

SWALLOWING DYSFUNCTION IN HEREDITARY NEUROPATHY WITH LIABILITY TO PRESSURE PALSIES

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Hereditary neuropathy with liability to pressure palsies (HNPP) is an autosomal dominant peripheral neuropathy characterized by recurrent episodes of paralysis of peripheral nerves, usually after a minor trauma to topographies prone to compression^{1,2}. Involvement of the cranial nerves has rarely been described in these patients³⁻⁸. Reports of swallowing dysfunction in patients with HNPP are even rarer.

We report a patient diagnosed with HNPP confirmed by molecular testing who presented with recurrent episodes of swallowing dysfunction (SD).

CASE

A 41-year-old man who presented with recurrent episodes of acute mononeuropathies affecting mainly the ulnar, radial and peroneal nerves followed by spontaneous improvement since the age of 12 years. In the years prior to diagnosis, the patient started experiencing sudden episodes of reversible SD without a specific trigger, but it worsening with progressive increased of volume and solid consistency of bolus food. The SD had a spontaneous improvement after few weeks, but with residual dysfunction when he drinking liquid. Some of his relatives (sisters and nephew) had similar symptoms, but none had SD. He denied episodes of aspiration (airway protection), exposure to drugs or toxic agents.

Cranial nerves showed mild weakness in posterior tongue during the swallow. Gag reflex, taste and sensation of tongue and oropharynx were normal. Mild asymmetrical muscle atrophy was observed in both hands and forearms while weakness was detected in the left first dorsal interosseus dorsal and flexor carpi ulnaris (grades 3 and 4, respectively, according to the Medical Research Council scale). Tendon reflexes were absent in both biceps and left brachioradial and ankle tendon reflexes were also absent. Pain, pinprick and light touch sensory impairment were detected on the territories of the left median, bilateral sural and superficial peroneal nerves.

Nerve conduction studies showed a nonuniform demyelinating neuropathy, mainly the ulnar, radial and peroneal nerves, together with evidence of asymmetrical acute and/or chronic denervation affecting predominantly the first dorsal interosseus, tibialis anterior and gastrocnemius muscles. Nerve conduction studies with similar findings were observed in the patient's sisters and nephew.

Laboratory tests as well as serological tests were normal. Biopsy of the sural nerve showed a reduction in the number of large myelinated fibers and focal thickening of the myelin sheath (formation of tomaculae). Biopsy of the gastrocnemius muscle biopsy showed recent and chronic denervation.

Phonoaudiological evaluation, videoendoscopic and fluoroscopic examination of deglutition revealed normal oral (preparatory and transport) phase; swallowing test (liquid, semisolid and solid consistencies) presented mild nasal escape, normal oral transit time, residual bolus in pyriform sinuses and valleculae cleared by dry swallow and cough, episodes of laryngeal penetration only after great volume of liquid, but with normal coughing reflex, and absence of aspiration or choking; asymmetrical stasis of the bolus (liquid consistency) in the pyriform sinuses and valleculae in the pharyngeal phase of swallowing with a decrease in pharyngeal constriction; penetration in airway remains above vocal folds with normal coughing reflex and no aspiration. Barium esophagography revealed symmetrical muscular hypotonia and hypomotility of the esophagus and bilateral asymmetrical pharyngeal stasis of the barium bolus in the pyriform sinuses and valleculae (Figure).

Cranial magnetic resonance imaging, abdominal ultrasonography and esophagogastroduodenoscopy were normal.

After informed consent was obtained, molecular genetic testing revealed deletion of the 17p11.2 region, which encompasses the *PMP22* gene, consistent with the diagnosis of autosomal dominant HNPP.

A diagnosis of HNPP associated with SD (pharyngeal and esophageal) was made on the basis of molecular, endoscopic

