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Case Report

Radiology Section

Lipoid Proteinosis in a Young Female: A Case Report

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ABSTRACT

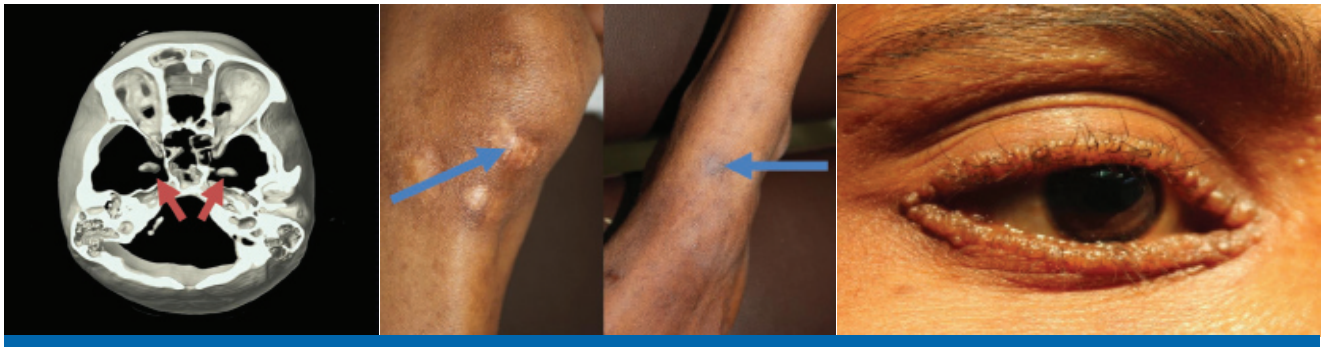
Lipoid proteinosis or Urbach-Wiethe disease is a rare autosomal recessive disorder. It is characterised by progressive deposition of hyaline substance in the mucous membranes, skin and internal organs. It is characterised by papular and nodular lesions on the face, elbows, knees and hands. The tongue is firm and hoarseness may be present at birth. We aim to describe one case of this disease in a 22 years old female who presented to the OPD for CT-scan of the brain post head injury. The essence of this case lies in its typical presentation with classic clinical features and also in the fact that this diagnosis was made incidentally in a patient presenting for a different complaint. A retrograde search leads to the identification of lesions of lipoid proteinosis in the patient. Since, very few such cases have been reported from our country we hope that this case report may lead to increased identification of this condition.

