Neuroimaging Findings in Acute Intermittent Porphyria

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The porphyrias are a group of rare inherited metabolic disorders of heme biosynthesis that lead to pathologic accumulation of various porphyrins and their precursors. Several classification schemes have been proposed to identify the different types which include: listing the specific enzymatic deficiencies, location of the excess precursors (liver or bone marrow), or acute and cutaneous forms depending on the predominant symptom[1]. However, most use a classification embodying acute and non-acute (or chronic) categories with acute forms presenting with severe neurovisceral symptoms and the non-acute varieties presenting as chronic disease (usually with cutaneous manifestations)[1]. The acute forms include acute intermittent porphyria (AIP), variegate porphria, hereditary coproporphyria and the very rare ALA (delta aminolevulinic acid) dehydratase deficiency porphyria; the most common is AIP[1].

The incidence of the acute porphyrias is estimated to be one to five per 100,000 in North America while the prevalence varies thoughout the world but has been estimated between one in 500 to one in 100,000 persons[1]. Most patients with AIP are asymptomatic except for intermittent attacks due to a sudden overproduction of porphyrins due to a deficiency of porphobilinogen deaminase. Such episodes are characterized by a wide variety of systemic and neurologic symptoms including pain in the abdomen and elsewhere, hypertension, tachycardia, obtundation, coma, seizures and psychiatric symptoms[1,2]. Generalized seizures are reported to occur in 2-20% of patients with acute AIP attacks, usually in association with other signs of encephalopathy including altered level of consciousness and behavioural abnormalities[2]. Acute attacks of AIP are precipitated by certain drugs, concomitant illness, metabolic changes and stress, but sometimes no cause can be identified. The diagnosis is made by finding elevated levels of urinary porphobilinogens[1,2]. There are just a few reports of the neuroimaging findings in patients with acute attacks of AIP and neurologic manifestations including seizures. Here we describe the computerized tomographic (CT) and magnetic resonance (MR) imaging findings in one such patient.

Case Report

A 21-year-old woman had recurrent abdominal pain that was attributed to endometriosis that had been previously confirmed by laparoscopy. She was treated with depot medroxy-progesterone acetate with no improvement and ultimately required admission to hospital for pain control with intravenous morphine. After five days of continued pain and anorexia she had a generalized seizure. Her blood pressure was never elevated. The initial CT scan demonstrated low density changes in the subcortical white matter in the frontal, parietal, and occipital lobes and no evidence of diffuse swelling (Figure 1 A,B). These findings were confirmed on MR imaging (Figure 1 C,D) with the additional demonstration that the hyperintense signal extended to the cortex. These MR features were highly suggestive of posterior reversible leukoencephalopathy syndrome (PRES)[3,4]. Given the patient's young age, her clinical symptoms and MR findings of PRES, the diagnosis of AIP was suggested by the imaging department. Urine porphobilinogens were elevated at 1660 μmol/L (normal < 9) and fractionated urine analysis revealed that urine coproporphyrins were not elevated. Upon clinical review, there were no cutaneous manifestations. Further analysis with enzymatic assays and DNA analysis was not done as this is not routine practice at our hospital. Although acute attacks can be seen with other acute porphyrias (such as hereditary coproporphyria (CP) and variegate porphyria (VP)), VP always has skin manifestations (photo-sensitivity) and one third of the cases of CP also have cutaneous findings[1]. Two thirds of the cases of CP present in an identical fashion to AIP but the significantly elevated urine porphobilinogens and normal urine coproporphyrins would suggest the diagnosis of AIP. It was later revealed that a paternal uncle was thought to have porphyria. The patient was placed on high concentration intravenous dextrose, but the abdominal pain persisted. She was then treated with hematin and total parenteral nutrition and the abdominal pain resolved. A MR study done three weeks later showed complete resolution of the abnormalities (Figure 1 E,F).

Discussion

Because of the relative rarity of acute attacks of AIP and the diverse and nonspecific nature of the symptoms, establishing this diagnosis is often delayed. When generalized epileptic seizures occur in a patient not known for having a seizure disorder, neuroimaging studies are usually performed, so it is important to know whether there are specific features that may

