Lipoid proteinosis

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SUMMARY

The case of a 37-year-old woman with lipoid proteinosis is presented. The first symptoms of hoarseness of voice occurred in puberty. Additional symptoms included beaded eyelid papules, macroglossia with yellowish papules, yellowish deposits of soft palate, popular eruption in the axillary area and tuberous nodules on the elbows.

KEY WORDS

lipoid proteinosis, hyaline material, macroglossia, affection of eyelids, hoarseness

Introduction

Lipoid proteinosis (LP), also known as hyalinosis cutis et mucosae or Urbach-Wiethe disease (OMIM 247100) is a rare, autosomal recessive disorder whose typical symptoms are generalized thickening of skin, mucosal membranes and certain viscera.

Classical features include beaded eyelid papules and laryngeal infiltration leading to hoarseness. Histologically, there is a widespread deposition of hyaline (glycoprotein) material and disruption/reduplication of the basement membrane. The etiology of LP is currently unknown. The hyaline material is periodic acid-Schiff-positive and Congo-red positive but diastase resistant. Perivascular deposits of collagens type IV and V are increased, whereas type I and II collagens are reduced (1,2).

Recently it has been shown that lipoid proteinosis results from mutations in extracellular matrix protein 1 (ECM1), a glycoprotein expressed in several tissues (including the skin) and composed of two alternatively spliced isoforms, ECM1a and ECM1b, the latter lacking exon 7 of this 10-exon gene (ECM1). The mutation maps onto chromosome 1q 21. To date, mutations that

either affect ECM1a alone or that disturb both ECM1 transcripts have been demonstrated in several cases. However, lipoid proteinosis is clinically heterogeneous with affected individuals displaying differing degrees of skin scarring and infiltration, variable signs of hoarseness and respiratory distress, and in some cases even neurological abnormalities such as temporal lobe epilepsy. Taken with the previously documented mutations in ECM1, studies of the disease have supported the view that exons 6 and 7 are the most common sites for ECM1 mutations in lipoid proteinosis. Clinically, it appears that mutations outside exon 7 are usually associated with a slightly more severe mucocutaneous lipoid proteinosis phenotype, but neurological features do not show any specific genotype-phenotype correlation (3, 4).

Case Report

A 37-year-old woman was referred to our hospital because of oral and chronic cutaneous lesions. She had suffered from hoarseness of voice due to thickening of the vocal cords since she was 16 years old. Over the following 20 years she developed oral and cutaneous lesions.

Examination revealed an otherwise healthy woman who presented oral symptoms such as macroglossia with lateral impressions, and small yellowish papules on the tongue (Fig. 1a). There were yellowish deposits on the soft palate (Fig. 1b). The teeth were not affected.

We found beaded papules on the thickened margins of the eyelids (Fig. 2), yellowish papules in the axillae and nodules of variable size at both elbows (Fig. 3).

A skin biopsy was taken from a papule. Hematoxylin-eosin and periodic acid-Schiff (PAS)-stains revealed an amorphous hyaline material in the walls of dermal vessels and around the eccrine sweat gland coils (Fig. 4). The material was PAS-positive but diastase negative.

There was no evidence of any internal involvement (brain, lung, intestine). Since no effective therapy is available, and the patient refused the laser or surgical removal of nodules and papules, no therapeutic action was taken.

Discussion

Lipoid proteinosis is a genetic disease, and a diagnosis can be established on the basis of characteristic clinical symptoms and confirmed by histopathology. A frequent symptom is hoarseness of the voice due to vocal cord deposits which manifests itself during the first years of life (5). Typical skin involvement includes whitish, moniliform papules on the eyelids (blepharosis moniliformis), and yellowish or waxy papules on the lips, over the knuckles, sides of the hands, on the knees, elbows or in axillae. Sometimes vesiculo-bullous eruptions or acneiform lesions may be present, which are followed by nodules or plaques or pock-like scars (6, 7) that are present, predominantly, on the face and the limbs. Patchy alopecia has also been observed (8). On the oral mucosa including gingiva firm, yellow-white papules or plaques are observed. Macroglossia and enlargement of the lips with fissuring has been reported. Diffuse infiltration of the larynx and pharynx can lead to dysphagia (5, 9). The yellowish papules on the tongue which we observed in the case cited above are less common.

Deposition of hyaline material in the eye may cause corneal opacities or secondary glaucoma (10). Calcifications of intracerebral para-sellar or hippocampal gyri may sometimes be associated with epilepsy and mental dysfunction (11-13). Deposits of hyaline material in the small bowel may cause intestinal bleeding (14). Lung and bronchial involvement has also been reported (15).

Erythropoietic protoporphyria has to be considered in the differential diagnosis: it may display similar skin symptoms, but not oral lesions (16,17). Increased values of protoporphyrin in erythrocytes are a key symptom.

There is no effective treatment available although in one case-study improvement after oral application of dimethyl sulphoxide was claimed. The initial dosage was 40 mg/kg/day, which was then increased progressively to 60 mg/kg/day. After 3 years of treatment, the patient's skin lesions, hoarseness of voice and abnormal esophageal function improved remarkably. No side-effects were noted except for a garlic-like smell of the patient's breath (18). Such favorable results were not, however, reproduced in three patients from Turkey (19). Further therapeutic attempts with etretinate (20) and D-penicillamine (21) have also been published.

