Generalized dystonia and striatal calcifications with lipid proteinosis

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Abstract—Lipoid proteinosis (LP) is an autosomal recessive disease that typically presents with papular, verrucous, poxlike, or acneiform scars and lesions and hoarseness. LP was recently mapped to the 1q21 locus and has been shown to result from mutations in the extracellular matrix protein 1 gene (ECM1). Epilepsy, mental retardation, and hippocampal calcifications can occur. The authors describe a patient with generalized dystonia caused by striatal calcifications.

Lipoid proteinosis (LP; OMIM 247100) was described in 1929 by Urbach and Wiethe.1 It is autosomal recessive and is also known as hyalinosis cutis et mucosae because of the progressive deposition of hyaline-like material (glycoprotein) that occurs in the skin, mucosae, and other tissues.2 Approximately 250 cases have been reported.2

Typically, clinical manifestations first appear in early childhood with hoarseness, followed by poxlike and acneiform scars, along with infiltration and thickening of the skin and other mucous membranes.2 In many affected individuals, intracerebral calcifications (particularly involving the hippocampi) are present. Neurologic and psychiatric manifestations include epilepsy and memory deficits, social and behavioral changes, paranoid symptoms, mental retardation, and aggressiveness.2,7

LP was recently mapped to the 1q21 locus and has been shown to result from mutations in the extracellular matrix protein 1 gene (ECM1).6,7

In this report, we describe a patient with LP who had skin lesions, mental retardation, and intracerebral calcifications—all typical for the disease—but in whom there was also severe generalized dystonia, a previously unrecognized and unreported clinical manifestation of LP.

Case report. A 24-year-old man was evaluated for mental retardation and dystonia. He was the product of an unremarkable full-term pregnancy, and there was no history of consanguinity. The patient was asymptomatic until age 2 years, at which time he developed hoarseness and yellowish skin papules over the body. Psychomotor and mental retardation was evident by age 6 years. Hoarseness worsened, and the patient became unable to speak during his teens. Bilateral foot dystonia then began in an ascending way, with axial, upper limb, oromandibular, and cervical compromise (anterocollis). Biperiden, 16 mg/d, and diazepam, 10 mg/d, were given with a slight response, but the dystonia progressed, and the patient became disabled and dependent on a caregiver.

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in exon 7, which is spliced out in the ECM1b isoform, can result in a slightly less severe skin and respiratory tract phenotype, but specific correlation between genotype and phenotype for neurologic manifestations has not been found.7

Epilepsy, particularly temporal lobe epilepsy, has been described as a common manifestation of LP. Our patient had no seizure history and a nonepileptiform EEG. The patient’s sister had epilepsy and hippocampal calcifications; her brain imaging study (CT scan) did not reveal the presence of striatal calcifications, unlike the findings described in our patient.

Bilateral temporal lobe calcifications within the amygdala, periamygdaline gyrus, and anterior and anteroposterior temporal horn may appear in up to 75% of the patients. These imaging patterns are highly suggestive of LP.3-5 Autopsy material shows dense amorphous masses of calcium and bone and multiple, haphazardly arranged small blood vessels with calcified walls and gliotic adjacent tissue. The cortex and white matter show isolated blood vessels completely occluded by fibrin, partial calcification, small perivascular areas of infarction, and demyelination.4

Mental retardation and memory deficits may be seen in patients with LP. Amnestic syndromes seem to be related to hippocampal calcifications.5 Our patient had severe mental retardation; thus, formal memory testing did not apply.

Our case is classified as heredodegenerative dystonia, with childhood onset and generalized dystonia. There is no evidence of primary and secondary dystonia or dystonia-plus syndromes. In the group of autosomal recessive heredodegenerative dystonias, other diseases could be considered, such as familial basal ganglia calcifications and mitochondrial encephalopathies, but their clinical picture is rather different. Finally, Fahr disease, hypoparathyroidism, and pseudohypoparathyroidism could be hypothetically considered in the differential diagnosis; however, we believe in our case they were efficiently ruled out by complementary tests as demonstrated.10

Our patient also has the unique clinical feature of dystonia and unreported imaging findings of bilateral symmetric striatal calcifications. These observations extend the possible clinicopathologic abnormalities that may occur in this inherited disorder and demonstrate that LP should be remembered as a possible cause of dystonia.

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References

Figure 1. Axial brain CT showing symmetric mesial temporal lobe (hippocampal) calcifications.

Figure 2. Axial brain CT showing symmetric striatal calcifications.
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