

URBACH WIETHE DISEASE: FIVE CASES WITHIN ONE FAMILY

Meimandii Simin,

Assistant Professor

Shamsadini Sadollah,

Associate Professor.

Dermatology Department

Kerman University of Medical Sciences,

ABSTRACT

Urbach Wiethé disease, or lipoid proteinosis, is a rare autosomal recessive disease in persons with a normal chromosomal pattern. It is characterised by a hoarseness of voice usually first noticed when the new-born infant starts to cry. We report five typical cases, four female and one male, within one family, nine of whose members are known to be heterozygous. We found hypertriglyceridemia in two cases but no severe complications.

Key words: Lipoid proteinosis, Urbach Wiethé, Hoarseness, genetical disease, autosomal recessive

INTRODUCTION :

Urbach-Weithe disease (UW), also known as lipoid proteinosis, is a rare autosomal recessively inherited disorder with a normal chromosomal pattern. It is characterised by hyaline infiltration of the skin and mucosae of the mouth, pharynx, larynx and internal organs^(1,2)

The first detailed clinical and histopathological



Fig. 1

P.O. Box 76135 - 784

Kerman, Iran

Short title : Lipoid proteinosis

description was given in 1929 by Urbach, a dermatologist, and Wiethé, an otolaryngologist⁽³⁾. Since then more than 300 cases have been reported worldwide⁽¹⁾ with the highest incidence being in South Africa and Sweden^(4,5,2,1,6). The disease presents in infancy with an unusually hoarse cry and appears more commonly in Caucasians, with both sexes being equally affected^(7,4,5,2,3). Consanguinity has been described in a number of reports^(8,9,2,10).

CASE REPORT

We were first alerted to severely closely related cases of UW disease by the appearance at the hospital of a 20-year-old girl with a long-standing history of multiple soft superficial papules on her eyelids and an unusually hoarse voice.

Physical examination showed multiple translucent bead-shaped papules along the margins of the eyelids with the eyelashes being fewer than usual. No hair loss was found elsewhere but there was mild scarring and thickening of areas of the facial skin. She had difficulty in protruding her tongue and there was obvious yellow, firm, waxy infiltration of the oral and lingual mucosae (Figs 1 & 2). A blue-tinged halo around the pupil, marginal eye lid pearly papules and corneal opacity with an undermined

