Phe 84 deletion of the PMP22 gene associated with hereditary motor and sensory neuropathy HMSN III with multiple cranial neuropathy: clinical, neurophysiological and magnetic resonance imaging findings

Introduction

Hereditary motor and sensory neuropathy (HMSN) comprises a heterogeneous group of peripheral neuropathies which are diagnosed on the basis of clinical, electrophysiological and neuropathological findings. HMSN III (Dejerine-Sottas disease, DSD) is a hypertrophic and demyelinating neuropathy with markedly reduced nerve conduction velocity (NCV), early onset and variable mode of inheritance. It is usually due to de novo mutations in genes such as that for peripheral myelin protein 22 (PMP22) or P0 [1, 2]. More recently the occurrence of a recessive transmission of a mutation in the PMP22 gene has been demonstrated in a Turkish family of DSD [3]. While peripheral nerve hypertrophy is essential in the diagnosis of HMSN, cranial nerve hypertrophy or neuropathy is very rarely seen [4, 5]. Here we present a genetically confirmed sporadic case of DSD with multiple cranial nerve hypertrophy shown by cranial magnetic resonance imaging (MRI).

Case report

A 19-year-old Turkish man was hospitalized complaining of unsteadiness, walking difficulty and deformity of the feet. His complaints had begun at the age of 2 years when he started to walk awkwardly, with thinning of the distal parts of legs, stepping on the sides of his feet. He was operated on in 1992 for his feet deformity when he was 15 years old. He was diagnosed as having DSD. Investigations at that time included slow motor and sensory NCV less than 4 m/s. Sural nerve biopsy revealed hypertrophic neuropathy findings: demyelinated and remyelinated axons were with onion-bulb formation, a
decrease in myelinated fibrils, an increase in intrafascicular area, a proliferation in Schwann cells, and an increase in fibroblasts. On the reticulin stain nerve fibres were decreased. CSF contained a high level of protein (400 mg/dl), with no cells. He was admitted to our clinic in 1996 for worsening of his gait and ataxia. On admission he was mentally well and was able to work full time in a private laboratory as a technician despite his ataxia.

Neurological examination found muscle atrophy of his legs, forearms and hands with clubfoot deformity. He had no cutaneous lesions such as café-au-lait. Bilateral oral and orbicular muscles seemed mildly atrophic with thick-lipped appearance. All other cranial nerve findings were unremarkable. Funduscopic examination and audiometry were normal. Deep tendon reflexes were absent. The distal parts of all extremities showed sensory disturbances of all modalities. Hypertrophy of small cutaneous nerve trunks was noted, such as the great auricular nerve, was palpable. He had decreased muscle strength on the distal parts of extremities, a positive Romberg sign, and an ataxic gait. His laboratory investigations including blood count, erythrocyte sedimentation rate, creatine kinase, serum immune globulins, thyroid function tests, serum ASO, C-reactive protein, rheumatoid factor, antinuclear antibodies, serological tests for brucellosis, syphilis and HIV were normal.

Electromyography showed denervation activity in distal muscles of extremities, extremely slow sensory and motor NCV of median and ulnar nerves, less than 4 m/s, with no sural nerve response. Facial NCV was also slow with velocity of 25 m/s with very late blink responses. Somatosensory evoked potentials could not be obtained, brainstem auditory evoked potential (BAEP) responses showed abnormality at the cochlear/auditory nerve level.

Cranial MRI revealed symmetric hypertrophy of the oculomotor, trigeminal, facial, vestibulocochlear and hypoglossal cranial nerves (Fig. 1). Bilaterally, Meckel caves and cavernous sinuses were enlarged with smooth margins and had isointense signal with grey matter on