Acute intermittent porphyria presenting as epilepsy

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The fact that acute intermittent porphyria may present as an acute abdomen is well known. Less well recognised is that it may present as a neuropsychiatric syndrome or fits. This is important because when porphyria presents with epileptic fits anticonvulsants may exacerbate the disease as most are inducers of hepatic enzymes. We report a case in which failure to recognise porphyria as the cause of fits led to profound motor polyneuropathy.

Case report

A 27 year old man was admitted having had two grand mal convulsions for the first time, which had been witnessed by his parents and his general practitioner. He did not have a history of fits, although three years previously he had been knocked unconscious in a road traffic accident. This had not led to any neurological sequelae. His brother had suffered with fits secondary to a craniopharyngioma, which had been controlled with anticonvulsants, and had died aged 19 six years previously. There was no other family history of convulsions or other neurological disease. The patient worked as a double glazer and smoked 30 cigarettes and drank six pints of beer a day. Before admission he had suffered some abdominal pain and vomiting for a few days, which had settled spontaneously, as had a similar episode four months previously.

On examination he was afebrile with a tachycardia of 120 beats/minute and a blood pressure of 110/60 mm Hg. General examination was unremarkable, and the abdomen was not tender. He was confused and disoriented in time but not in space. There were no other neurological signs. Three hours after admission he complained of abdominal pain and had mild epigastric tenderness, which settled with antacids.

During the next two days he had two further grand mal fits. He had a slight fever up to 38° C and tachycardia and was hypertensive (blood pressure 180/120 mm Hg). A full blood count was normal, and biochemical screening showed a sodium concentration of 129 mmol(mEq)/1, which improved spontaneously. Skull and chest x ray films were normal, and blood cultures were sterile. In view of his fever computed tomography was performed and excluded a cerebral abscess. An electroencephalogram was normal. His temperature settled spontaneously, and phenytoin 300 mg a day was started. He was discharged having had no further fits.

He was readmitted 10 days later with profound weakness of the arms and legs. He had felt tired three days after discharge, and his general practitioner had therefore changed his treatment to sodium valproate 500 mg thrice daily. The tiredness had progressed to pronounced weakness, and he became unable to stand or pick up a cup.

On admission he was conscious and oriented. He had a tachycardia of 120 beats/minute and a blood pressure of 180/120 mm Hg. General examination was otherwise normal. The cranial nerves were intact. There was wasting of the deltoid muscles but no fasciculation. He had a profound symmetrical flaccid proximal weakness of both arms and legs: there was no movement at all at the shoulders, and he was unable to lift his legs off the bed against gravity. Grip strength and ankle movements were normal. It was impossible

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Acute intermittent porphyria may sometimes present as fits. Items in the history and examination may enable the disease to be identified

to elicit any reflexes in the arms; the right knee jerk was present but not the left. His ankle jerks were normal and the plantar responses flexor. On sensory testing there was reduced sensation to pinprick over the shoulders and the hips with sparing of sensation more distally. Proprioception and vibration sense were normal.

Over the next few days the weakness progressed. He became dyspnoeic and confused, although not hypoxic, and ventilation was not required. Free porphyrins were found in the urine and acute intermittent porphyria diagnosed. This was subsequently confirmed by assay of red cell enzymes. His tachycardia and hypertension were treated with propranolol, and he was given a high carbohydrate diet. Anticonvulsants were withdrawn, and he had no further fits. He made a slow recovery but was left with a pronounced weakness of his arms, although he could walk and feed himself.

Discussion

Acute intermittent porphyria is a hereditary disorder characterised by deficiency of activity of the enzyme porphobilinogen deaminase (uroporphyrinogen-I-synthetase). It is transmitted in an autosomal dominant manner, and in 90% of cases the disease is latent. Under normal conditions the reduced enzyme activity is insufficient to lead to a build up of precursors. If enzyme inducers are taken, however, the enzymes proximal to uroporphyrinogen-I-synthetase increase in activity, leading to increased concentrations of δ -aminolaevulinic acid and porphobilinogen. These precursors produce neuronal degeneration followed by myelinolysis.