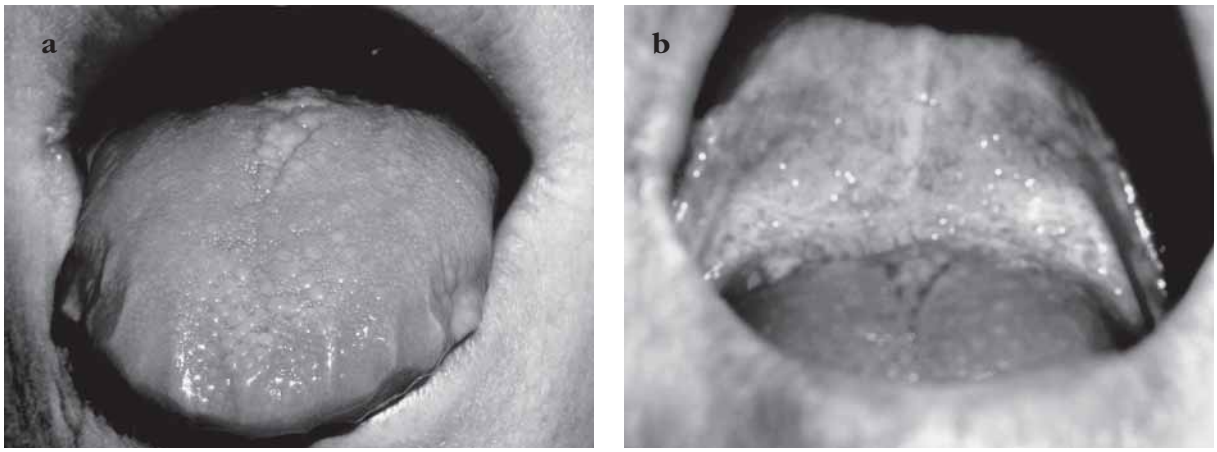

Figure 1. Oral manifestations of lipoid proteinosis:
(a) Macroglossia with lateral impressions and multiple yellowish papules. (b)Yellowish deposits on the soft palate.

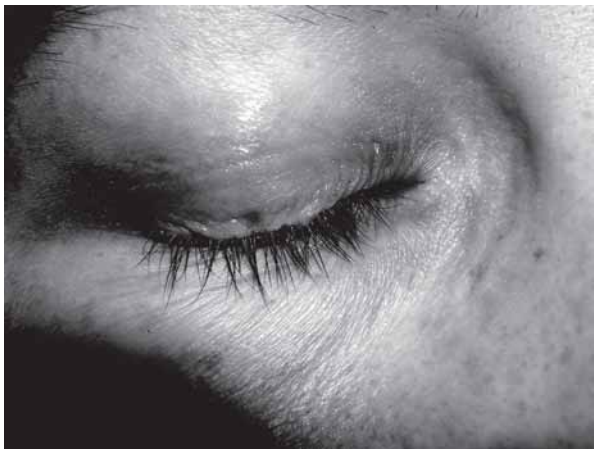

Figure 2. Candida-like whitish papules on the margins of eyelids (moniliform blepharosis).

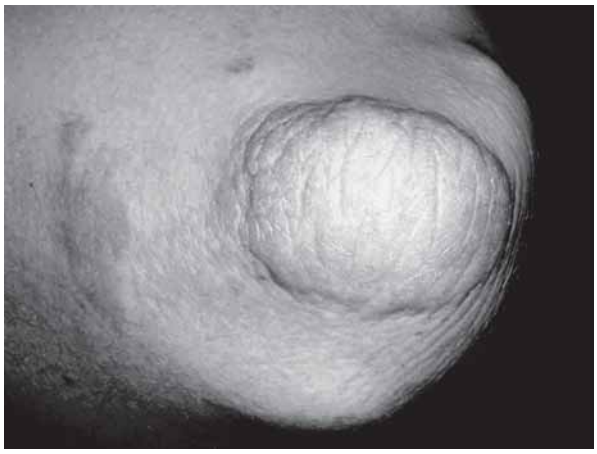

Figure 3. Papulonodular eruptions in lipoid proteinosis on the elbow.

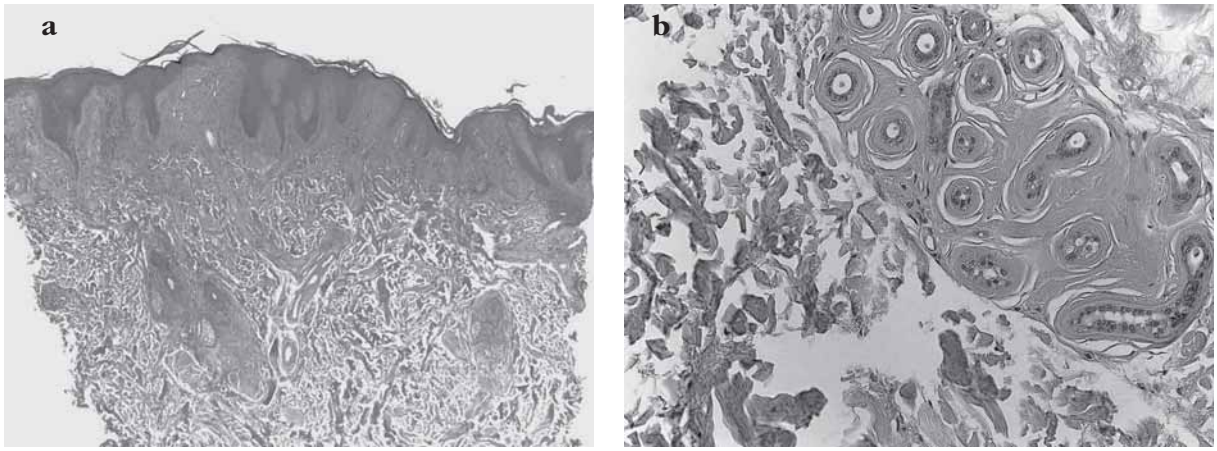

Figure 4. Histopathology: HE-stain showing hyaline material surrounding (a) dermal vessels and (b) eccrine sweat gland coils.

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