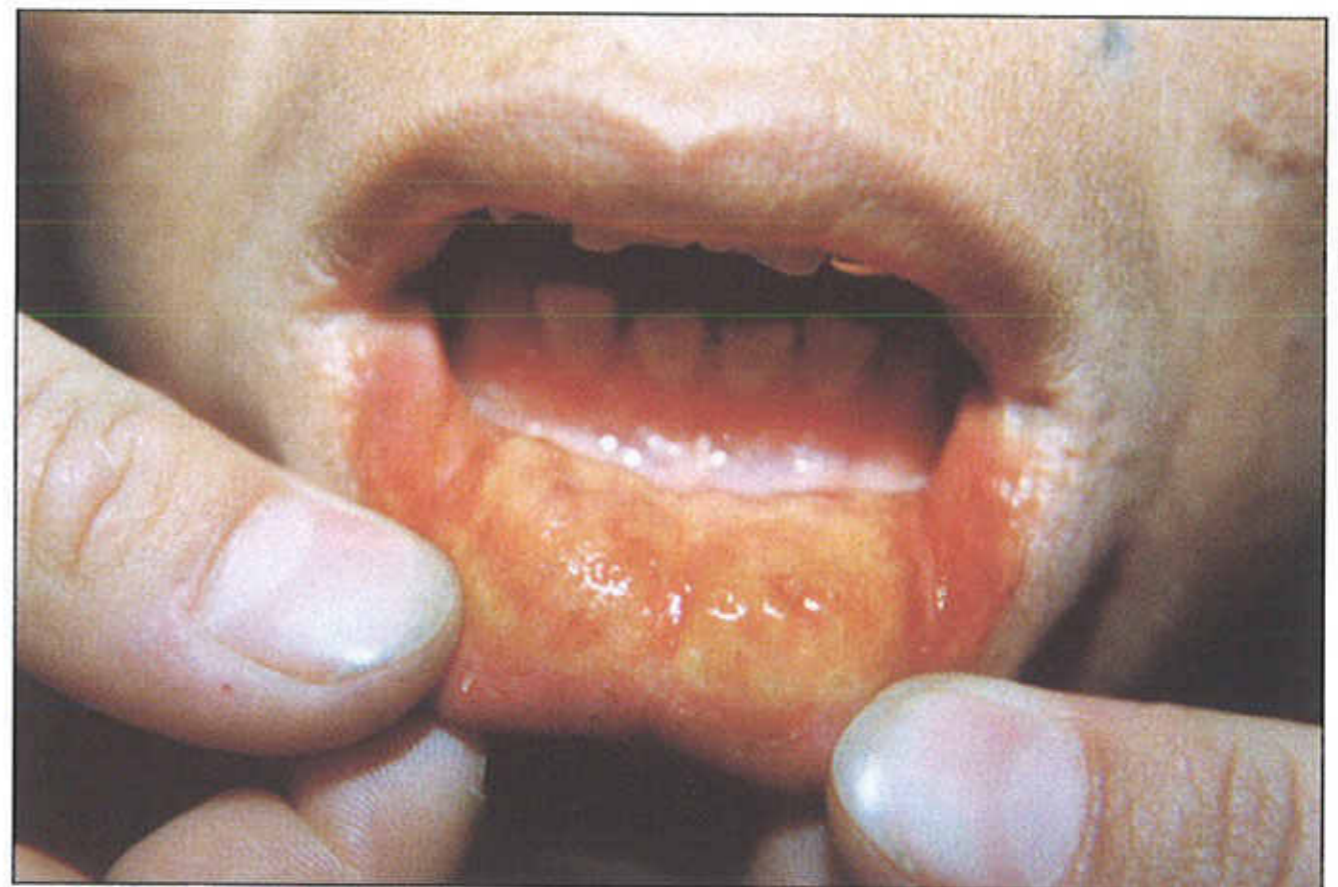


Fig. 2

margin were visible in both eyes but were more prominent in the left (Fig. 3).

Laboratory tests showed a hypertriglyceridemia ranging from 437 to 611 mg/dl with normal levels of serum cholesterol. The total protein in a 24-hour sample of urine was 1590 mg in a volume of 1400 ml. There was also a mild anaemia with anisocytosis.

Sonography of the kidneys showed a mild dilation of the calyx in both kidneys with partial duplication in the right.

Her intellect and language ability both appeared normal but she complained of a persistent mild bitemporal headache. An EEG was normal and a computerised brain scan showed no calcification in the cerebral parenchyma although the ventricles were collapsed.

Biopsy of an infiltrative mucosal lesion showed dispersed spongiosis and stroma with a homogenous eosinophilic background perpendicular to the surface. A few vessels showed hyalinisation of the wall consistent with hyalinosis cutis et mucosa (Figs 4,5,6) Later, a physical examination and questioning of the girl's family revealed a very close consanguinity and several more cases of UW disease (three female and one male) amongst her relatives

(diagram 1). By then, three were adult but one was still an infant. They had a common history of a hoarse voice from an early age, oligodontia, tongue rigidity, lesions on the eyelids and various skin and mucosal lesions, with the exception of the infant in which perhaps the lesions had not yet developed (Diagram 1).

DISCUSSION :

Altogether we found five cases of UW disease in this consanguinous family living in Kerman, Iran. Although other authors have reported that the sexes are equally affected (7,2), in our small sample four of the five cases were female. In various degrees, all had the hoarse voice and showed many of the infiltrative skin and mucosal lesions described by other authors (Diagram 1) but none had gingival hyperplasia, xerostomia or keratoconjunctivitis sicca^(11,12).



