**Desafios em Neurologia**

**Casos Clínicos do XXX Congresso Brasileiro de Neurologia**

**Lipoid Proteinosis (Urbach-Wiethe Disease)**

**ID:** Male, 38 years old, white, born and resident in São Paulo – SP

**Diagnostic Hypotheses:**

> Syndromic: Convulsive Syndrome

> Topographic: Bilateral mesial temporal lobes

> Nosological: Genetic

> Etiologic: Urbach-Wiethe Disease (Lipoid Proteinosis)

**Clinical History:**

A 38-year-old male patient with a history of hoarseness since birth (Video 1), anosmia since childhood (can only smell alcohol), aggressive behavior and irritability (without learning impairment) since he was a teenager, and alopecia since he was 18, was referred to our center for evaluation of uncontrolled seizures that started at age 22.

Seizures were characterized by dizziness and déjà vu sensation, with subsequent loss of awareness and oral automatisms. Attacks were short-lasting and followed by a postictal confusion state. There was no family history of seizures. He started treatment only at age 27, initially only with phenobarbital, followed by association with multiple other anti-epileptic drugs, with questionable adherence and maintaining crises uncontrolled

During the first evaluation he was being treated with lamotrigine (LMT) 300 mg daily, valproic acid (VPA) 750 mg daily, Clobazam 10 mg daily, and Clonazepam 1 mg daily, with seizures still occurring 7 to 8 times a month. His neurological assessment was normal, and so were his EEG, and laboratory tests. Brain CT was not performed due to the patient missing his appointment. In the next follow-ups, the doses of LMT and then Clobazam were increased, while Clonazepam was gradually tapered and discontinued. An MRI was ordered, and the patient was instructed to return for regular follow-ups.

**EEG:** Normal background activity and no epileptiform patterns

Due to the COVID-19 pandemic, the patient failed to follow up and returned to our institute 2 years later. Fortunately, he became seizure-free after the adjustment of AEDs. Brain magnetic resonance imaging (MRI) was subsequently performed for further evaluation.

**Brain MRI:** Bilateral, symmetric, comma-shaped hypointense lesions in both mesial temporal lobes on T1- and T2-weighted images (Image 1)

The radiological aspects were pathognomonic of Urbach-Wiethe disease. On detailed interrogation, there was no history of cognitive dysfunction, visual impairment, photosensitivity, dysphagia, or respiratory obstruction. In a test of emotion recognition (Ekman faces), the patient performed 19 out of 35 (normal range: 23 to 33). His family history revealed the consanguineous marriage of his parents. None of the other family members were affected. Meticulous clinical examination revealed beaded papules around the eyelids (also pathognomonic), as well as areas of hyperkeratosis on the buccal and labial mucosa, with a nodular appearance. Atrophic scarring and skin thickening were noted over the elbows, dorsum of hands, and fingers (Image 2)

Given the history, dermatological and neuroimaging findings, the diagnosis of Urbach-Wiethe disease was made with further testing confirming a novel mutation (NM\_004425:exon7:c.733\_734del:p.C245fs) in the ECM1 gene. Subsequently, the patient was referred to a dermatologist and monitored by a multidisciplinary follow-up.