A Novel Association of the Additional Intracranial Calcification in Lipoid Proteinosis: A Case Report

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ABSTRACT
Lipoid Proteinosis (LP) is a genetically linked, autosomally transferred, rare, chronic multisystem disease which is characterized by a normal lipid profile, but with abnormal deposits of lipids and proteins in the body, which slowly but steadily leads to systemic manifestations. Although it affects almost all the systems of the body, it predominantly manifests as lesions on the skin and it has characteristic intracranial calcifications. Although, the intracranial calcifications can be classified, based on their aetiopathogenesis, as age-related and physiologic, congenital, infectious, endocrine and metabolic, vascular, and neoplastic; the symmetric calcifications in LP are a distinct entity. To one who is aware of this entity, LP is usually an incidental diagnosis. No permanent cure is available for LP till date. Only symptomatic medical treatment is being given. With the increasing awareness on this entity, LP can now be detected in its early phase and it can be better managed.

As this condition is rare, it is necessary to spread awareness on this entity in the scientific community and hence this case is being reported. This case report is the first to demonstrate a novel association of an additional intracranial calcification in Lipoid Proteinosis.

INTRODUCTION
Lipoid Proteinosis (LP) is a radiologically rare genodermatosis which is caused by the abnormal deposition of lipids and proteins in various systems of the body, even though the lipid profile is normal [1,2].

Although multiple systems of the human body are affected by it, the most predominant manifestations which are seen in the dermatology practice are lipid laden skin lesions and eye lesions and in the radiology practice, symmetric, intracranial, medial, temporal calcifications are seen. To one who is aware of this entity, LP is usually an incidental diagnosis. As this condition is rare, it is necessary to spread awareness on this entity in the scientific community. Hence, a case of LP which was diagnosed incidentally in a 52 years male who was referred for CT scan of the head with complaints of occasional headache has been reported here.

CASE REPORT
A 52 years male was referred for CT scan examination of the head for headache that was troubling him for the past 6 months.

Clinically, he was conscious, co-operative and well oriented to the time, place and persons. He had no prior history of any systemic diseases. Yellowish patches [Table/Fig-1] were seen on his skin, over the forearm. There was absence of any hyperkeratosis of the skin and depigmentation of the lips. The tongue was freely mobile. There was no hoarseness of the voice.

There was neither any significant family history, nor was he a product of a consanguineous marriage.

His blood counts and lipid profile were within normal limits. His serum cholesterol was 144 mg/dl (normal < 200 mg/dl), his serum triglycerides were 96 mg/dl (normal < 170 mg/dl) and his serum HDL cholesterol was 53 mg/dl (normal < 70 mg/dl).

The plain radiograph of the skull in the lateral view [Table/Fig-2] showed an irregular intracranial calcification in the posterior cranial fossa region. The plain CT scan brain window images showed subtle, symmetric, comma shaped hyperdensities with a CT attenuation value of 84 – 92 H.U. which were suggestive of calcifications in the medial aspect of the temporal lobes [Table/Fig-3(a), 3(b)], in addition to the irregularly shaped, posterior fossa intracranial calcification [Table/Fig-3(c)]. Hence, a radiological diagnosis of LP was put forth.

The histopathology of the punch biopsy from the yellowish plaques on the skin which was done outside by the referring physician, reported them as ‘an abundant deposition of amorphous eosinophilic material in the thickened papillary dermis.’ The hyaline like material was diastase resistant and PAS positive [Table/Fig-4]. These findings were consistent with the radiological findings of LP.
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**DISCUSSION**

Although Seibman first reported Lipoid Proteinosis in 1908 [3], Urbach and Weithe scientifically studied it and named it as “Lipoidosis cutis et mucosae” in 1929 [3,4].

Hamada et al. [5] mapped LP to chromosome 1q21 at D1S498 [6] and concluded that the mutations outside the exon 7 exhibited the more severe mucocutaneous LP phenotype [7].

LP has a slow but steady and a progressive course. Histologically, the material which is deposited in the tissues resembles lipids and proteins. Hence, this entity was erroneously labeled as LP.

Very few cases have been reported from Asia and most of the cases have been seen in South Africa and Central Europe [3,8]. Such is the rarity of the disease that till date, not more than 500 cases have been reported worldwide. Therefore, the actual picture on its incidence and prevalence is not completely known.

No definitive age, sex or race predilections exist. There is a documented autosomal recessive inheritance as there is usually a history of consanguinity among the unaffected parents [9]. A mental subnormality is seen only when it is transmitted by autosomal dominant inheritance due to the mutant genes [3].

In the gene which encodes the extracellular matrix protein 1 (ECM1) on the chromosome band 1q21, loss of function mutations occur. The patients with the exon 7 mutations display slightly milder clinical features, while the mutations in exon 6 result in a more severe phenotype [5,6]. This data continues to get modified and recently, a novel nonsense mutation in the ECM1 gene was identified in a Pakistani family [7].

A glycoprotein which is produced by the normal ECM1 gene is expressed in the skin, mucosa and in multiple internal organs. The mutations in this gene lead to the deposition of a hyaline like material in the skin and the viscera in abnormal amounts, which is the cause of the clinical manifestations. These deposits stain positive with the Periodic Acid-Schiff stain and they are Diastase resistant and negative for Congo red [10].

Due to the deposition of this hyaline like material in the oesophagus, a barium swallow examination shows filling defects in the upper...
To conclude, although LP is not always a life threatening entity, it can at times be quite distressing. An appropriate radio-pathological workup can lead to an early detection so that a team effort of multiple specialties can render a proper management.

The novelty in the case which has been reported here, is the association of the posterior fossa calcification in addition to the routinely seen medial temporal calcification of LP.

REFERENCES