Keywords: CT-scan, ECM1 mutation, Urbach-Wiethe disease

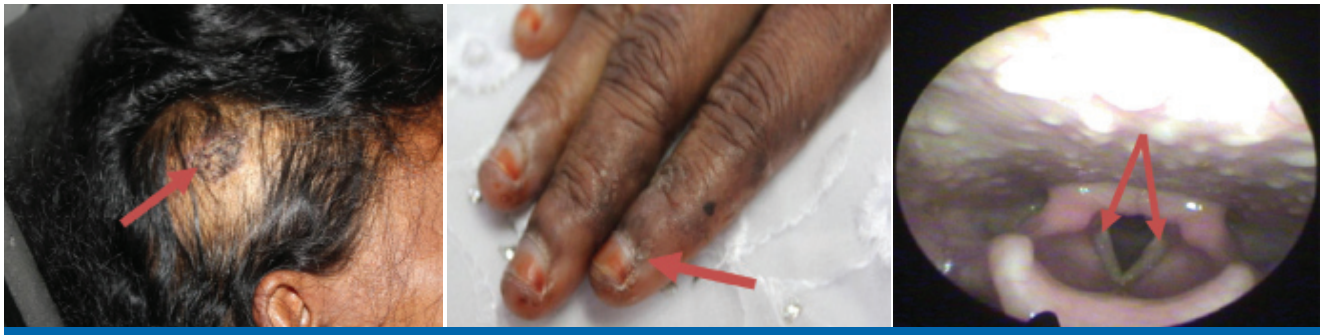
CASE REPORT

A 22-year-old female was referred to us for CT imaging of brain for a history of head injury. She was born of a consanguineous marriage and developed husky voice with skin and mucous membrane lesions at a young age. CT brain showed bilateral intracranial bean shaped calcification within the amygdala and hippocampal region of the temporal lobes [Table/Fig-1]. She had hoarseness of voice since 18 months of age. She also had multiple vesicular and pustular lesions in the skin which on resolution formed permanent scars with hyperkeratosis at the site of trauma [Table/Fig-2]. A thickened row of yellowish papular lesions was seen along the eyelid margins with loss of eyelashes [Table/Fig-3]. Her hair was sparse with scarring alopecia [Table/Fig-4]. She also reported frequent loss of temper of recent onset with a generalised disgust affect, mostly due to depression. There was no history of seizures, visual disturbances, photosensitivity or respiratory obstruction. There was no history of similar complaints or lesions among her immediate family members. It is pertinent to keep in mind a differential diagnosis of porphyria, xanthoma and amyloidosis while diagnosing this condition.

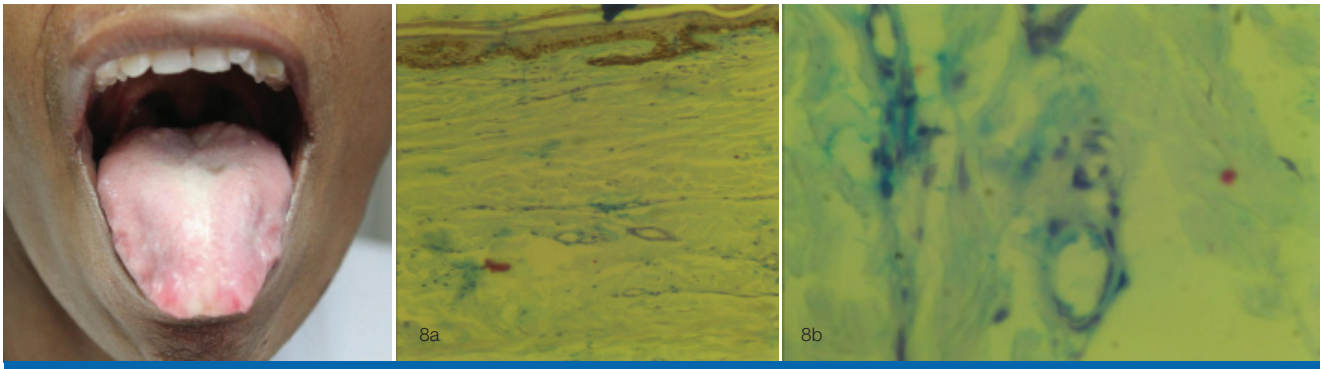
With these clinical presentations and the presence of bilateral, intracranial, bean-shaped calcifications within the hippocampal region of the temporal lobes (pathognomic sign), she was diagnosed as having lipoid proteinosis. Skin biopsy showed moderate fibrosis in the dermis and focal moderate



[Table/Fig-1]: 3D CT BRAIN – showing B/L bean shaped intracranial calcification in the hippocampal region of temporal lobe. **[Table/Fig-2]:** Permanent pox like atrophic scarring on resolution of skin lesions. **[Table/Fig-3]:** Monoliform blepharosis (pathognomic sign) thickened row of beaded papular lesions in the eyelids with loss of eyelashes. (Images from left to right)



[Table/Fig-4]: Scarring alopecia. **[Table/Fig-5]:** Hyperkeratotic verrucous lesion at the sites of trauma. **[Table/Fig-6]:** Diffuse thickened vocal cord due to infiltration in the lamina propria layer. (Images from left to right)



[Table/Fig-7]: Infiltrated tongue with impaired mobility. **[Table/Fig-8a&b]:** Skin biopsy showing diastase resistant, Alcian blue and PAS-D positive, moderate fibrosis in the dermis and focal moderate hyalinisation around few adnexal glands. (Images from left to right)

hyalinisation around few adnexal glands which was diastase resistant, alcian blue and PAS-D positive, confirming diagnosis [Table/Fig-8a&b]. She was treated symptomatically for the skin lesions and genetic counselling was given. Informed consent was taken from the patient prior to examination and for taking of pictures.

