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Case Report:

Hereditary coproporphyria

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Hereditary coproporphyria, a form of acute hepatic porphyria, is a rare Mendelian autosomal dominant inherited condition with incomplete penetrance. The acute attack is usually followed by complete remission, but death may occur. Latent cases are recognised, and the characteristic neurovisceral symptoms and signs are shared by many other conditions. Acute porphyria should be considered in the differential diagnosis of any patient presenting with abdominal pain and neuropsychiatric upset.

CASE REPORT. A 21 year old female presented with a one week history of "'flu-like" illness, characterised by dry cough, generalized weakness and sore throat. Five days prior to her admission she had developed crampy central abdominal pain, which radiated to both loins. Trimethoprim was prescribed for a possible urinary tract infection. Her symptoms did not improve, and she was referred to her local hospital for investigation.

Examination revealed generalised abdominal tenderness, but no palpable mass. Bowel sounds were normal. She was apyrexic; blood pressure 140/110 mmHg. Haemoglobin concentration was 14.8 g/dl with normal indices, white cells 12,000 x 10^9/l. A routine biochemical profile showed values within the reference limits for sodium, potassium, urea, bilirubin and hepatic transaminases. Serum calcium was 2.46 mmol/l, glucose 8.3 mmol/l. Routine Stix testing of urine was positive for protein and blood. Urine culture for micro-organisms was negative. Ultrasound scan of the abdomen showed right-sided renal agenesis with hypertrophy of the left kidney. Gastroscopy was reported as normal.

Two days after admission she was found unconscious on the ward. Her blood pressure was 160/110 mmHg, and she had sinus tachycardia of 100 beats per minute. Fundoscopy revealed retinal artery spasm, but no haemorrhages or exudates. There were no lateralising signs. She was apyrexic and there was no neck stiffness. Over the next few hours blood pressure rose to 180/130 mmHg and pulse rate to 150 beats per minute. She then had a generalised tonic-clonic seizure lasting three minutes, which resolved spontaneously. Intravenous labetalol was commenced. Three further generalised seizures occurred over the next ten hours. The patient was then referred to our unit at the Royal Victoria Hospital.

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CT scan of the brain showed no focal lesion. A 24 hour urine collection for catecholamines was commenced and the specimen was noted to turn a dark red colour on standing. Catecholamille levels were later reported as normal. Urine tests for porphyrins revealed d-aminolaevulinic acid 209 μmol/l (normal=0.8-34.3) and porphobilinogen 316 μmol/l (normal < 8.8). An initial diagnosis of acute hepatic porphyria was made.

She was managed conservatively with a 10% dextrose infusion and oral glucose solutions.[1] Blood pressure fell to 130/100 mmHg on the labetalol infusion, which was discontinued when she became normotensive. The second day after transfer she complained of feeling weak. Physical examination showed proximal muscle power symmetrically reduced to Grade 4 in upper and lower limbs. Deep tendon reflexes were diminished. Serum sodium was 112 mmol/l, and plasma osmolality 236 mOsm/kg, with urinary sodium 27 mmol/l, and urine osmolality 542 mOsm/kg. These findings suggested the syndrome of inappropriate ADH secretion. Fluid restriction to 1000 ml per 24 hours returned the serum sodium level to normal within five days. Recovery over the next week included one episode of syncope, but was otherwise uneventful. She was discharged after sixteen days in hospital.

Subsequent results showed an excess of both coproporphyrin and protoporphyrin in a faecal sample, which confirmed a diagnosis of hereditary coproporphyria. Her parents and three younger brothers are currently being investigated in order to detect any latent cases of porphyria.

DISCUSSION

The porphyrias are a heterogeneous group of inborn errors of metabolism caused by enzyme defects in the biosynthetic pathway of haem. The acute clinical picture occurs secondary to the over-production of porphyrin precursors. These disorders are classified into acute and non-acute forms.

The acute porphyrias include acute intermittent porphyria, variegate porphyria, hereditary coproporphyria and plumboporphyria. All are inherited in an autosomal dominant fashion with the exception of plumboporphyria, which is autosomal recessive. Acute attacks may be precipitated by infection, alcohol, endogenous hormones and a variety of commonly used drugs, particularly those which are inducers of hepatic microsomal enzymes.[2,3] In plumboporphyria, heterozygotes are liable to illness after moderate exposure to lead.[7] Excretion of porphyrins in the urine is markedly increased in the acute phase, and can remain so for months afterwards. Faecal analysis is required to classify the biochemical subtype.

Hereditary coproporphyria was first described in 1955 by Berqer and Goldberg.[4] There is reduced coproporphyrinogen oxidase activity. The clinical manifestations are accompanied by the excretion of d-aminolaevulinate and porphobilinogen in urine and coproporphyrinogen III in faeces and urine. Genetic studies have shown the defect to be located on chromosome 9. A recent paper[5] reports an amino-acid substitution (Arg to Trp) resulting from a single base change, in a patient homozygous for hereditary coproporphyria. This is the first mutation that has been found in this condition. Similar methodology may be used in the future to determine the spectrum of mutations responsible for hereditary coproporphyria and could be used for diagnostic purposes.

The acute attack is managed with supportive therapy and a high carbohydrate intake. In severe cases infusions of haem arginate and tin protoporphyrin may be given. This induces a rapid biochemical remission.[6] They are thought to work by suppressing the rate-determining enzyme in haem biosynthesis as it repletes the hepatic pool of haem. During the recovery phase patient and family education are vital. It is necessary to supply the patient and their general practitioner with a list of drugs which must be avoided.[7] Essential too is the screening for latent cases amongst the relatives.

A large number of the classical clinical features found acutely with this disease were illustrated in this case. It is interesting that there was no evidence of any dermatological complaint. Approximately one-third of patients with hereditary coproporphyria will develop a photosensitive bullous skin eruption,[8] and these often have abnormal liver function tests, which were not found in this case. Our patient has nevertheless been counselled regarding possible problems on exposure to the sun; the use of a sun-block cream may be required.

We were unable to determine the precipitant leading to the development of this particular crisis. It is tentatively suggested that the preceding "'flu-like" illness or the initial trimethoprim therapy may have been responsible.

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