Acute intermittent porphyria and epilepsy

R. BIAGINI, R. TIGNANI, A. R. FIFI, AND L. NAPPINI
Divisone Pediatria, Ente Ospedaliero di Arezzo, Italy

SUMMARY A 14-year-old boy had suffered from intermittent acute hepatic porphyria, myoclonic convulsions, and mental retardation (Lennox-Gastaut syndrome). The porphyria was treated by stopping the administration of phenobarbitone and phenytoin. Sodium valproate at a dose of 70 mg/kg per day lessened the severity and frequency of convulsive crises.

Acute intermittent porphyria (AIP) is rare in children, but is not unknown. In a survey of reports on such children, Barclay (1974) found 37 cases but these were not all fully documented. In our opinion the age of the patient is of particular interest as is the association of AIP with epilepsy. The only 4 cases of hepatic metabolic disorder of porphyrins to have been fully described in infants associated with epilepsy are 3 of hereditary coproporphyria (Birchfield and Cowger, 1966; Haeger-Aronsen et al., 1968; Houston et al., 1977) and one of hepatic porphyria not better identified (Houston et al., 1977).

Case report

A 14-year-old boy (born 4.12.1963) was the second child in an otherwise apparently healthy family with two other children. However, when examined his 39-year-old mother was found to have latent AIP.

During early infancy our patient had been moderately retarded in his psychomotor development, especially walking and speech. At 3 years he had generalised convulsions; during the chronic phase these mainly affected the right side. He was put on a course of phenobarbitone and phenytoin, or one of these, and although this treatment was changed and reassessed periodically, his condition did not improve. The length and frequency of the attacks increased and there was concurrent and progressive slowing down of his psychomotor development and learning ability, until at age 5, his IQ was 75. Because of his mental retardation and the fact that his repeated convulsive crises did not respond to drugs, he was sent to an institution and by age 11 his IQ was at a 5-year level.

Before coming to our attention, this child had three times been admitted to surgical departments with acute abdominal symptoms and constipation.

At age 13 he was admitted to a medical department with bronchopneumonia and underwent haemodialysis for anuria. Then, for the first time, in addition to the generalised convulsions, petit mal crises of variable length were recorded. The first was noted on the 14th day after admission. From the EEG findings, the neuropsychiatrist interpreted the neurological symptoms as Lennox-Gastaut syndrome. When the anuria ceased, despite the fact that the boy's urine was dark brown, no further diagnosis of AIP was registered.

We first saw this child in 1977 when he was aged 14. He had been admitted for clinical observation because of renewed episodes of abdominal pains and constipation. At that time there was a clinical picture of an acute attack of AIP.

We stopped those drugs which are now known to provoke acute crises of AIP and were able to reduce the number of seizures and ameliorate the acute clinical symptoms. By giving him sodium valproate alone (70 mg/kg per day) we have been able to reduce the frequency, duration, and gravity of the fits. With this diminution of fits and, subsequently, almost complete elimination of such crises, the patient's mental condition has improved.

Table 1 Urinary porphyrins and precursors and uroporphyrinogen-1-synthetase enzyme activities in erythrocytes

<table>
<thead>
<tr>
<th>Urinary porphyrins and precursors</th>
<th>Uroporphyrinogen-1-synthetase enzyme activities in erythrocytes</th>
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<tbody>
<tr>
<td></td>
<td>ALA (mg/24h)</td>
</tr>
<tr>
<td>Propositus</td>
<td>14</td>
</tr>
<tr>
<td>Mother</td>
<td>38</td>
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ALA = 5-Aminolaevulinic acid normal less than 3.5 mg/24h. PBG = porphobilinogen normal 0µg/24h. URO = uroporphyrin normal 0-30 µg/24h. COPRO = coproporphyrins normal: male 130-248 µg/24h, female 92-176 µg/24h. Uroporphyrinogen-1-synthetase enzyme activities in erythrocytes, normal 220-380 pmol/mg URO per mg protein per hour.
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Discussion

The following points are of interest. (1) The mental handicap in our patient was the same as that described in 3 of 5 other cases (Birchfield and Cowger, 1966; Houston et al., 1977). (2) There is a continuous need to adjust the treatment. (3) The severity of the epilepsy was such that the paroxysmal activity was 2.5 Hz on the EEG, suggesting a seizure disorder such as the Lennox-Gastaut syndrome. The epilepsy was equal in severity to the other cases (Birchfield and Cowger, 1966; Houston et al., 1977). (4) The symptoms became much less when barbiturates and phenytoin were stopped and sodium valproate given alone at a dose of 70 mg/kg per day.

We, therefore, believe that our case lends further support to the claim of Houston et al. (1977) that there is a correlation between epilepsy and acute porphyria. In fact, the failure to diagnose AIP early and the unsuccessful anticonvulsive therapy probably hastened the acute crises which were attributed to AIP only in retrospect.

Table 1 gives the amounts of urinary porphyrins and precursors and uroporphyrinogen-1-synthetase enzyme activities in erythrocytes found both in the patient and in the mother on which the diagnosis is based (using the method of Grandchamp et al., 1976).

Table 2 gives the principal clinical findings in our patient and those previously reported.

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References


Correspondence to Dr R. Tignani, Divisione Pediatria, Ente Ospedaliero di Arezzo, Via Curtatone, n. 54, Arezzo, Italy.
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R Biagini, R Tignani, A R Fifi and L Nappini

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