Fig. 3

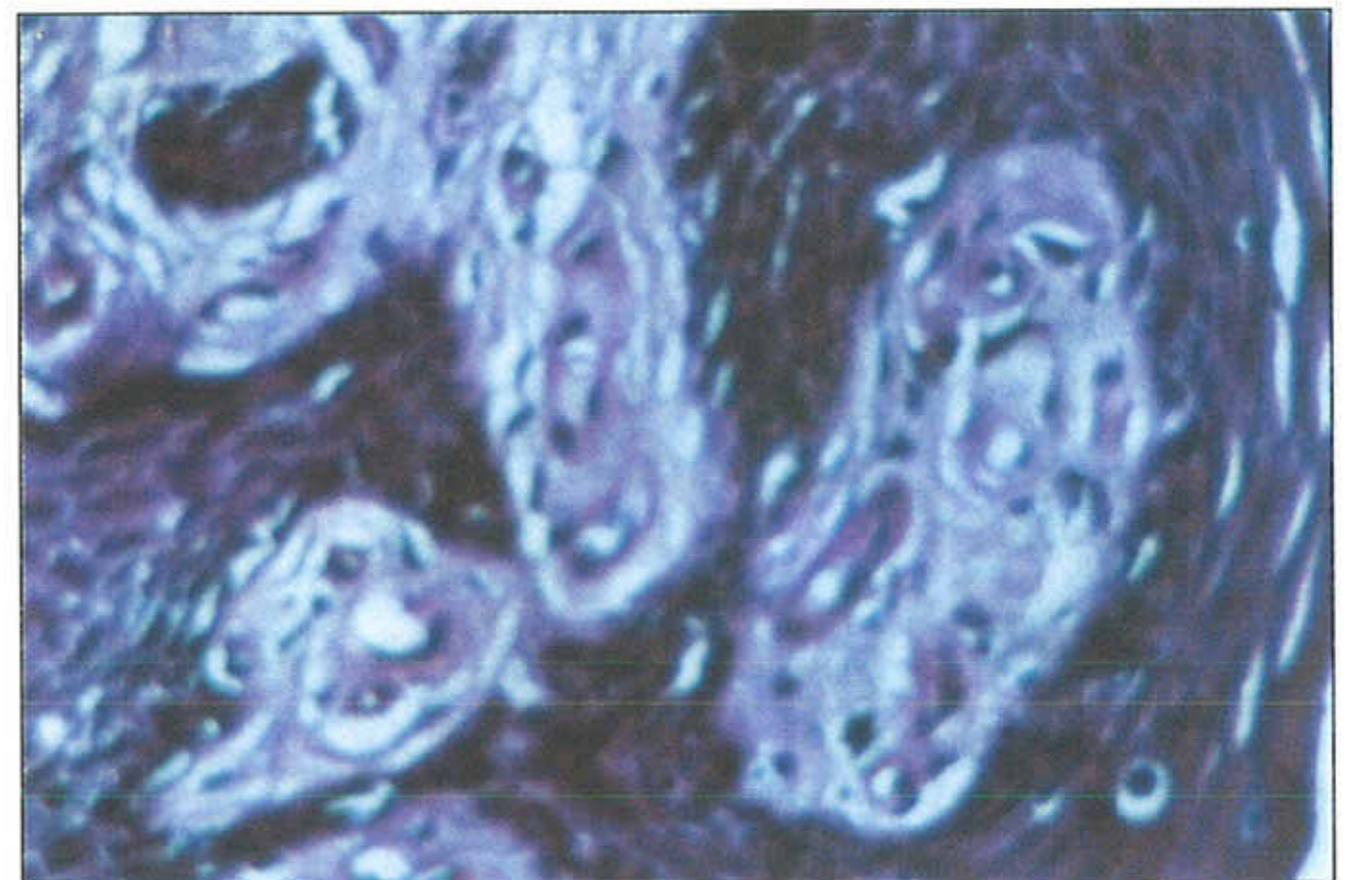


Fig. 4

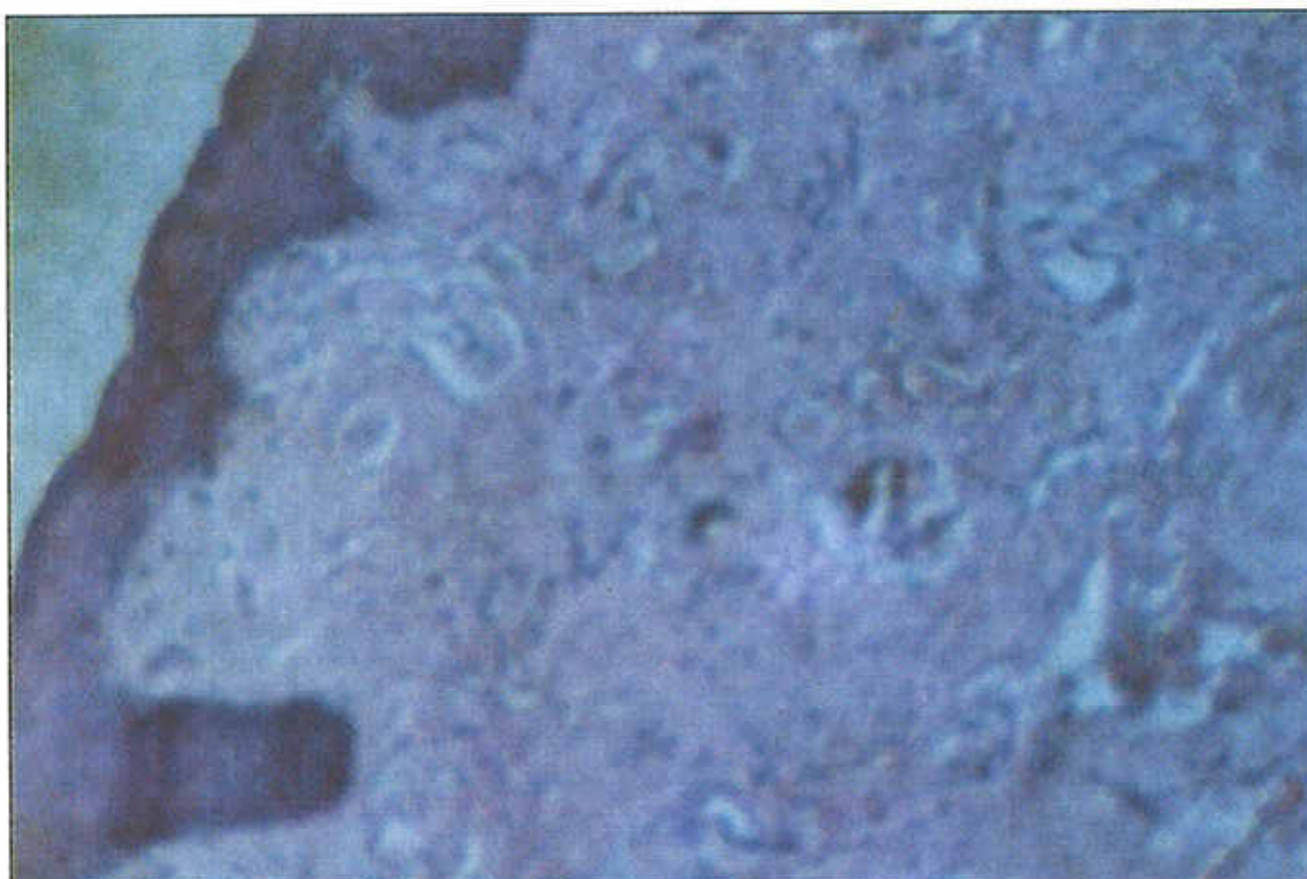


Fig. 5

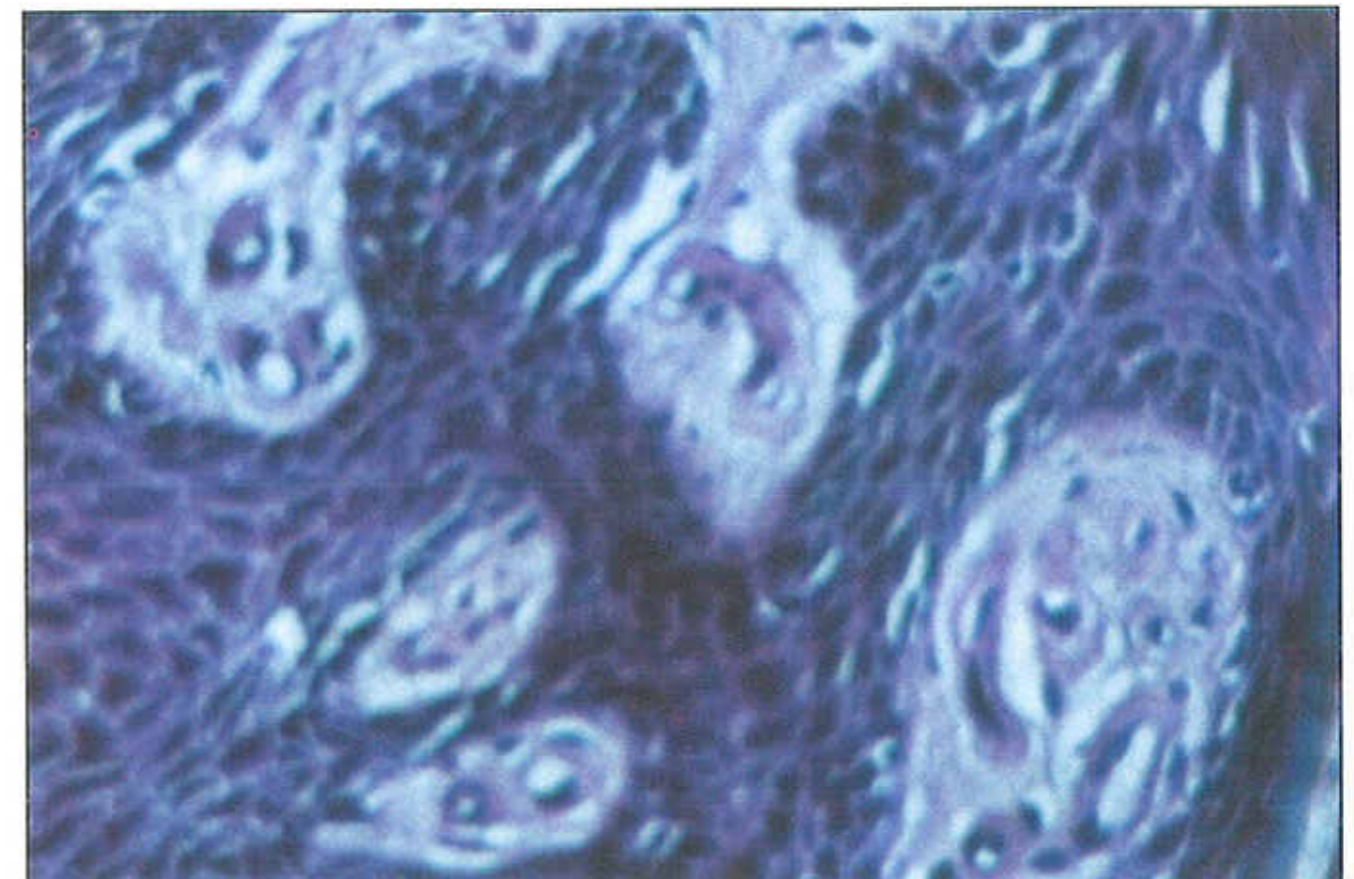


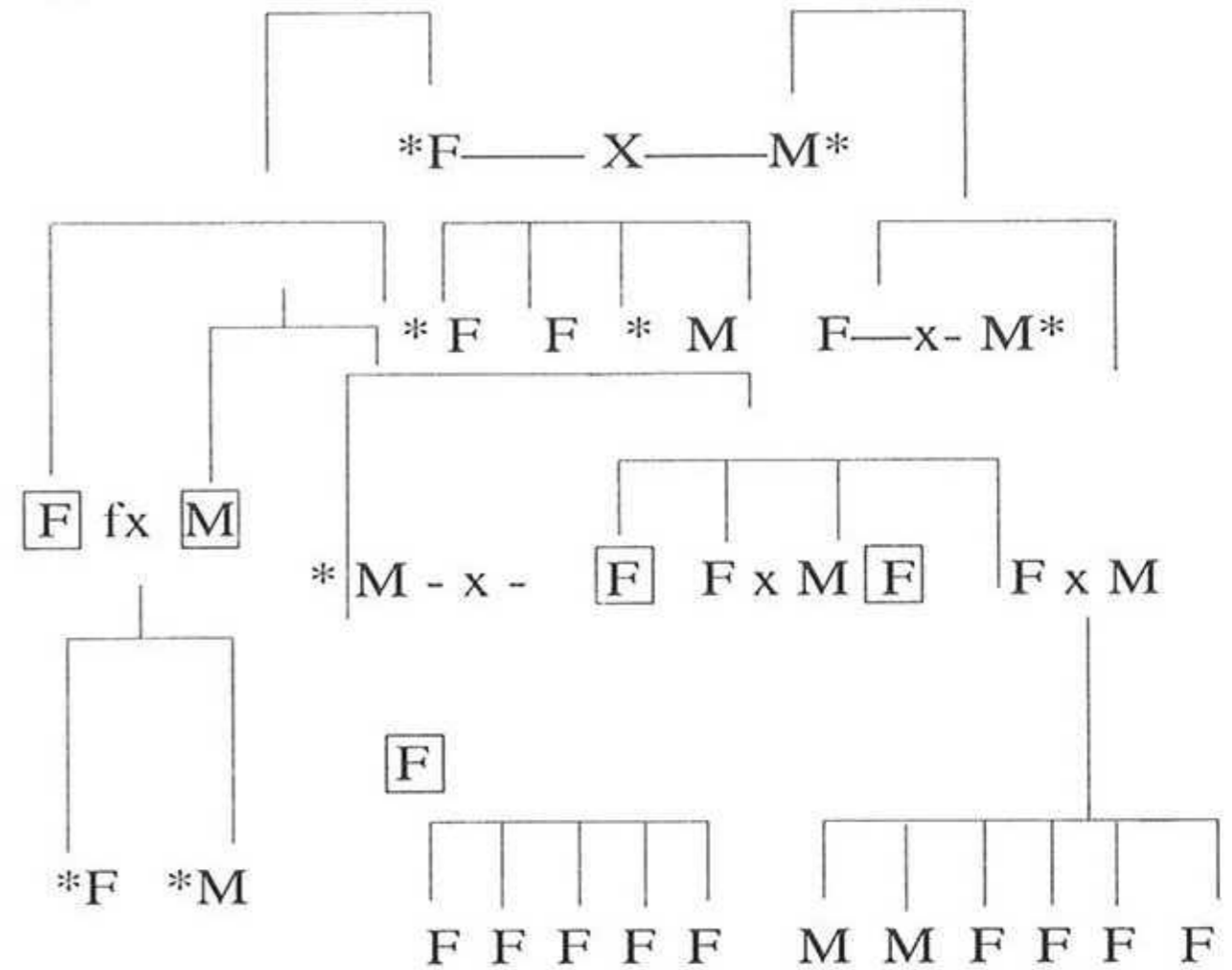
Fig. 6

Our principal patient reported chronic headache but we found no significant abnormality to account for it although hypocampal calcification has been reported in this disease ⁽¹³⁾.

Amongst homozygous individuals the morbidity is likely to be high but the mortality is no more than in non-affected individuals ^(14,15) except that in the neonate massive infiltration of the vocal cords by hyaline masses of lipid proteins is known to cause inability to cry and might cause respiratory obstruction ⁽²⁾. It has even been suggested that the prognosis is "good" because the condition appears to be progressive only until early adulthood ^(16,7)

Recently, Moe and co-workers have demonstrated ultrastructural and phenotypic changes in the fibroblasts of lipid proteinosis cases and they suggest that these changes might be relevant to the pathology of this condition ^(17,18), but the nature of the hyaline material and the underlying metabolic defect are still unknown. Inevitably, this makes attempts at treatment rather empirical. Wong and Lin reported remarkable success with demethylsulphoxide in a single case ⁽²⁰⁾ and Dowlati and co-workers obtained a good response to etretinate ⁽²¹⁾. Our experience with etretinate 25 mg daily in one case only was that it led to a marked increase in circulating triglycerides and for that reason we discontinued treatment.

Diagram one :



Pedigree of a family with 5 affected individuals
 F = non affected phenotypical female (unknown genetically involved).
 f = non affected phenotypical and non consanguinity female (unknown genetically involved).
 F* = heterozygote female. M = non affected male (unknown genetically involved).
 M* = heterozygote male
 [F] = affected female [M] = affected male

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