Clinical manifestations of acute intermittent porphyria are numerous, the most common being abdominal pain and vomiting. Motor neuropathy occurs in over half of cases and sensory abnormalities in 40%. Seizures occur in only 10-20% of cases.¹ Hyponatraemia has been recorded and is attributed to inappropriate secretion of antidiuretic hormone.²

Seizures, when they occur, are a difficult problem because all the commonly used anticonvulsants—including barbiturates, phenytoin, carbamazepine, sodium valproate, ethosuxamide, and clonazepam—may precipitate attacks of acute intermittent porphyria⁴⁵; a delay of months or years may occur before the attacks are precipitated. Bromide appears to be the drug of choice⁴⁵ and has been used successfully,⁵⁶ although careful monitoring of drug concentrations is essential. Status epilepticus may be treated with either diazepam or paraldehyde, although both have been reported to be porphyrinogenic in chick embryo hepatocyte culture (unlike bromide and magnesium sulphate). Magnesium sulphate has been recommended for both long and short term control of seizures.^{7 8} Other treatment in acute intermittent porphyria consists of withdrawing any precipitant and controlling hypertension and tachycardia with propranolol and a high carbohydrate diet. Some authorities advocate using haematin to reduce the activity of the rate limiting enzyme aminolaevulinic acid synthetase.

This case shows that acute intermittent porphyria may present as seizures and that failure to recognise this may lead to devastating neuropathy. To screen for porphyria everyone presenting with fits is not justified or necessary, but certain clinical pointers should be looked for. A history of episodes of abdominal pain or vomiting should be sought carefully. During the examination persistent tachycardia or hypertension should raise suspicion of the disease. Motor neuropathy and absent tendon reflexes are found in over half of cases. Patients with the disease will have increased porphobilinogen and free porphyrins in the urine.

Finally, after the diagnosis has been proved the relatives must be studied as the condition is autosomal dominant and affected family members are at risk throughout their lifetime of having an attack precipitated by many of the commonly used drugs.¹

Testing for porphyrins and their precursors in the urine will identify only some relatives with latent disease. Direct analysis of red cell enzymes for uroporphyrinogen-I-synthetase is helpful. In those with latent disease activity is reduced to 50% of normal, although one kindred with normal activity has been reported.⁹ Further discrimination of those with latent disease was attained when erythrocyte uroporphyrinogen-I-synthetase activity was combined with estimations of leucocyte δ -aminolaevulinic acid synthetase activity, which is increased.¹⁰

We have established that our patient's father has latent acute intermittent porphyria; further study is in progress.

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Letter from . . . Chicago

Seagulls or exports

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A man minding his business in the streets of Seattle was suddenly hit on the head by a falling rock. While surgeons stitched up his scalp eyewitnesses described how a seagull had come out of an open window carrying a paperweight; it then shot up into the air before letting it drop. Bird experts explained that its motives were culinary rather than criminal, this being how seagulls crack open the shells of long neck clams before having their soft inner contents for dinner. Some people predicted that the injured man would sue the owner of the rock, the seagull, or the branch of government that was allowing these dangerous birds to roam free. Others, seeing an opportunity to cut down on the surplus of malpractice lawyers, wanted to train seagulls to project their missiles selectively at prearranged targets.

At this brutal suggestion the health maintenance organisations were appalled. Heavily committed to marketing, promoting, and advertising, they could hardly afford to pay for fixing thousands of cracked skulls. Not that they would have otherwise objected, now that they too are being sued. Thus there had been a recent case in litigation of a doctor who refused to authorise a child to be examined in an emergency room, insisting instead that the mother bring him to his office in the morning. That would avoid the health maintenance organisation having to pay the hospital for services

Cook County Hospital, Chicago, Illinois GEORGE DUNEA, FRCP, FRCPED, attending physician rendered. Otherwise, how is market profitability to be maintained and the shareholders kept satisfied? For competition is fierce out there, with everybody fighting for a piece of the action, and the insurance companies are now coming up with new plans that do not tie down the patients to any particular doctor or hospital. Some people indeed do resent the lack of choice offered by health maintenance organisations-and sometimes the lack of service too. "It's like socialised medicine," said one patient recently. "It's good for people who are not ill," explained a district nurse; and now the employers are discovering that health maintenance organisations do not necessarily save them money. Even in that Mecca of the health maintenance organisation, Minneapolis, "where it all began," enrolment has been declining for the first time in years. Although some 20 million people throughout the United States are enrolled in health maintenance organisations, the heightened competition has given rise to much talk of marketing blitzes, mergers, consolidations, and even bankruptcies.

Similar problems beset some of the large "for profit" hospital chains. Four large companies (Humana, Hospital Corporation of America, American Medical International, and National Medical Enterprises) own or manage 12% of all United States hospitals and hope to expand further through a network of clinics and doctors treating the patients enrolled in their plans. Various health gurus, looking into their crystal balls, see a rosy corporate future, predicting that eventually a few chains will control American medicine, providing cost efficient and readily available though somewhat regimented care. So far investors have been rewarded with annual earnings as high as 20%—until that black day when