Radiologic presentation of lipid proteinosis with symmetrical medial temporal lobe calcifications

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Lipoid proteinosis is a rare, autosomal-recessive, genetic disorder characterized by multisystem involvement due to intracellular deposition of amorphous hyaline material. The disease is due to a mutation in the extracellular matrix of the protein 1 gene. The skin, mucosa, and central nervous system are commonly affected. Hallmark findings in the brain are calcifications, mostly occurring in the amygdala, hippocampus, parahippocampal gyrus, and striatum. Moniliform blepharosis, a dermatologic condition that is present in 50% of patients, is a pathognomonic finding. In the other 50% of patients, imaging assists in the diagnosis. We present a case of lipid proteinosis with its characteristic features.

Introduction

Lipoid proteinosis, also known as Urbach-Wiethe disease or Hyalinosis cutis et mucosae (1), is a rare, autosomal-recessive disorder characterized by multisystem involvement with deposition of protein, lipid, and carbohydrates in various tissues like skin, blood vessel, brain, vocal cord, pharynx, and esophagus (2). Lipoid proteinosis is caused by a mutation of the extracellular matrix protein 1 gene (ECM 1) (3).

The skin manifestations are the first symptoms to appear in most of these patients. Patients with lipid proteinosis also characteristically develop hoarseness. Many patients also develop a variety of neurologic manifestations that reflect central nervous system involvement (4). Migraine, seizure disorder, depression, and anxiety disorder are the frequently occurring neuropsychiatric presentations in this disease. We describe the characteristic radiologic features of lipid proteinosis in a patient with biopsy-proven disease.

Case report

A 37-year-old female, born of nonconsanguineous parents, came for CT imaging with a chief complaint of giddiness; she had been referred from the neurology outpatient department. Her neurologic examination and psychiatric evaluation were essentially normal. Her other complaints were facial scars (poxlike lesions) and hoarseness—both apparent since childhood. The patient had not received any prior consultation for her hoarseness or skin problems.

CT images showed bilateral, symmetric, fairly dense, comma-shaped calcifications in both the hippocampi and amygdalae. Calcifications were also seen in the left basal ganglia (Figs. 1A and B).

In the MRI brain study, T2-weighted images showed hypointense lesions in the mesial temporal lobes bilaterally (Fig. 2A). The gradient echo images showed hypointense lesions symmetrically in the amygdalae, the heads of the hippocampi, the parahippocampal gyri, and in the left basal ganglia (Figs. 2B, 2C).

Otolaryngologic examination demonstrated that both her vocal cords were thickened. A dermatologic opinion revealed poxlike scarred lesions in her face with dry and wrinkled skin (Fig. 3). Ulcerations were noted in the angles of her mouth. Maculopapular, beaded lesions were also noted in her lower eyelids—typical of moniliform ble-
Lipoid proteinosis was first described by Urbach and Wiethe in 1929 under the name “hyalinosis cutis et mucosae.” It is a rare, autosomal-recessive genodermatosis with around 300 cases described globally so far (5). The condition is due to a mutation in the ECM1 gene on chromosome 1q21. ECM is a glycoprotein with three varieties—ECM1a, ECM1b, and ECM1c. ECM1 is expressed in the dermis, basal keratinocytes, endothelial cells, and developing bones and is associated with keratinocyte differentiation, basement membrane regulation, collagen composition, and growth factor binding (3).

The mutation of the ECM1 gene leads to deposition of hyaline material in the dermis, with thickening of the skin and mucous basement membranes, blood vessels, and adnexal epithelia. Patients present with abnormal scarring and wound healing, and premature aging of the skin (3, 6). Hoarseness is present at birth or early infancy in approximately two-thirds of patients and is due to infiltration of
the larynx with hyaline material. The condition progresses with time (7).

Lipoid proteinosis is a multisystem disease, and CNS involvement is seen in 50-75% of individuals. Infiltration of the CNS occurs predominantly in the hippocampal capillaries, with resultant wall thickening, later progressing to perivascular calcium deposition. Microscopic findings are amorphous calcifications surrounded by gliotic tissue and calcified, thickened capillary walls (8). Neurologic manifestations range from migraine, seizure disorder, and depression to anxiety disorder. Lipoid proteinosis patients were found to have an increased incidence of mood, anxiety, and psychotic disorders (9, 10). The patients also had varying degrees of mental retardation, as well as disturbances in decision making and memory, and abnormal social interaction. This multitude of neuropsychiatric symptoms may prompt CT or MR evaluation of patients, which in symptomatic individuals can lead to a proper diagnosis.

The typical imaging finding in lipoid proteinosis is intracranial, fairly dense calcifications in the bilateral medial temporal lobes. Amygdala involvement is pathognomonic and is more prominent with a longer duration of the disease. Commonly involved sites are the amygdalae, hippocampus, the parahippocampal gyrus, and the striatum.

In CT, these calcifications appear as curvilinear or comma-shaped hyperdense lesions symmetrically in both medial temporal lobes and corpus striatum. On MRI, these lesions appear hypointense in T1 and T2 and are well brought out in T2* GRE images. In the absence of brain calcifications, the CT or MRI features of these patients are unremarkable.

Moniliform blepharosis is a pathognomonic dermatologic finding that is found in 50% of patients with lipoid proteinosis, and the diagnosis can be confirmed after dermatologic consultation. In the other 50% of patients, CT and MRI can aid in the diagnosis because of the typical sites involved in calcification.

The differential diagnosis for medial temporal lobe calcifications includes the following:

- Calcified gliomas in the amygdalohippocampal region in the pediatric population, but these are usually neither bilateral nor symmetrical.
- Raine syndrome—a very rare autosomal-recessive, sclerotic, bone dysplasia, characterized (among other findings) by intracranial calcifications. The calcifications rarely affect blood vessel walls and mainly affect the basal ganglia. There were no records of calcification in the amygdalae.
- Healed herpes encephalitis. Dystrophic temporal lobe calcifications can occur as a late sequelae of herpes encephalitis (9).
- Amygdalae, as a part of the limbic system, play a key role in mediating emotions, especially fear recognition in relation to possible danger and threat, modulation of attention, perception, learning, and emotional long-term memory (10, 11).
- Generalised dystonias have been described in patients with striatal calcifications (2).

**Conclusion**

Selective brain parenchymal calcification is pathognomonic of lipoid proteinosis, with calcifications occurring in
very specific sites such as the amygdala, the hippocampus, the parahippocampal gyrus, and the corpus striatum. These locations help explain the myriad neurologic signs in these patients. CT and MRI of the brain help in identifying this pathognomonic pattern of calcification, leading to the correct diagnosis in the proper clinical setting.

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