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Lipoid Proteinosis – A rare autosomal recessive genodermatosis

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Abstract

Lipoid proteinosis also known as "Urbach-Wiethe disease" is a rare autosomal recessive disorder with about more than 300 cases noted in literature till 2015 data [(1)]. It is characterized by the deposition of eosinophilic hyaline like material in the skin and the mucous membrane [(2)] .The first clinical manifestation is the progressive hoarseness of voice due to the infiltration of the vocal cords. Skin manifestations are not usually present at birth and develop later in life [(3)] .Presence of bead like papules on the upper eyelid k/a "moniliform blepharosis" is the pathognomic feature of the disease. Extracutaneous manifestation including the ophthalmic and central nervous system and have been noted. Here we present a case of lipoid proteinosis for its rarity.

Keywords: Lipoid proteinosis, genodermatoses, moniliform blepharitis, Urbach-Wiethe disease.

Introduction

Lipoid Proteinosis (LP), a rare genodermatosis which is caused by deposition of eosinophilic hyaline like material in the skin and the mucous membrane [2]. Although multiple systems of the human body are affected, the most predominant manifestations in dermatology are lipid laden skin lesions known as "moniliform blepharosis". Radiological manifestations include symmetrical, intracranial, medial and temporal calcifications. LP is usually an incidental diagnosis.

Considering its rare occurance, It is necessary to spread awareness on this entity in the scientific community.

Case Report

A 13 year old female, born out of non-consanguineous marriage presented with complaints of pearly white lesion on eyelid and recurrent spontaneous erosions all over the body which, healed by hypo to depigmented scar since 2 years. On enquiry, patient gave history of hoarseness of voice. Patient received various treatment for the same with no improvement. No history of seizures, cognitive or behavioral impairment, visual impairment, respiratory difficulty or dysphagia was present. No history of similar complain was noted in family. On examination, multiple pearly white papules were seen on upper and lower eyelid like string of pearl appearance or moniliform blepharosis (Figure 1).

Figure 1: Skin lesions on eyelid

Hypo-depigmented scars were present over face, elbow and back. Intraoral examination shows thickened and stiff tongue(Figure 2).

Figure 2: Thick and stiff tongue

Nasopharyngolaryngoscopy with stroboscopy showed normal base of tongue, epiglottis, pyriform fossa, aryepiglottic fold and arytenoids. Bilateral vocal cords were mobile. Complete blood counts, liver profile were within normal limits.

H & E stain revealed mild irregular acanthosis and elongation of rete ridges in the epidermis . Dermis showed eosinophilic homogenous acellular deposits extending upto the upper dermis, multiple small blood vessels with scanty peri-vascular lymphocytic infiltrate. Dense collagenization was seen in deeper dermis.

Homogenous pink acellular material was seen subdermally on PAS staining (Figure 3).

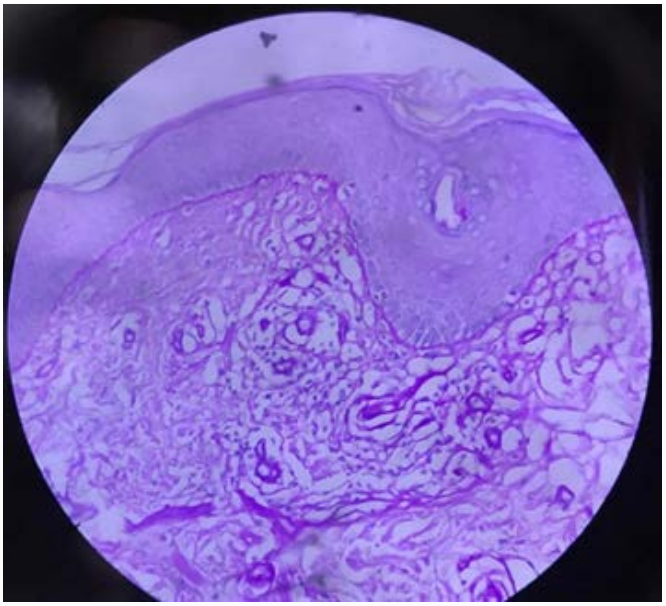

Figure 3: PAS staining

Patient was started on isotretinoin 20mg daily for 2 months and then shifted to 20mg alternate day. she showed significant improvement after 2 months of treatment. Voice therapy for hoarseness of voice provided significant improvement. Till last follow up he was receiving voice therapy.

