



## Nadir Bir Nöbet Nedeni; Lipoid Proteinozis (Urbach-Wiethe hastalığı): Olgu Sunumu

### A Rare Cause of Seizure; Lipoid Proteinozis (Urbach Wiethe disease): A Case Report

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#### ÖZET

Urbach-Wiethe hastalığı olarak bilinen Lipoid Proteinozis (LP) nadir görülen otozomal resesif geçişli genodermatozudur. Hastalar genellikle ses kısıklığı ve cilt- mukoza anormallikleri ile başvururlar. Lipoid Proteinozis merkezi sinir sistemini nadiren tutar. Temel görüntüleme bulgusu çoğunlukla medial temporal loblarda meydana gelen atipik intrakranial kalsifikasyonlardır. Bu yazıda nöbet ile başvuran nadir bir LP olgusunun bilgisayarlı tomografi (BT), manyetik rezonans görüntüleme (MRG) bulguları patolojik confirmasyon eşliğinde sunulmuştur.

**Anahtar Kelimeler:** Bilgisayarlı tomografi, Lipoid proteinozis, Manyetik rezonans görüntüleme, Nöbet

#### SUMMARY

Lipoid Proteinozis (LP) known as Urbach-Wiethe disease is a rare autosomal recessive inherited genodermatozis. Patients usually present with hoarseness and skin-mucosa abnormalities. Lipoid Proteinozis involves the central nervous system (CNS) rarely. The essential imaging finding in LP is appearance of atypical intracranial calcifications, mostly occurring in the medial temporal lobes. Herein we report a rare case presenting with seizure accompanied computed tomography (CT), magnetic resonance imaging (MRI) findings and also with pathological confirmation.

**Key words:** Computed tomography, Lipoid proteinozis, Magnetic resonance imaging, Seizure

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**Başvuru Tarihi/Received:** 19-10-2015  
**Kabul Tarihi/Accepted:** 29-10-2015



## INTRODUCTION

Lipoid Proteinozsis (LP) is a rare autosomal recessive inherited facomatosis with a wide clinical spectrum and typical neurological, dermatological and neuroradiological features, resulting from mutations in extracellular matrix protein (*ECM1*) gene (1). Patients usually present hoarseness and skin-mucosa abnormalities. Herein we report a rare case presenting with seizure accompanied computed tomography (CT), magnetic resonance imaging (MRI) findings and also with pathological confirmation.

## CASE PRESENTATION

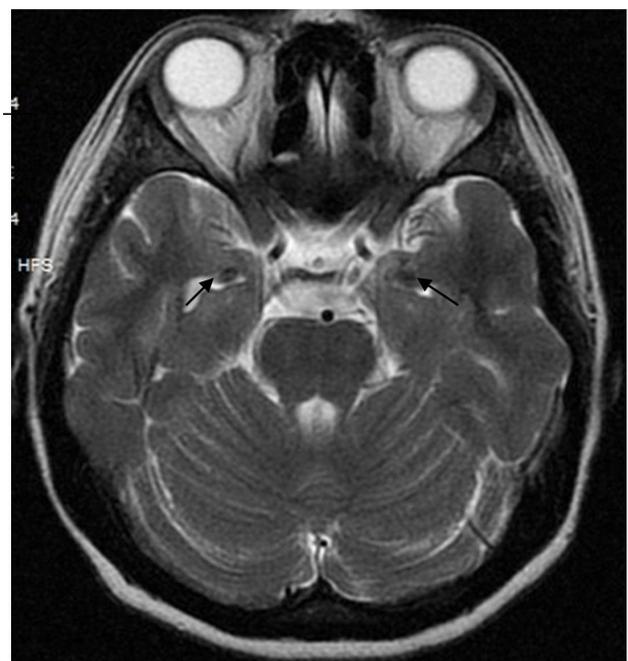
A 28-year-old female patient admitted to neurology department with complaint of smell of burning on her nose and buzzing noises on her ears. Her complaints had started as recurrent episodes 3 months before those were going once a week. Seizures came in the shape as complex partial and never turned to generalized seizures. After beginning of episodes she had developed panic attacks also. Her clinical history was unremarkable and neurological examination was normal. No abnormality was noted on electroencephalography (EEG). To exclude a possible organic intracranial pathology brain CT and MRI were requested. Computed tomography revealed bilateral extensive horn shaped calcifications (arrows) in medial temporal lobes, amigdala and hippocampus region (Figure 1).

T2 weighted MRI showed bilateral symmetric hypointense lesions representing calcification in amigdala (Figure 2).

Because of typical calcified lesions in mesial temporal lobes, LP was considered initially in the differential diagnosis. She had referred to an otorhinolaryngologist who noticed weak hoarseness on her voice. Later she stated that her hoarseness had been since early infancy. By detailed history it was learned that her parents were first degree relatives. On her exacting dermatological and ear, nose-throat examination, small yellow lesions were seen on the inner mucosa of lower lip (Figure 3). Her urogynecological and cardiological examinations were normal. Other than small yellow lesions and hoarseness there was no positive examination finding.



