Porphyric neuropathy: a clinical, neurophysiological and morphological study

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A case of neuropathy in the course of an attack of acute intermittent porphyria was studied from the neurophysiological and morphological points of view. The neurophysiological findings (acute neuropathy with almost complete denervation despite normal or slightly reduced conduction velocity) and the morphological findings (no segmental demyelination after teasing, conservation of the linear fiber diameter/internodal distance ratio, mainly axonal damage on ultrastructural study) seem to indicate that the disease process is chiefly an axonal neuropathy.

Key-Words: Porphyria — neuropathy

Introduction

Acute intermittent porphyria (AIP) is a genetic disorder of the porphyrin metabolism characterized by urinary overexcretion of the precursors of porphyrins (delta-aminolevulinic acid and porphobilinogen) both in the course of attacks and during the symptom-free periods. It manifests clinically by impairment of the nervous system, both central and peripheral, especially the latter. Although the underlying biochemical anomaly (deficiency of uroporphyrinogen-1-synthetase) is now known, there is still uncertainty about the mechanism of the nervous involvement. Nor is there complete agreement on the type of anatomical lesion underlying porphyric neuropathy. A recent case of neuropathy in a patient with AIP enabled us to investigate this controversial point.

Case report

A 54-year-old man with no relevant family history and a personal history of hypertension treated with diuretics (chlorthalidone) since the age of 48 began to complain of violent and continuous abdominal pain in the absence of precipitating factors. 13 days after the onset of these pains the patient noted weakness of the upper limbs, especially of the shoulder girdle, and later of the lower limbs. Walking became impossible. 18 days later he became restless and sleepless and complained of pains and paresthesias in all four limbs and over the trunk. On admission he was in poor health, having lost 15 kg, and was anxious and distressed. AP was 180/120 mmHg and heart rate 120/min. Neurological examination showed moderate dysphonia, severe and diffuse amyotrophy affecting mainly the shoulder girdle and loss of strength commensurate with the amyotrophy. The deep reflexes were abolished in the upper limbs but spared in the lower limbs. Superficial sensation was reduced on the trunk and thighs according to a pattern reminiscent of “Long John’s distribution” described by Ridley [14]. Laboratory tests confirmed the diagnosis of AIP: the urinary excretion of porphobilinogen, measured on several consecutive days, was 12-15 mg/24h.
Fig. 1. Relationship between fiber diameter and intranodal length (50 fibers).

Fig. 2. Semithin section showing a marked reduction in number of myelinated fibers of all sizes (100 x).

(NV<2 mg/24h), of delta-aminolevulinic acid 3.2-4.5 mg/24h (NV<0.54 mg/24h) and of uroporphyrins 640-122 µg (NV<20 µg). The coproporphyrins were increased in the urine: 105-120 µg (NV<5 µg) but not in the feces: 820-950 µg (NV 400-1000 µg). This finding is important because it rules out other types of porphyria: hereditary coproporphyria and mixed or variate porphyria, in which the fecal excretion is increased [15]. The clinical course was favorable: pain, restlessness and insomnia ceased two days after the beginning of treatment with perfusions of hypertonic glucose (240 g/24h) and general health improved. The regression of the sensory and motor symptoms was much slower but at follow-up a year later recovery was complete.

Neurophysiological data. The first EMG (one month after onset of the disease) showed severe denervation in the deltoid and quadriceps on the right, less severe denervation in the tibialis anterior and extensor digitorum brevis. Motor conduction velocity (MCV) was 47 m/sec on the ulnar nerve, 48 m/sec on the common peroneal nerve. Two months later EMG confirmed the severe neurogenic impairment of the above muscles and some slowing of the NCV: 40 m/sec on the ulnar and 33 m/sec on the common peroneal nerve. The orthodromic NCV of the right sural nerve (biopsied 4 days later) was 56.2 m/sec.