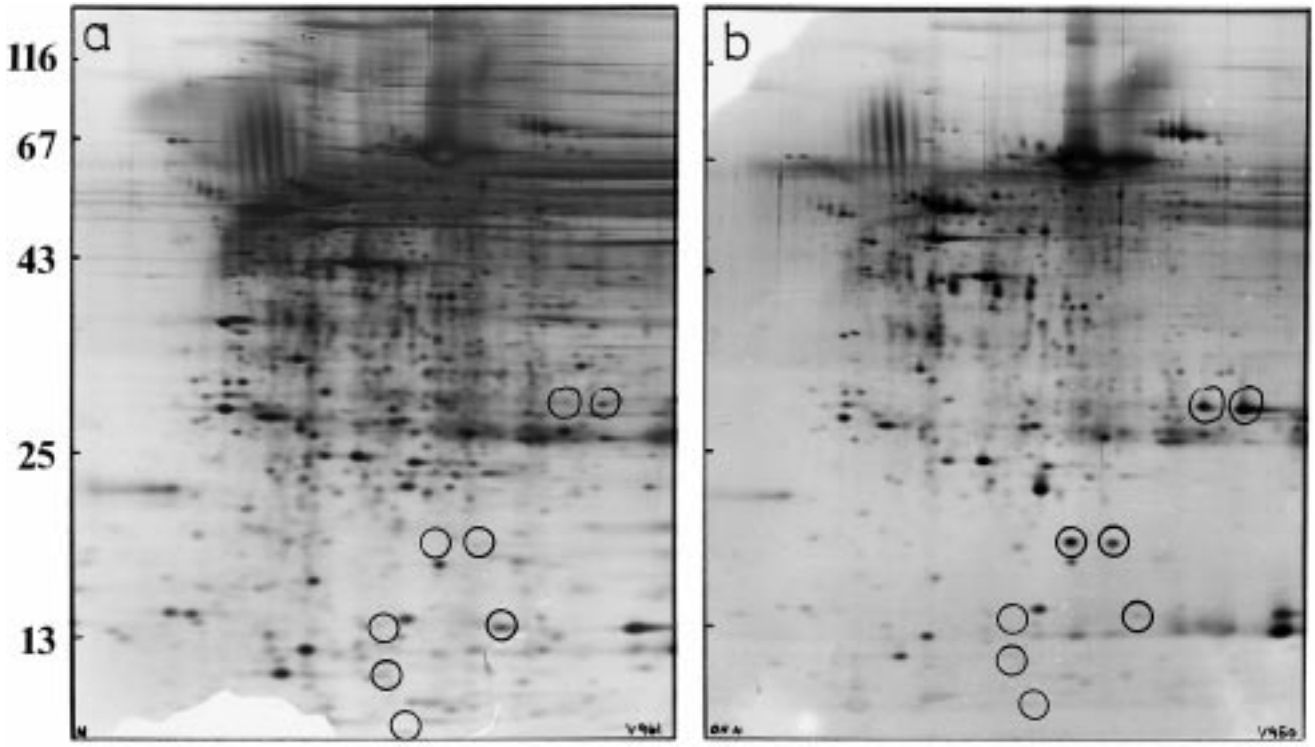
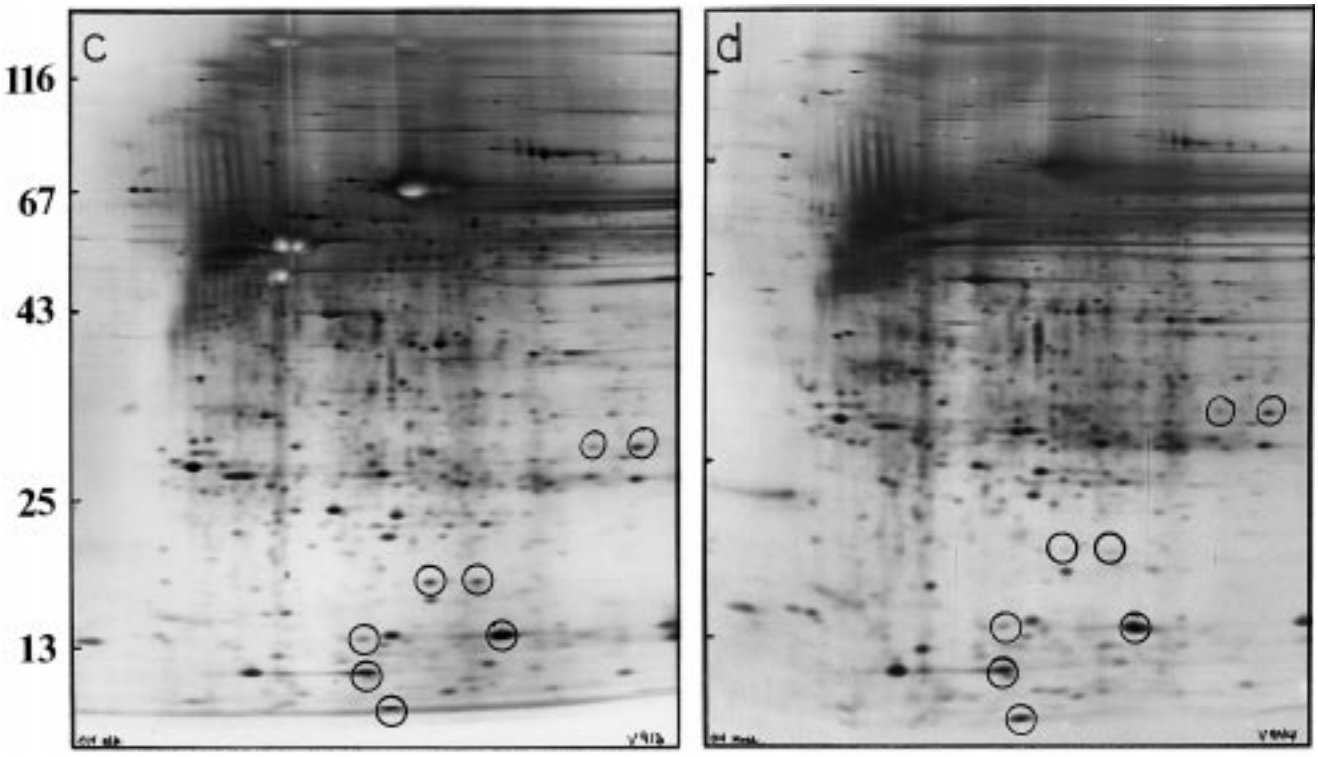


Fig. 1. Two-dimensional electrophoresis polypeptide patterns of (*a*) the skin of a normal control person, (*b*) unaffected skin, (*c*) affected skin on the elbow and (*d*) affected skin on the knee from a patient with lipoid proteinosis. The gels are oriented with the acidic end to the left, and the approximate molecular mass (in kDa) is indicated along the vertical scale. The marked spots indicate some of the differences in the patterns (see text).



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