Discussion

The Lipoid proteinosis also known as "lipogylcoproteinosis", "lipid proteinosis", "Urbach-Wiethe disease" and "hyalinosis cutis et mucosae" was first described by Urbach and Wiethe in 1929 as "Lipoidsis Cutis et mucosae" which was later changed to "lipoid proteinosis cutis et mucosae" by Urbach based on the histological findings(4). It has been described to be caused by loss of function mutation in the extracellular matrix protein (ECAM), especially ECAM 1&E gene on chromosome 1q21 which encodes for secretory glycoprotein. (5)

The first clinical manifestation is hoarse gravelly voice due to infiltration of the vocal cords with eosinophilic hyaline like material (4). Cutaneous manifestations tend to develop in the first 2 years of life or even later (3). They are characterized by waxy, yellowish-white papules or nodules primarily distributed on the face and the extremities with thickening of the skin due to infiltration(4) . The most pathognomonic cutaneous manifestation is the presence of beaded papules on the upper eyelid margins known as "moniliform blepharosis". It is seen in about two third of the patients (3). The skin lesions sometimes also consist of blood/ pus filled vesicles or bullae which rupture to form pockmarked scars, whereas acneiform scarring is usually seen on the face and the trunk(4) . Xanthoma like hyperkeratotic (verrucous) papules have been observed in areas of repeated friction like hands, elbows and the knees.(6) Other cutaneous manifestations include alopecia, progressive thickening of the sub-lingual frenulum with reduced tongue movements observed in a few cases (4).

Extracutaneous manifestations include epilepsy, severe generalized dystonia, memory loss, schizophrenia and mental retardation(7) which are radiologically characterized by bean or comma shaped intracranial calcifications in the temporal lobes (8). Abnormalities in the facial expressions may also occur (4). Due to deposition of eosinophilic hyaline like material in the oesophagus, filling defects in the upper aero-digestive tract has been observed (8). Symptoms of hyposalivation or xerostomia are sometimes present leading to poor oral hygiene, oral ulceration due to involvement of the submandibular and parotid gland. Ocular involvement has been noted in the form of glaucoma, uveitis, epiphora, keratoconus and lens subluxation with cauliflower like lesions in the lower puncta (7). Infiltration and thickening of the epiglottis and the arytenoids have also been observed in endoscopic examination of larynx in certain cases (2)

Histology reveals a cystic wall lined by stratified squamous epithelium along with deposition of

amorphous eosinophilic hyaline like PAS+ material around the appendages particularly the capillaries, sweat glands and hair follicles and in the papillary dermis (7). Disruption or duplication of the basement membrane resulting in thickening of the lamina densa has been noted.

PCR studies followed by direct sequencing was suggestive of homozygous C>T transition with a few cases showing heterogenous transition most commonly located within exon 6 and 7. Differential diagnosis include erythropoietic porphyria, xanthomatosis, popular mucinosis, amyloidosis (2).

No specific or effective treatment has been available for the disorder. Patients with lipoid proteinosis are often under the care of multiple specialists, including dermatologist, paediatrician, neurologist, otolaryngologist (ear, nose, throat specialist), Geneticist and psychologist.

Acitretin is being used for hoarseness of voice, tracheostomy can help aid the respiratory obstruction. Acitretin at a dose of 0.5 mg/kg/day for up to 6 months may show improvement in the hoarseness, appearance of vesiculobullous lesions, and palmoplantar hyperkeratosis. After consent, D-penicillamine can also be considered, which is taken empty stomach 300mg twice a day along with work up including complete blood cell counts and complete urinalysis performed every 4 weeks, and a chemistry panel performed every 3 months. As D-penicillamine might take several months to become effective, the patient is reevaluated after 6 months by means of a clinical and pathologic examination. Oral dimethyl sulfoxide 60mg/kg/day shows good result (9).

Chemical peeling, CO2 laser and dermabrasion have been tried and is effective for cosmetic improvement. Blepharoplasty has been the treatment of choice for eyelid lesions. Systemic treatment modalities include oral dimethyl sulfoxide, retinoids and intralesional heparin. Severe cases leading to change in the quality of voice can be treated with laser micro-laryngoscopy, mucosal stripping or dissection the vocal cords (10). Seizures, if present, may be treated with appropriate anticonvulsant medications. Overall prognosis of the disorder is good.

Statement of Ethics

Published research must comply with the guidelines for human studies and should include evidence that the research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. In the manuscript, authors should state that subjects (or their parents or guardians) have given their written informed consent to publish their case (including publication of images). If applicable, also state that the study protocol was approved by the institute's committee on human research. Information revealing the subject's identity is to be avoided. All patients should be identified by numbers or aliases and not by their real names.

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