Neurological complications of porphyria

Saroj Gupta, Sunil Dolwani

A 20-year-old girl presented with a three-year history of recurrent colicky abdominal pain associated with the passage of reddish urine. During the past three months she had also noticed progressive weakness and wasting of her right hand and forearm. There were no sensory symptoms. There was no history of photosensitivity or any skin changes. On examination she had wasting of the small muscles of the hand, predominantly on the right side (figure 1). Deep tendon reflexes were diminished in the upper limbs but normal in the lower limbs. Plantar reflexes were bilaterally flexor and there was no sensory, cranial nerve or cerebellar involvement. All routine investigations including biochemical tests of thyroid function were normal. Ehrlich's test for porphobilinogen in urine was repeatedly positive. A clinical diagnosis of acute intermittent porphyria was confirmed by further laboratory tests. Electrophysiological studies revealed bilateral median nerve axonal neuropathy. She was appropriately treated and discharged with advice to take certain precautions.

Seven months later she was re-admitted with additional features of increase in the weakness and wasting of the left hand, brisk deep tendon reflexes in the lower limbs and bilateral consistently extensor plantar reflexes. X-Rays of the cervical spine and CV junction as well as magnetic resonance imaging (MRI) of the cervical spine (figure 2) were normal. Her third admission a month later was with the presenting features of hoarseness, nasal regurgitation and dysphagia along with abdominal pain and reddish urine. Her blood pressure was 150/100 mmHg with a drop to 130/80 mmHg on standing. On neurological examination she had a bilateral 9th and 10th cranial nerve palsy which resolved completely over the next 10 days.

Figure 1 Marked wasting of the hands

Figure 2 MRI of cervical spine

Department of
Internal Medicine,
Lady Hardinge
Medical College &
associated SK
Hospital, New Delhi,
India
S Gupta
S Dolwani

Correspondence to Dr Saroj
Gupta, P-41 NDSE Part II,
Ring Road, New Delhi-
110049, India

Accepted 3 October 1995

Questions

- 1 What is the diagnosis and how would you confirm it?
- 2 What are the neurological manifestations of this disorder?
- 3 What is the treatment indicated and the long-term outcome?
- 4 What precautions do these patients have to take?
- 5 List two other conditions which could present with similar neurological manifestations?

Answers

QUESTION 1

Motor neuropathy in porphyria. Delta-amino-laevulinic acid (ALA) and porphobilinogen levels are increased in plasma and urine during acute attacks. Urinary porphobilinogen levels are usually 220–880 $\mu\text{mol/day}$ (normal 0–18 $\mu\text{mol/day}$), and urinary delta-amino-laevulinic acid is 150–760 $\mu\text{mol/day}$ (normal 8–53 $\mu\text{mol/day}$). The excretion of these compounds generally decreases with clinical improvement, particularly after haematin infusions. A normal urinary porphobilinogen during an acute attack effectively rules out acute intermittent porphyria. Faecal porphyrins are usually normal or minimally increased in acute intermittent porphyria in contrast to hereditary coproporphyria and variegate porphyria. The enzyme deficiency of hydroxymethylbilane synthase is detectable in erythrocytes from most acute intermittent porphyria heterozygotes and is a useful screening test for family members.

QUESTION 2

The neurological manifestations of the disorder are given in box 1.

QUESTION 3

During acute attacks narcotic analgesics may be required for abdominal pain and phenothiazines for nausea, vomiting, anxiety and restlessness. Chloral hydrate can be given safely for insomnia. Intravenous glucose (at least 300 g daily) ameliorates the acute attacks. Intravenous haem 3–4 mg/day in the form of haematin, haemalbumin or haem arginate is more effective than glucose in reducing porphyrin precursor excretion and leads to more rapid recovery. This is infused daily for four days beginning as soon as possible after the onset of the attack. Clonazepam is safer than phenytoin or barbiturates for seizures. Recovery from the acute attack is rapid with prompt therapy. In general, the prognosis for ultimate recovery from neuropathy is excellent although it may sometimes take up to two years. Relapse of the porphyria may result in further involvement of the peripheral nervous system (relapsing polyneuropathy).

Neurological manifestations of motor neuropathy in porphyria

- cranial neuropathy (predominantly lower cranial nerves)
- peripheral neuropathy (predominantly motor)
- autonomic neuropathy (cardiovascular, bladder, bowel)
- sensory loss over the trunk
- neuropsychiatric manifestations (anxiety, depression, insomnia, disorientation, hallucinations, paranoia)
- seizures, due to direct neurological involvement or hyponatraemia
- rarely: cerebellar involvement, basal ganglion involvement, pyramidal tract involvement

Box 1

Known precipitating factors

- low calorie diets
- porphyrinogenic drugs (including anaesthetic agents)
- gonadal steroids (endogenous and exogenous)
- infections

Box 2

QUESTION 4

Patients should identify and avoid those agents known to precipitate an attack (box 2).

QUESTION 5

A neurological presentation with lower motor neuron signs in the upper limbs and upper motor neuron signs in the lower limbs may also be found in cervical spinal cord compression and in amyotrophic lateral sclerosis (motor neuron disease). In our patient, however, these are ruled out by the normal MRI scan and the findings on electrophysiology. Pyramidal tract signs are very rare in porphyria.

Final diagnosis

Motor neuropathy in porphyria.

Keywords: porphyria, neurological disorders

1 Berman S. Neurologic disorders in porphyria. A brief clinical survey of 81 cases. Proceedings of the VII International Congress in Neurology, Rome, 1961; p 33.

2 Goldberg A, Moore MR, McColl KEL, Brodie MJ. Porphyrin metabolism and porphyrias. In: Weatherall DJ, Ledingham JGG, Warrell DA, eds. *Oxford textbook of medicine*, Vol 1, 2nd edn, ELBS/Oxford University Press, 1987; p9.136–45.

3 Weller R, Cervos-Navarro J. *Pathology of peripheral nerves*. London: Butterworths, 1977.

4 Asbury AK, Johnson PC. *Pathology of peripheral nerve*. Philadelphia: Saunders, 1978.

5 Walton J. *Brain's diseases of the nervous system*. 9th edn, ELBS, 1985; p449.

6 Hierons R. Changes in the nervous system in acute porphyria. *Brain*, 1957; 80: 176.