Axillary skin biopsy: Diagnostic for Lafora's disease

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Dear Editor,

A 19-year-old man presented with progressive myoclonus, generalized tonic-clonic seizures, and mental decline to Emam Reza Hospital, Kermanshah, Iran. His past history was remarkable for tonic-clonic seizures nine years earlier, initially during sleep, which finally culminated in progressive cognitive decline, forgetfulness, personality deterioration, strange behavior, and dissociated crying or smiling episodes in past year. He had no family history of seizures. Physical examinations were normal with no hepatosplenomegaly or skin lesions. Neurologic evaluation revealed partial cooperation and orientation, with occasional absurd behavior. Cerebellar, pyramidal, extra pyramidal, and peripheral nerve system evaluations were all normal. Routine blood, urine and magnetic resonance imaging (MRI) were normal. Biochemical tests demonstrated decreased levels of calcium, parathyroid hormone (PTH), and 1,25-dihydroxy vitamin D. Electroencephalography (EEG) evaluation revealed diffuse and non-localized multiple spikes with slow wave forms. Progressive myoclonus epilepsy with an onset in late childhood raised the suspicion of Lafora's disease (LD) in the neurologist. Although there were no skin lesions, a biopsy of the axillary skin was performed by a dermatologist. Periodic acid-Schiff stain (PAS) stain with diastasis was requested to detect Lafora's bodies (LBs). Microscopic examination of the hematoxylin and eosin stained sections of the axillary skin biopsy showed no obvious abnormalities. PAS with diastasis demonstrated round to oval intracytoplasmic PAS-positive, diastase-resistant inclusions within the acinar cells of the apocrine and eccrine glands, which was consistent with the diagnosis of LD. LD is an autosomal recessive progressive myoclonus epilepsy characterized by seizures, myoclonus, and dementia that leads to death in 5-10 years in most patients. Symptoms mostly begin during adolescence [1]. The neuropathology of LD is characterized by neurodegeneration due to progressive formation of LBs which are PAS-positive intracellular inclusion bodies with resistance to diastasis. They are composed of aggregates of many proteins and an abnormal form of glycogen without branching and spherical structure of normal glycogen, termed as polyglucosan [2]. LD is caused by mutations in one of two genes: epilepsy, progressive myoclonus type 2A (*EPM2A*) and epilepsy, progressive myoclonus type 2B (*EPM2B*), which code for laforin and malin, respectively [3]. Lack of these enzymes can impact glycogen metabolism and result in the formation of LBs [3-5]. In addition to LBs, a mild loss of granule and Purkinje cells, and loss of neurons in some of the basal ganglia and cerebral cortex may be present. In patients with LD, there are no abnormalities of the blood, CSF, or urine. Differential diagnosis should consider Unverricht-Lundborg disease, neuronal ceroid lipofuscinoses, sialidosis, myoclonic epilepsy with ragged red fibers (MERRF), subacute sclerosing panencephalitis (SSPE), and schizophrenia. Younger age at onset, slow disease progression,

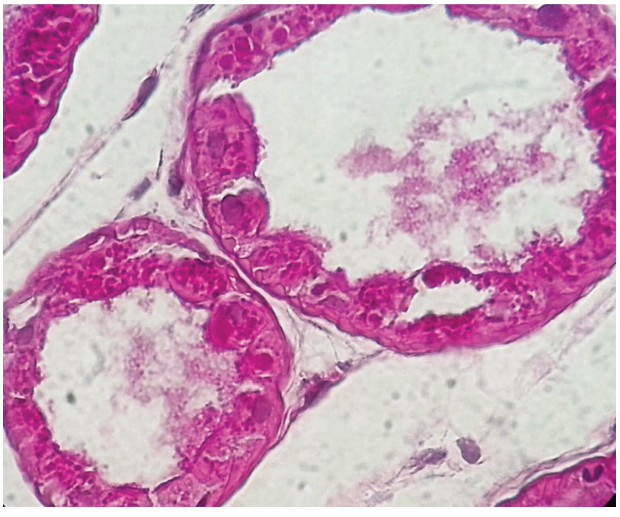

Figure 1. Periodic acid-Schiff (PAS) positive, diastase-resistant intracytoplasmic bodies in the axillary apocrine glands. (PAS; ×400)

and lack of LBs differentiate Unverricht-Lundborg disease from LD [6]. To rule out neuronal ceroid lipofuscinoses and sialodosis, electroretinography is useful. Lactate levels in the CSF can be helpful in determining the possibility of MERRF. For diagnosis of SSPE, titers of measles antibodies are useful. Visual hallucinations and cognitive decline without seizures and abnormal EEG differentiates schizophrenia from LD [6,7]. Despite advances in genetic and metabolic pathway studies, skin biopsy is a primary diagnostic method. Skin biopsy is more effective, easier and the least invasive method compared to biopsies from other involved tissues, such as the brain. Although LD is very rare, it can be easily distinguished from other differential diagnoses by a axillary skin biopsy that shows PAS-positive intracytoplasmic inclusion bodies (Figure 1).

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