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A Rare Case Report Of Lipoid Proteiniosis

KEYWORDS: Lipoid proteinosis, Urbach-Wiethe disease, periodic acid-Schiff , ECM1

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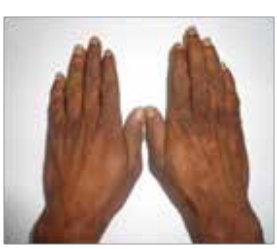
ABSTRACT *Lipoid proteinosis (Urbach-Wiethe disease and Hyalinosis cutis et mucosae) is a rare, autosomal recessive disorder, characterized by infiltration of PAS positive hyaline material into the skin, oral cavity, larynx and internal organs. The clinical manifestations include hoarseness of voice, beaded papules along the eyelid margins, skin scarring and an inability to protrude the enlarged and thickened tongue. It has been mapped to the chromosome 1q21 and pathogenetic loss of function mutations have been identified in the extracellular matrix protein 1 gene (ECM1). We report a case of 30 yr male presented with seizures to casuality. The patient also had beading of papules around the eyelids, scarring on the skin and verrucous plaques over knees and elbows. A*

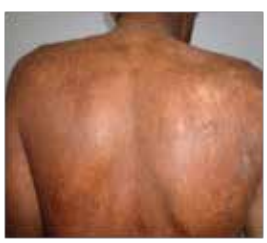
INTRODUCTION

Lipoid proteinosis (Urbach Wiethe Disease and Hyalinosis cutis et mucosae or Lipoglycoproteinosis) is a genetic disorder with autosomal recessive inheritance [1,2] characterized by the deposition of an amorphous hyaline material in the skin, mucosa and viscera.[3] The disease is caused by mutations which cause loss of function at chromosome 1q21 (extracellular matrix protein 1)[4]. It is characterized by hoarseness of voice from early infancy, together with various cutaneous manifestations including acneiform scarring, waxy papules, eyelid beading etc and other manifestations which are attributed to infiltration of hyaline material into the skin, larynx and various organs[5].This hyaline-like material is periodic acid-Schiff (PAS) positive and diastase resistant and is believed to be the result of the deposition of non-collagenous proteins and glycoproteins[6].

CASE REPORT

A 30-years-old male patient came to casualty of SVS Medical College & Hospitals, Mahabubnagar with seizures and altered sensorium and was given symptomatic treatment. On examination, hoarseness of voice and numerous atrophic scars over forehead, face and back were noted. Hyperkeratotic, verrucous papules were present on both the elbows, knuckles, buttocks, natal cleft, scrotum and extremities. Bilateral upper and lower eyelid beading was present. Tongue, lips, and frenulum were thickened and infiltrated. Hypopigmented erythematous plaques were present over hard palate and angle of mouth. Scalp had patchy alopecia. He was born to non consanguineous parents and had no history of similar illness in the family.





Clinical Pictures showing characteristics features of Lipoid proteinosis

Skin biopsy from right elbow was done. H & E and PAS staining done. H & E showed deposition of hyaline like material at the level of the basement membrane (resulting in its thickening at the dermoepidermal junction), papillary dermis and surrounding blood vessels. PAS showed the hyaline material eosinophilic, PAS-positive, diastase resistant, indicating the presence of glycoproteins.

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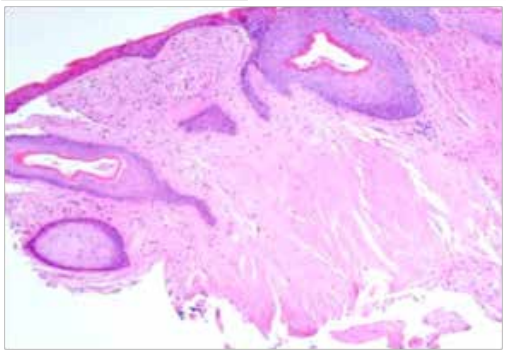
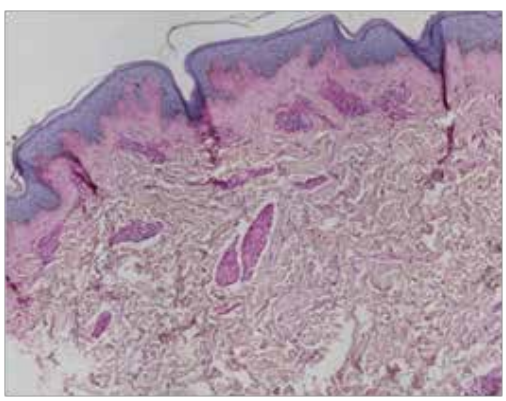
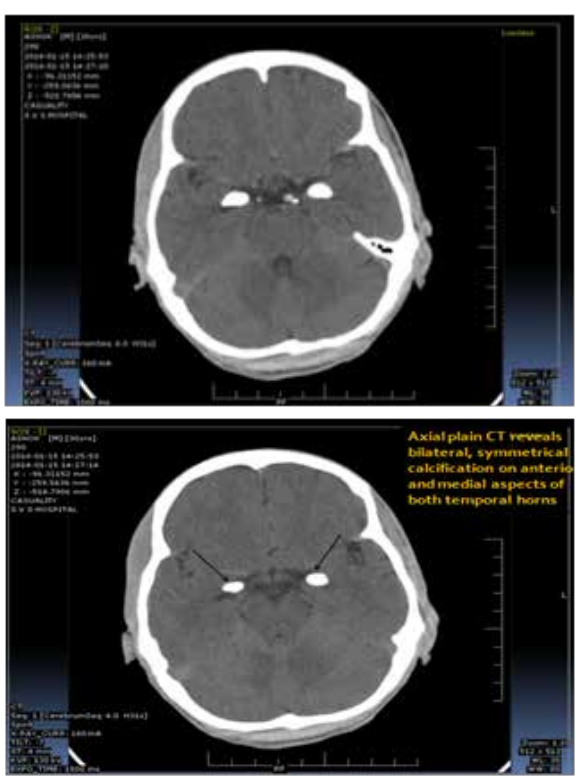