**Figure 1.** Axial CT image shows bilateral symmetric horn shaped calcifications in medial temporal lobes, amigdala and hippocampus region

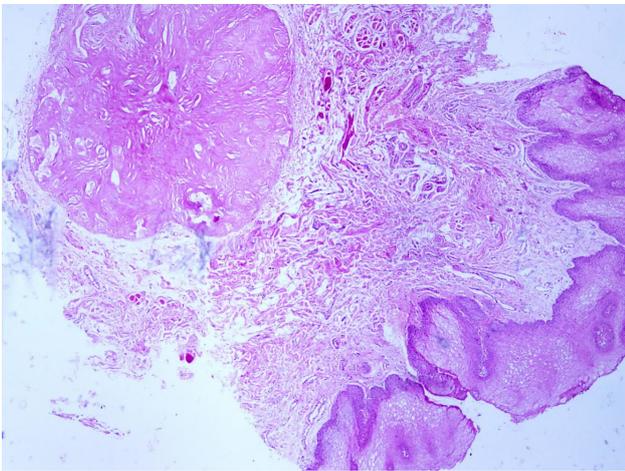


**Figure 2.** Axial T2-weighted MR imaging reveals bilateral symmetric hypointense lesions in the medial temporal lobes (arrows)

After the biopsy, pathological examination confirmed our preliminary diagnosis. Histological analysis showed the typical deposition of eosinophilic PAS-positive hyaline material (Figure 4).



**Figure 3.** Close view of patient shows small yellow lesions on the inner mucosa of lower lip



**Figure 4.** 200x-Deposition of eosinophilic hyaline material in the stroma

In the examination of the psychiatry department she had been diagnosed as anxiety disorder, because of anxiety attacks due to seizures escitalopram drug therapy was started. Seizures were controlled with antiepileptic drug therapy by caphamazepine 400 mg (twice daily) and lev-etirasetam 250 mg (twice daily).

## DISCUSSION

As a multisystem disease, LP involves the central nervous system (CNS) rarely. Perivascular calcium deposition occurs as a result of infiltration and wall thickening of capillaries around the hippocampus. Gross amorphous calcifications encompassed by gliotic tissue and calcified thickened capillary walls are seen as microscopic findings (2). Histopathological examination confirms the clinical diagnosis is confirmed by hematoxylin and eosin stained sections by the entity of extracellular amorphous and eosinophilic hyaline material which is PAS positive and diastase resistant (3). Subsequent calcium accumulation, gliotic tissue and architectural distortion of medial temporal lobes can lead to reported neurologic manifestations, which range from migraine, variable degrees of mental retardation, seizures, depression, anxiety, and panic attacks to disturbances in decision making, memory, and abnormal social interaction patterns (4, 5). These varied symptoms frequently lead to radiologic evaluation by sectional imaging with CT and MRI, which, in unsuspected patients, may indicate the convenient diagnosis. The essential imaging finding in LP is appearance of atypical intracranial calcifications, mostly occurring in the medial temporal lobes. The most commonly affected sites are amygdalae, hippocampus, parahippocampal gyrus, or even the striatum. Amygdalae involvement is considered pathognomonic, being more prominent with longer disease duration. Curvilinear hyperattenuated horn-shaped lesions are well depicted by CT in the amygdaloid bodies. On MRI such lesions are hypointense in all pulse sequences, especially in GRE T2\* weighted images. CT or MRI findings may be unremarkable in patients with LP in the absence of brain calcifications (2). CT findings can be more striking as in our case because of calcification. We think that because of lesions symmetry, mild lesions can be overlooked near sella. In our case MRI findings were weak and there were no prominent dermatological complaints suggestive of LP as a cause of seizures. So preliminary diagnosis was made after CT imaging.

Epilepsy, particularly temporal lobe epilepsy, has been described as a common manifestation of LP, especially in combination with intracerebral calcifications, principally in the anteromedial temporal lobe (6). Clinically, our patient presented smell and sound hallucinations indicating temporal lobe epilepsy but EEG was not noted any abnormality. This can be explained by deeply localization of the lesions or may be related to timing of EEG as it was not achieved during the seizure.

In majority of studies hoarseness of voice and skin and mucosal involvement were main clinical presentations of the disease (7). In this case we introduce a patient with only neurologic symptoms and weak vocal hoarseness without any specific dermatological signs or symptoms. Only a few studies had been reported the neurological involvement without any dermatological presentation (6, 7). Due from absence of the specific dermatological findings they were diagnosed after many years from the beginning of

the seizures. Our patient's seizures' onset was subakut. She had not been treated because of seizures yet. This was the first appealing to the hospital. Radiologists should be familiar with imaging findings of LP. Therefore they will be the first clinician suggesting the diagnosis and may provide control of seizures promptly.

## CONCLUSION

Involvement of very specific sites such as the amygdalae, hippocampus, parahippocampal gyrus, and the striatum by calcification is the hallmark of LP. These lesions can explain many varied neurologic symptoms in these patients. The recognition of this pathognomonic lesion pattern can support the accurate diagnosis in unsuspected patients with seizures.

## Disclosure

The authors disclosed no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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