GENETIC CREUTZFELDT-JAKOB DISEASE MIMICKING CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

Creutzfeldt-Jakob disease (CJD) is a relentlessly progressive neurodegenerative disorder, belonging to the transmissible spongiform encephalopathies. It is characterized by the deposition of the abnormal isoform of the prion protein (PrPsc), causing spongiform neurodegeneration. The disease is classically known to mainly affect the gray matter of the CNS. However, involvement of the peripheral nervous system (PNS) has been described.1–3 Herein, we describe a patient with genetic CJD, in whom the disease presentation was a demyelinating neuropathy reminiscent of chronic inflammatory demyelinating polyneuropathy (CIDP).

Case report. A 55-year-old man with a history of psoriasis was seen at our center because of progressive numbness and paresthesias in his feet, accompanied by gait difficulties since 2 months. A few weeks earlier, he was diagnosed and treated for a suspected Guillain-Barré syndrome in another hospital. He was referred to our center because of disease progression, despite an initial favorable response to IV immunoglobulins. On neurologic examination, evidence of a sensory ataxic neuropathy with distal sensory deficits, diminished deep tendon reflexes in the lower limbs, sensory ataxia, and an unsteady gait were found. Nerve conduction studies confirmed the presence of an inhomogeneous demyelinating neuropathy, with conduction blocks, temporal dispersion, prolonged terminal latencies, reduced conduction velocities, and prolonged F-wave latencies, and were therefore suggestive of a diagnosis of CIDP (figure, A). He fulfilled the European Federation of Neurological Societies criteria of definite CIDP. On lumbar puncture, we found an albuminocytologic dissociation (albumin 1,830 mg/L; normal range 139–246 mg/L). Infectious and paraneoplastic causes were excluded. Anti-GM2 antibodies (titer 1/2,000) were present. We administered further treatment with IV immunoglobulins every 6 weeks, but no significant response to this treatment was observed. Therefore, a trial with oral corticosteroids was initiated. However, his condition quickly worsened, and 8 months after the initial CIDP-like presentation, he clearly developed cognitive problems, together with a further worsening of the gait difficulties. Mini-Mental State Examination score was 23/30, cerebellar ataxia in the limbs was noted together with hyperreflexia in the upper limbs and increased muscle tone in the 4 limbs. In the following month, Mini-Mental State Examination score decreased to 18/30, after which the patient became bedridden and apathic. Consecutive MRI of the brain showed bilateral diffusion-weighted and fluid-attenuated inversion recovery imaging hyperintensities in the medial thalamus and basal ganglia (figure, B).4 Several EEGs showed diffuse slowing, but no periodic discharges were found. Protein 14-3-3 in CSF was negative, but total tau levels were clearly elevated (>1,200 pg/mL, upper limit of normal 367 pg/mL). The patient died of pneumonia 11 months after the onset of symptoms. In the neocortical and subcortical regions, we observed various degrees of spongiform change (figure, C). Immunostaining for PrP (antibody 12F10) revealed prominent synaptic (figure, C) and perineuronal immunoreactivity for the disease-associated PrP. In addition, peculiar intraneuronal globular immunoreactivity (figure, D) was observed in the deeper layers of the neocortex and in the brainstem neurons; this immunomorphology was strongly suggestive of a genetic etiology. Indeed, genetic analysis revealed a p.Glu200Lys mutation in the PRNP gene on chromosome 20, which is a frequently found pathogenic mutation in patients with CJD. Unfortunately, no peripheral nerve tissue was available for examination.

Discussion. Our findings support the notion that CJD can present as a subacute demyelinating neuropathy and underscores the idea that PNS involvement is an integral part of CJD in a subset of patients. Although a manifest axonal or demyelinating peripheral neuropathy is rare in CJD (up to 15% of E200K genetic CJD cases),2,4,5–7 subclinical PNS involvement can be documented using nerve conduction studies in patients with sporadic CJD.1 Axonal sensorimotor polyneuropathy and CIDP-like neuropathy have been described as presenting...
symptoms in cases with sporadic CJD.\(^3\)\(^5\) We expand these findings by reporting a genetic CJD presenting with a CIDP-like phenotype 8 months before overt CNS involvement. This suggests that Schwann cells and peripheral nerve cells are also vulnerable to prion-induced damage.

CJD should be considered as rare CIDP mimic in patients with fast disease progression and lack of response to immunotherapy and particularly if additional symptoms suggesting CNS involvement appear.

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