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Cessation of Drug-resistant Seizures with Clobazam in a Patient with Lipoid Proteinosis

Lipoid Proteinosis Hastasında İlaca Dirençli Nöbetlerin Klobazam ile Sonlanması

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Anahtar Kelimeler: Lipoid proteinosis, epilepsi, ilaca dirençli nöbet, medial temporal lob kalsifikasyonu, klobazam

Dear editor,

Lipoid proteinosis (LP) is a very rare autosomal recessive disease caused by *ECM1* mutations, which lead to the loss of protein–protein interaction, resulting in the deposition of hyaline material in the mucous membranes, skin, and other organs. Some of the easily recognizable mucocutaneous manifestations of the disease are hoarseness due to the infiltration of laryngeal mucosa, fragile skin with blisters, and beaded eyelid papules. Common neuropsychiatric manifestations are seizures, headache, psychosis, panic attacks, anxiety, memory impairment, and abnormal emotional responses to fear and danger (1). The prominent medial temporal lobe calcifications in neuroimaging studies are considered pathognomonic (2). Epilepsy is reported in approximately 30% of cases, with most patients experiencing temporal lobe seizure characteristics (3).

Our patient was a 26-year-old man who was admitted to our neurology clinic as a result of drug-resistant epileptic seizures. His first seizure was a generalized tonic–clonic convulsion at the age of 15. This was his only generalized seizure. Afterward, he developed focal seizures with impaired awareness. Some of his seizures were preceded by a rising epigastric sensation. His past medical history revealed a weak cry and hoarseness since infancy. He had fragile, easily damaged skin. He developed scars on his face, elbows, buttocks, and hands, which tended to increase when he was exposed to the sun (Figure 1A). He also had a thickened, firm, and enlarged tongue (Figure 1B). His neurological examination was unremarkable. He was born to first-degree consanguineous parents. Nobody in his family had similar symptoms or a diagnosis of epilepsy. An interictal electroencephalography (EEG) revealed slow background activity over the left temporal region with occasional sharp waves at the T3 electrode. Ictal EEG findings also involved the left temporal lobe. Cranial computed tomography revealed calcification of both amygdalae (Figure 2A), accompanied by millimetric calcifications in the basal ganglia. His magnetic resonance imaging showed bilateral amygdaloid hypointensities that were compatible with LP (Figure 2B). A punch biopsy taken from his lower lip demonstrated pale eosinophilic deposits of hyaline-like material in the dermis and around the capillaries on hematoxylin and eosin-stained sections. The deposits were

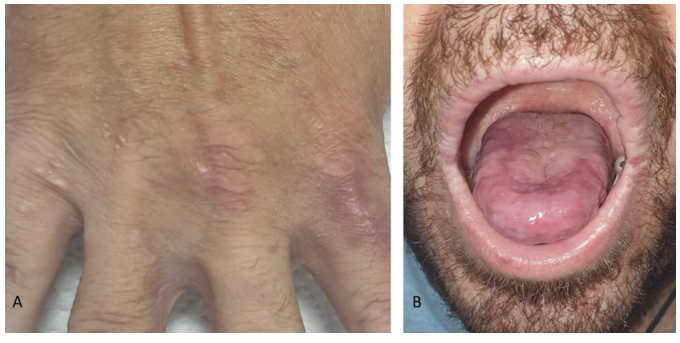

Figure 1. Scar-like lesions on the dorsum of the right hand (A); thickened, firm, and enlarged tongue (B)

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strongly positive with periodic acid-Schiff (PAS) and PAS diastase stain (Figure 2C, D). Due to the intractable course of his seizures, the patient was prescribed vigabatrin, oxcarbazepine, lamotrigine, topiramate, and levetiracetam in various doses and combinations with minimal or no impact on seizure frequency or severity. His temporal lobe seizures continued to occur once a week. In 2017, clobazam (20 mg/day) was added to the existing anti-seizure medications (levetiracetam 3.000 and lamotrigine 400 mg/day). The patient has been seizure-free with these medications since then.

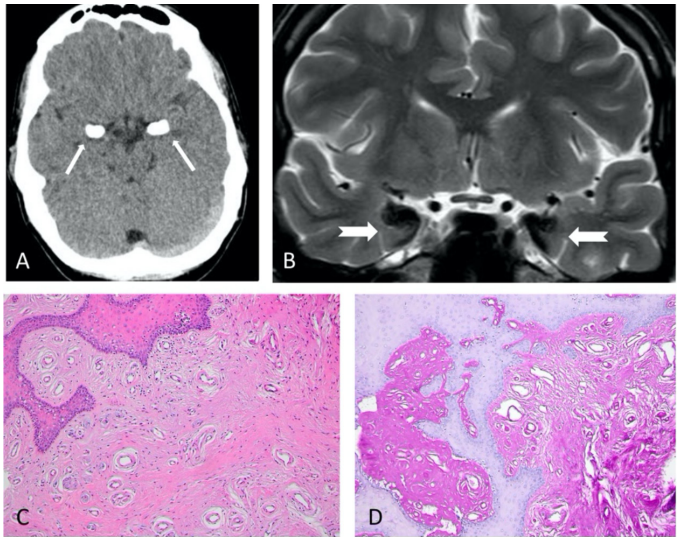

Figure 2. Bilateral amygdaloid calcifications (arrows) detected by cranial computed tomography scanning (A); bilateral comma-shaped hypointense lesions (arrows) on brain magnetic resonance imaging (B); homogenous eosinophilic material around blood vessels and in the dermis. H & E x 200 (C); hyaline-like material is periodic acid-Schiff (PAS) positive and diastase resistant. d-PAS x 200 (D)

H & E: Hematoxylin and eosin, PAS: Periodic acid-Schiff

In a previous case series, 57% of patients with bilateral medial temporal involvement had seizures that were not correlated with the severity of calcifications (4). In the literature, most patients are reported to be drug resistant. Older and newer generation drugs have been tried, but none of them is superior to the others (4). Only one previous paper reported a patient who "dramatically improved" with a combination of carbamazepine (1.200 mg/d) and levetiracetam (1.000 mg/d) (5).

Ethics

Informed Consent: Obtained.

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Authorship Contributions

Concept: N.D., Design: N.D., Data Collection or Processing: Ö.G., E.D.Ö., Analysis or Interpretation: N.D., Literature Search: E.D.Ö., Writing: N.D., E.D.Ö.

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References

1. Mcgrath JA. Lipoid proteinosis. Handb Clin Neurol 2015;132:317-322.
2. Gonçalves FG, de Melo MB, de L Matos V, Barra FR, Figueroa RE. Amygdalae and striatum calcification in lipoid proteinosis. AJNR Am J Neuroradiol 2010;31:88-90.
3. Meletti S, Cantalupo G, Santoro F, et al. Temporal lobe epilepsy and emotion recognition without amygdala: a case study of Urbach-Wiethe disease and review of the literature. Epileptic Disord 2014;16:518-527.
4. Oguz Akarsu E, Dinçsoy Bir F, Baykal C, et al. The characteristics and long-term course of epilepsy in lipoid proteinosis: a spectrum from mild to severe seizures in relation to ECM1 Mutations. Clin EEG Neurosci 2018;49:192-196.
5. Omrani HG, Tajdini M, Ghelichnia B, et al. Should we think of Urbach-Wiethe disease in refractory epilepsy? Case report and review of the literature. J Neurol Sci 2012;320:149-152.