DISCUSSION

Lipoid proteinosis, initially described as "hyalinosis cutis et mucosae" [1] is a rare autosomal recessive genodermatosis due to a mutation in the ECM1 gene on chromosome 1q21. Till date only around 300 cases have been reported. This makes an interesting case owing to its low visibility. ECM1 is a protein coding gene involved in maintaining the structural integrity of the skin. It is linked to differentiation of keratinocytes, collagen composition, basement membrane regulation and growth factor binding [2].

The ECM1 gene mutation leads to hyaline material deposition in the dermis. This results in thickening of skin and mucous basement membrane around blood vessels and adnexal epithelia. The patient will eventually present with abnormal wound healing, premature skin aging and scarring [3]. Over time, the larynx is infiltrated with hyaline material. As a result of this around two-thirds of patients show the presence of hoarseness at birth or in early infancy [4].

Skin manifestations include recurrent, variably sized vesicles, pustules, bullae, and haemorrhagic crusts that arise on the skin, mouth and throat. The most commonly affected sites are the face and distal extremities. Upon resolution, the lesions heal with pox like atrophic scarring that is permanent. Sites of trauma may show the development of hyperkeratotic, verrucous plaques especially at the elbows, knees and dorsum of the hands [Table/Fig-5]. Moniliform Blepharosis- a row of beaded papules along eyelid margins resembling a string of pearls is considered a pathognomonic finding present in 50% of the patients [5].

Hoarseness of voice, dysphagia and airway obstruction results from infiltration of the larynx, vocal cords and surrounding structures [Table/Fig-6] [6]. Infiltration of tongue results in woody firmness and impaired mobility [Table/Fig-7]. Pebbling of lip mucosa imparts a cobblestone appearance.

Skin biopsy is used to confirm the diagnosis. The distinguishing histological feature of lipoid proteinosis is the accumulation of extracellular hyaline material in areas such as the upper cutis, around the secretory sweat ducts, excretory ducts, small blood vessels and hair follicles. The hyaline material while strongly PAS positive, was also slightly digested by diastase. It stained faintly for collagen with Gomori's trichrome. Within the hyaline material fat stains were negative. Most of the PAS positive material was removed following pepsin digestion.

This suggests that the carbohydrate component is probably linked to a protein. Since this protein is susceptible to pepsin digestion and contains tryptophan, it does not appear to be collagen.

The infiltration around the hippocampal capillaries in the central nervous system results in wall thickening. This is followed by perivascular calcium deposition. Microscopic findings include gross amorphous calcifications encompassed by gliotic tissue and calcified thickened capillary walls [7]. Subsequent medial temporal lobe architectural distortion with gliotic tissue and calcium accumulation can lead to a constellation of reported neurologic manifestations, which range from migraine, variable degrees of mental retardation, seizures, depression, anxiety and panic attacks to disturbances in decision making, loss of memory and abnormal social interaction patterns [8].

These varied symptoms frequently lead to radiologic evaluation by CT or MR imaging which may indicate the proper diagnosis. The bilateral bean-shaped intracranial calcification in the amygdala and hippocampal areas is pathognomic of LP and can support the correct diagnosis in unsuspected patients [9].

CONCLUSION

Lipoid proteinosis or Urbach-Wiethe disease is a rare disorder without curative treatment. It is essentially a diagnosis based on clinical presentation. The clinical triad of typical skin lesions, early onset of hoarseness of voice and the presence of beaded papules around the eyelids confirms the diagnosis. Bilateral bean shaped intracranial calcification in the hippocampal region of temporal lobe on CT scan is the hallmark of this disease. Supportive measures and appropriate precautions will help to avoid worsening of disease. The disease has not been shown to reduce the lifespan of the affected individual.

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