H & E -40X



PAS-40X

Patient underwent X ray Skull And CT Brain. Skull radiography revealed bean-shaped calcification in the suprasellar area. Curvilinear hyper attenuated horn-shaped lesions are well depicted by CT in the amygdaloid bodies. So epilepsy may be related to these calcifications.



CT brain: Curvilinear hyper attenuated horn-shaped lesions

DISCUSSION

Lipoid proteinosis was first of all reported by Seibenmann[7] in 1908, but was characterized as a clinical entity in 1929 by Urbach and Wiethe[7,8] and named as 'lipoidis cutis et mucosae'. Later on it was rechristened by Urbach as 'lipoid proteinosis'. Lipoid proteinosis is a genetic disease and diagnosis can be established on the basis of characteristic clinical symptoms, confirmed by histopathology. The exact aetiology and pathogenesis of lipoid proteinosis is not known. Mutations in the gene encoding extracellular matrix protein 1 (ECM 1) gene on band 1q21 have been recently identified as the cause of lipoid proteinosis. Frameshift and non-sense mutations have been described throughout the gene, although exons 6 and 7 are the most common locations.

The clinical manifestations of LP are protean and vary considerably between affected individuals. The clinical manifestations of lipoid proteinosis are usually progressive hoarseness of voice caused by infiltration of hyaline material in the mucosa of the vocal cords[9]. Skin lesions follow hoarseness, includes waxy papules on the face, trunk, flexures, and extremities. Acneiform or pock like scarring may occur predominantly on face and trunk. Infiltration of the eyelids gives rise to characteristic beaded appearance (*moniliform blepharosis*). Infiltration of oral cavity leads to thickened, wood-hard tongue along with thickened lips and frenulum resulting in inability of tongue to protrude out of mouth**.**

Extracutaneous features may include epilepsy, mental retardation, and other neuropsychiatric illnesses. In a few cases, calcifications of the temporal lobe or hippocampi appear as bean-shaped opacities on skull radiography and are considered to be pathognomic of the disease. Hyaline deposits have also been described in the conjunctiva, cornea, trabeculum, and retina, sometimes leading to corneal opacities or secondary glaucoma.[10]Hyaline deposition in the small bowel may lead to intestinal bleeding.

The exact pathogenesis is not known but has been postulated to be the result of either a lysosomal storage disorder involving multiple enzyme defects or from a disturbance in collagen synthesis, as evidenced by decrease in the ratio of type-1 to type-3 collagen associated with a decrease in mRNA for type-1 procollagen. There is also an increase in mRNA for type-4 procollagen resulting in underproduction of fibrous collagens and an overproduction of basement membrane collagens, which tend to deposit in the skin and various organs, the hallmark of the disease.

Recent studies have shown that LP is due to reduced expression of Extracellular-matrix-protein (ECM-1) gene (composed of two alternatively spliced isoforms, ECM-1a and ECM-1b, the latter lacking exon 7 of this 10-exon gene) mapped to chromosome 1 in the fibroblasts. Extracellular-matrix protein 1, has physiological and biological roles in epidermal differentiation, in binding of dermal collagens and proteoglycans, and in regulation of angiogenesis. Homozygous-nonsense mutation in exon 2 of the ECM1 gene, Q32X, was identified by direct sequencing of genomic DNA of an affected member of a Libyan family**.**

Histologically, lipoid proteinosis is characterized by PAS positive and diastase resistant basement membrane thickening at the dermoepidermal junction, surrounding blood vessels and adnexa[11]. Immunofluorescence labeling with anti-type IV collagen antibody shows bright, thick bands of staining at the dermoepidermal junction and around the

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blood vessels consistent with basement membrane thickening[12].Ultrastructurally, there are multiple concentric rings of basement membrane around the blood vessels and irregular reduplications of lamina densa at the dermoepidermal junction. Abnormal lysosomes containing curved tubular inclusions have been reported in histiocytes and eccrine sweat glands [13]. Demonstration of pathogenetic mutations in the ECM 1 gene in lipoid proteinosis provides a definite means of establishing diagnosis. Mutations have been detected in all the exons of ECM 1, but more than half of the mutations have occurred in exon 6 or the alternatively spliced exon 7. [14] Epilepsy, when present, may be related to these calcifications. Patients should be followed with MRI/CT in order to identify these abnormalities[15].

Lipoid proteinosis has to be differentiated from some other clinical entities including erythropoietic protoporphyria, amyloidosis, xanthomatosis, myxoedema and lichen myxedematosus.

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