

## Urbach--Wiethe Disease: A Rare Cause of Bilateral Mesial Temporal Lobe Involvement and Cerebral Hemorrhage

Dear Editor,

Two siblings born from consanguineous parents were admitted to our hospital with the complaint of seizures. The seizures were in the form of unresponsiveness attacks that lasted less than 1 min. Before these seizures, the patients described an aura with an unusual bad smell. No ictal motor phenomenon was described.

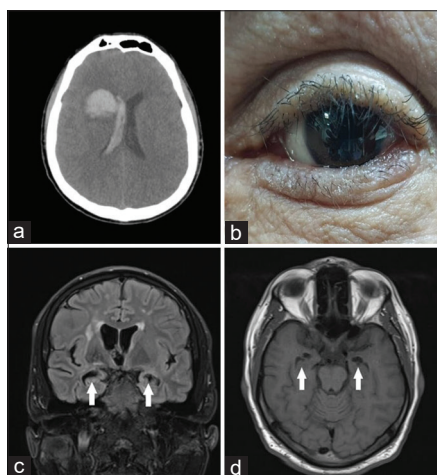
The first patient was a 37-year-old man. In addition to the seizures, he also had behavioral changes. The patient was no longer afraid of animals that he used to fear. He had irritability and aggressive behaviors, as well as increased libido and hypersexuality. He had sex with multiple partners multiple times despite being married. In his past medical history, he had a putaminal hemorrhage at the age of 33, despite not having hypertension or an aneurysm [Figure 1a]. The patient also had hoarseness since early childhood. His neurological examination was normal. On physical examination, he had alopecia. There were multiple papules on the eyelid margins and the malar region (moniliform blepharosis) [Figure 1b]. Cranial magnetic resonance imaging (MRI) showed

bilateral, symmetrical calcification of the hippocampus and parahippocampal regions, which had a hypointense appearance on T1 and Fluid-attenuated inversion recovery (FLAIR) sequences [Figure 1c and d]. Cranial MRI features were compatible with Urbach--Wiethe disease. Extracellular matrix protein 1 (ECM-1) gene mutation was shown by genetic testing. Electroencephalography (EEG) did not show any abnormalities.

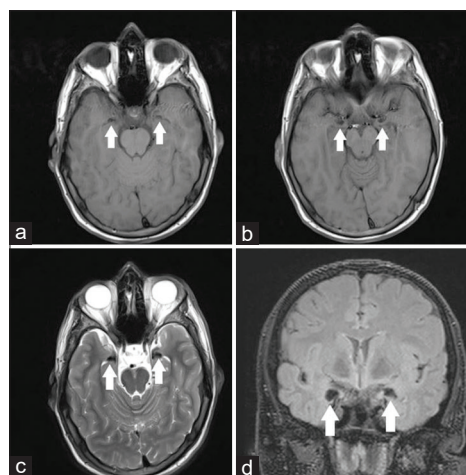
The second patient was a 23-year-old man. Although he did not have any neuropsychological complaints, he had hoarseness and alopecia. His neurological examination was normal. He also had bilateral, symmetrical calcification of the hippocampus and parahippocampal regions [Figure 2]. The genetic testing showed ECM-1 gene mutation. EEG did not show any abnormalities.

Valproic acid was the preferred drug for the patients. The seizures were controlled with valproic acid therapy.

Urbach--Wiethe disease (also known as lipoid proteinosis; hyalinosis cutis et mucosae) is a rare disorder caused by mutations in ECM-1.<sup>[1]</sup> ECM-1 is an extracellular protein



**Figure 1:** (a) Putaminal hemorrhage on a brain computerized tomography image. (b) Moniliform blepharosis. (c) Bilateral amygdala calcification on a coronal FLAIR sequence. (d) Bilateral amygdala calcification on an axial T1 sequence



**Figure 2:** (a) Bilateral amygdala calcification on an axial T1 sequence. (b) Bilateral amygdala calcification on an axial T1 sequence. (c) Bilateral amygdala calcification on an axial T2 sequence. (d) Bilateral amygdala calcification on a coronal FLAIR sequence

that takes part in angiogenesis.<sup>[1]</sup> Autopsy studies have shown calcified vessel walls and gliotic tissues in the amygdala.<sup>[1]</sup> Bilateral symmetrical temporal lobe calcification can be seen in up to 75% of patients with Urbach--Wiethe disease.<sup>[1]</sup> Temporal lobe calcifications are visible on T1, T2, and FLAIR images.<sup>[1]</sup>

Epilepsy and behavioral changes are the most common neurological manifestations.<sup>[2]</sup> The most common seizure type is focal seizures with impaired awareness, which may manifest as motionless staring with an epigastric aura.<sup>[2]</sup> The neuropsychological findings are aggressive behavior, anxiety, hypersexuality, and decreased ability to identify emotional expressions.<sup>[3]</sup> The neuropsychological findings and radiologic findings can evolve over time.<sup>[1,3]</sup> Valproic acid is one of the effective drugs in temporal lobe epilepsy.<sup>[4]</sup> Also preferred was valproic acid, so as to take advantage of its impulse control effect.<sup>[5]</sup>

Urbach--Wiethe disease is associated with intracerebral hemorrhage.<sup>[6,7]</sup> A small number of Urbach--Wiethe disease patients with intracerebral hemorrhage were reported in the past.<sup>[6,7]</sup> Patients may develop a large brain hematoma or small cerebral hemorrhages.<sup>[6,7]</sup> The ECM-1 gene is expressed around the vessels.<sup>[8]</sup> The ECM-1 protein stimulates blood vessel formation.<sup>[1]</sup> Mutations in the ECM-1 gene cause a glycoprotein deposition and calcium mass in the vessels.<sup>[1,8]</sup> Moreover, it reduces collagen protein expression and stimulates the overexpression of non-collagenous proteins.<sup>[8]</sup> These alterations affect the structure of the vessel walls and may explain the intracerebral hemorrhage risk in patients with Urbach--Wiethe disease.<sup>[1,8]</sup>

The disease also has a broad range of dermatological and head and neck symptoms.<sup>[1]</sup> Moniliform blepharosis is pathognomonic.<sup>[9]</sup> Neurologists should keep Urbach--Wiethe disease in mind due to its neurological manifestations, despite its rarity.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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