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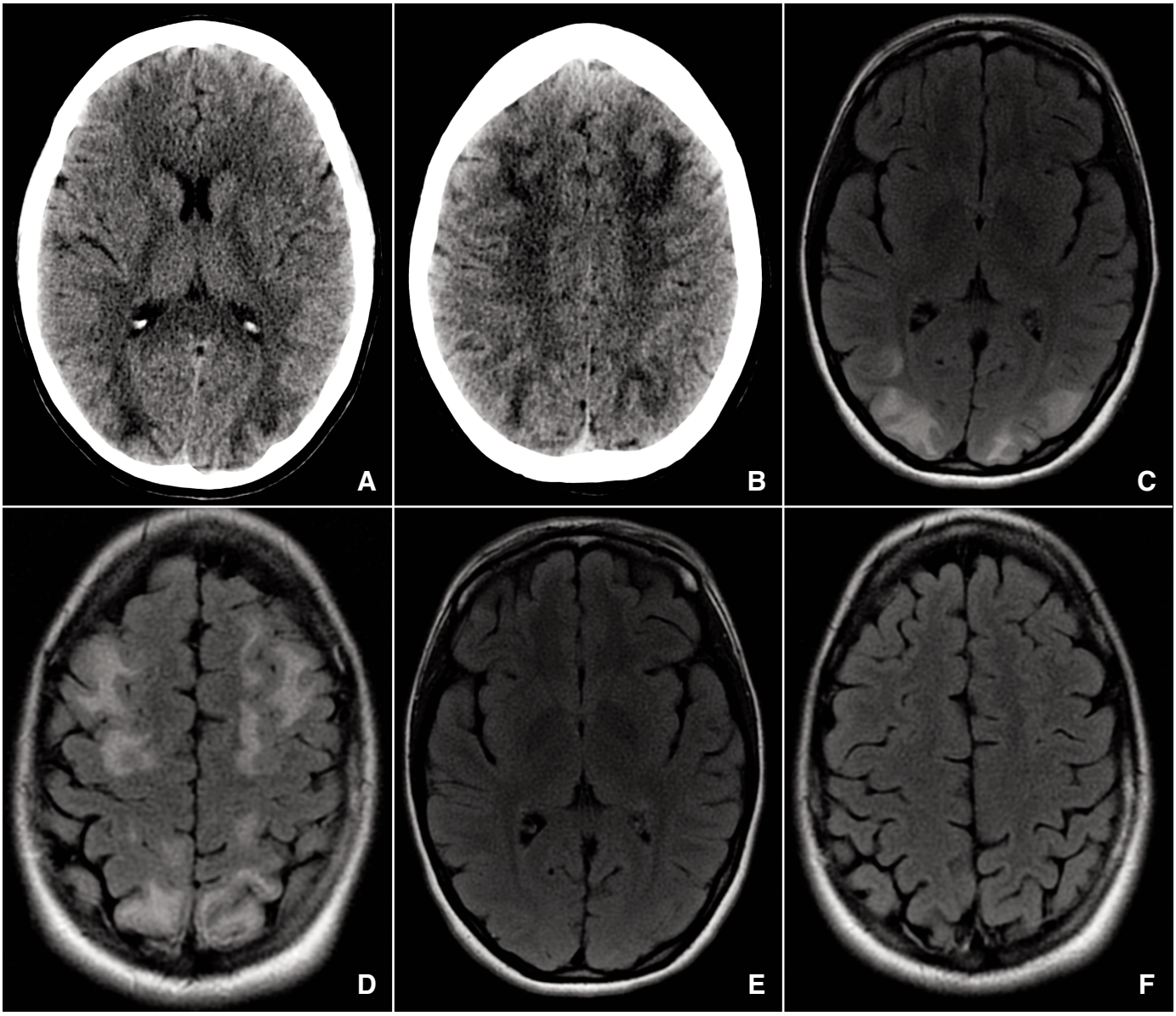

Figure: *(A) and (B) Axial CT scans demonstrate bilateral low density changes in the subcortical white matter of the frontal, parietal, and occipital lobes. (C) and (D) Axial MR FLAIR images confirm the findings seen on CT scan and show that the hyperintense signal extends to the cortex. (E) and (F) Axial MR FLAIR images performed three weeks after the seizure and following treatment shows complete resolution of the abnormalities.*

point to the diagnosis of AIP. There are a few descriptions of patients with AIP and transient, reversible changes involving the cerebral white matter and cortex on MR imaging, characteristic of the posterior reversible leukoencephalopathy syndrome[2,5-9]. In our patient, it was the appearance of PRES on the MR imaging, in a patient who was not hypertensive, that suggested the diagnosis of AIP. The MR findings of PRES were first reported in patients with eclampsia, on cyclosporine treatment for organ transplantation, severe hypertension, high dose chemotherapy, shock and sepsis, but a variety of other illnesses can be associated with PRES[3,4]. A less frequently described MR abnormality in patients with AIP and hyponatremia is central pontine myelinolysis[10].

In summary, it appears that the most frequent imaging abnormality seen in AIP is that of PRES, so this diagnosis should be added to the expanding list of causes of this neuroimaging syndrome. These findings, in the context of a patient with generalized seizures combined with other systemic and encephalopathic symptoms, particularly abdominal pain, may be valuable clues to the diagnosis of AIP.

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