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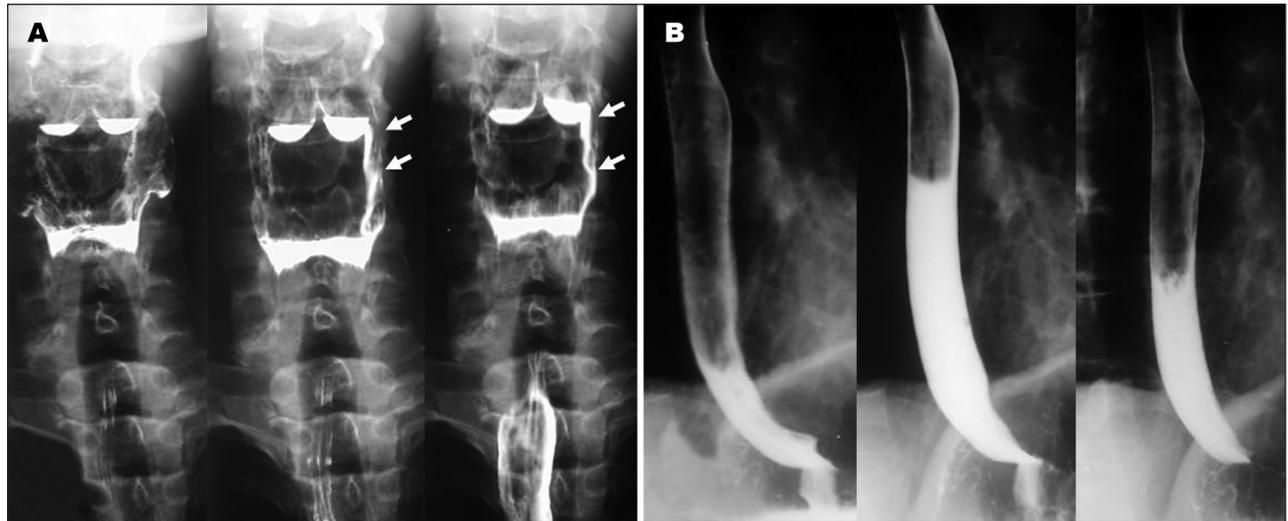


Figure. Barium esophagography showing diffuse symmetrical muscular hypotonia and hypomotility of the esophagus in cervical (A) and thoracic (B) segments. Also, bilateral pharyngeal stasis of the barium bolus in bilateral the pyriform sinuses and valleculae (A), mainly on the left side (arrows).

and radiological findings. During the follow-up period, the patient continued to have acute recurrent episodes of mononeuropathies and SD.

DISCUSSION

HNPP is an uncommon hereditary neuropathy with an estimated prevalence of at least 16/100,000 people⁹. The disease is usually caused by a heterozygous 1.5-megabase deletion of the *PMP22* gene on chromosome 17p11.2, but several point mutations associated with HNPP have been reported^{10,11}. The onset is around the second or third decade of life and 15% of carriers remain asymptomatic². Carriers are predisposed to focal neuropathies that most frequently involve the brachial plexus and peroneal, ulnar, radial, and median nerves^{5,12}. Several authors have reported involvement of the facial, trigeminal, hypoglossal and recurrent laryngeal nerves³⁻⁸. The attacks usually stop within days or weeks and are triggered by compression, slight traction or other minor trauma^{1,12}.

The electrophysiological pattern in patients with HNPP consists of prolonged distal motor latencies in some nerves, multiple conduction slowing at compression sites and only mildly reduced conduction velocities in other segments of the motor nerves^{11,13}. There is also a diffuse reduction in sensory nerve action potential amplitudes^{11,13}. Asymptomatic carriers frequently have prolonged distal motor latencies and abnormal results in sensory conduction studies¹².

The mechanism of this susceptibility to compression is unknown. Distal myelinopathy or a simple length-dependent process can not explain the abnormal electrophysiological findings of HNPP¹⁴. The typical pathologic finding in nerve biopsies is a focal sausage-shaped thickening of

the myelin sheath in about 25% or more of the internodes, referred to as 'tomaculae'^{15,16}. This finding however is not specific to HNPP and can occur in Charcot-Marie-Tooth disease and acquired neuropathies¹⁶.

SD are frequent in neurological diseases and may arise from pharyngeal or esophageal dysphagia¹⁷. Deficits of the lower cranial nerves (nerves IX, X, XI and XII) may cause disabling SD³. Pharyngeal dysphagia has previously been reported in HNPP, mainly related to a transient hypoglossal mononeuropathy or associated with recurrent laryngeal nerve palsy^{3,6,8}. Winter and Juel reported an HNPP patient with evident hypoglossal nerve palsy which could partially explain the pharyngeal dysfunction in our patient⁸. The weakness in the tongue during swallowing, caused by hypoglossal neuropathy could result in pharyngeal dysfunction with stasis in the pyriform sinuses and valleculae^{3,8}.

Esophageal dysphagia may be caused by mechanical lesions or motility disorders¹⁷. Our patient presented with an esophageal motility dysfunction, and other causes, such as drugs, achalasia, diffuse esophageal spasm, diabetes mellitus, Chagas' disease and scleroderma were all excluded.

To our knowledge esophageal dysphagia in HNPP has not previously been reported, but in bovine tomaculous neuropathy it has been attributed to bilateral vagus nerve degeneration, with nerve lesions similar to those seen in tomaculous neuropathy in humans¹⁸. We suggest that HNPP should be considered in the differential diagnosis of patients with atypical swallowing dysfunction.

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