Chapter 4
Porphyria

S. Jann, D. Facchetti, and I. Costi

The porphyrias are a group of metabolic diseases caused by an enzyme defect involved in heme biosynthesis which is the main product of porphyrin metabolism.

In addition to hemoglobin and myoglobin, heme is a metalloprotein integrated in microsomal cytochrome P450 in the liver and is involved in the transport chain of mitochondria electrons. It participates in the metabolism of many substances and drugs, some of which can trigger porphyria attacks [1].

The reduction of heme concentration leads to activation of δ-aminolevulinic acid (ALA) synthetase enzyme, which increases the metabolic pathway of porphyrins. The induction of cytochrome P450 by some substances, such as barbiturates, alcohol, or the reduced supply of carbohydrates, determines a stimulation of ALA synthetase.

The accumulation of precursors of the heme metabolism, ALA and porphyrins, and the reduction of the heme synthesis itself are responsible for the porphyrias, some of which are

S. Jann (✉) • D. Facchetti • I. Costi
Department of Neurology and Stroke Unit, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy
e-mail: stefano.jann@ospedaleniguarda.it

E. Agostoni (ed.), *Emergencies in Neuromuscular Disease*, Emergency Management in Neurology,
DOI 10.1007/978-3-319-56654-2_4

characterized by neuropathies.Acute neuropathy during a porphyria attack is usually secondary to delays in diagnosis and therefore in the treatment of acute attacks. Neuropathy usually occurs after several attacks which are characterized by unexplained abdominal pain, nausea and vomiting, emission of dark urine, possible episodes of psychomotor agitation, possible seizures, and frequent bullous skin lesions.

This neuropathy is predominantly motor and mostly axonal, with rapid onset. It predominantly affects the proximal limb muscles and can worsens up to a complete tetraplegia with dysphagia and respiratory failure.

It is associated with autonomic neuropathy, which is responsible for abdominal pain, constipation, and pseudo-obstruction as well as tachycardia and orthostatic hypotension. There are seldom sphincter disorders. The mechanism of the neuropathy is not known but appears to be associated with a neurotoxicity of accumulated precursors or with a disorder of the fast axonal transport which is heavily energy dependent [2].

There are three forms of porphyria of neurological interest: they can be differentiated by the different enzyme deficiency involved and are transmitted through an autosomal dominant disorder. They are acute intermittent porphyria, hereditary coproporphyria, and variegate porphyria. These are called acute porphyrias and are characterized by acute attacks with the characteristics mentioned above, alternated by periods of quiescence.

The attacks are usually triggered by drugs (mainly cytochrome P450 inductors), alcohol, and fasting. Attack prevention is therefore linked to the removal of these risk factors, but acute attack management involves the administration of glucose and intravenous hematine.

The diagnosis involves dosage of urinary porphobilinogen.

The characteristics of the electrodiagnostic study are those of an axonopathy, reduced amplitude of motor potential compounds (AMPC), motor conduction velocity preserved or slightly reduced (CV), and normal distal latency of CMAP [1].

Conduction blocks or time dispersion is usually absent. If present, F waves and H reflex have normal latencies [2]. The sensory action potentials (SAP) and sensitive CV can be preserved even in nerves with marked motor involvement.

Electromyographic examination with needle concentric electrode (EMG) in the initial stages shows only a reduction in the recruitment of motor units, which are activated at high frequency. This reduction is proportional to loss of strength.

The signs of active denervation characterized by abundant fibrillation activities appear after approximately 3 weeks. They start from the proximal muscles and often display a patchy distribution of affected and spared muscles. In the recovery phase short, polyphasic, low-amplitude rising potentials may be recorded.

In the acute phase, potentials in the proximal muscles are reported as having reduced amplitude and duration and as being quickly recruited. These features, together with the presence of fibrillation and positive slow waves, may be confused with a myopathic picture (1). Electromyographic studies after clinical recovery may show findings of a residual chronic subclinical neuropathy.

Acute neuropathy during a porphyria attack needs the same attention and multidisciplinary management that is used for other acute neuropathies, such as GBS. It is not rare to find that some patients who have been diagnosed with Guillain-Barre syndrome actually suffer from porphyria neuropathy. Where necessary, admission to an ICU is required.

The neuropathy should be treated with i.v. heme arginate as soon as possible because although this does not improve the previous nerve damage, it prevents further damage. A daily infusion of 3 mg/kg is initially required and must therefore be reduced in both dose and frequency in accordance with clinical improvement.

References

1. Albers JW, Fink JK (2004) Porphyric neuropathy. Muscle Nerve 30:410–422
2. Lin CSY, Krishnan AV, Lee MJ, Zagami AS, You HL, Yang CC et al (2008) Nerve function and dysfunction in acute intermittent porphyria. Brain 131:2510–2519