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Acute Porphyria: Between Errant Diagnosis and Unusual Associated Metabolic Disorders; Case Report

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Abstract

Background: Acute intermittent porphyria (AIP) is a rare inherited metabolic disorder. It presents with acute episodes of neurovisceral symptoms which are non-specific, therefore diagnosis is frequently missed or delayed. AIP is rarely associated with dyslipidemia, and is exceptionally accompanied by copper disorders, or non-iatrogenic hepatic iron overload. We report one case.

Case Report: A 20-year-old female was referred to us for a recurrent attack of abdominal symptoms associated with neurological manifestations, that were first linked to a psychiatric origin. Laboratory test revealed electrolyte disorders moderate liver cytolysis, acute renal failure, dyslipidemia, slightly low ceruloplasmin with high urinary copper levels. Urinary porphobilinogen and ADA levels came back very high. Hepatic and cerebral-MRI showed an iron and copper overload. The diagnosis of AIP associated with hepatic iron overload, copper overload, and dyslipidemia was made. Haemin was unavailable, so she was put on symptomatic treatment. Symptoms have resolved within a week. Three months later, she had another attack due to exposure to a solvent eventually resolved under treatment. Conclusion: AIT is rare, misdiagnosed disease. Its association with copper and iron overload outside of heminic-treatment is exceptional; coincidence or cause-and-effect relationship? This remains to be elucidated.

Introduction

Acute intermittent porphyria AIP is a rare autosomal dominant disease of heme biosynthesis due to a mutation in the porphobilinogen deaminase gene. Characterized by a deficiency of hydroxymethylbilane synthase (HMBS), thereby causing an accumulation of heme precursors (δ-aminolaevulinic acid and porphobilinogen) [1, 2]. These neurotoxic

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heme precursors elicit acute neurovisceral attacks consisting of episodes of abdominal pain, neuropathies, vomiting, tachycardia, and hypertension, but, unlike most other porphyrias, patients with AIP do not develop a cutaneous rash. The acute attacks of AIP are more frequent in women and they are typically triggered by certain factors; several drugs, steroid hormones… etc. [1]. AIP diagnosis gets usually delayed due to nonspecific symptoms and similarities with other diseases [1]. AIP is a rare disease with an estimated European prevalence of 1/2000 [1]. While associated dyslipidaemia is rarely described in patients with porphyria [7], the association of AIP with copper disorders and hepatic iron overload unrelated to haemin is unusual and exceptional, and has not yet been described in the literature. Here, we report the case of a 20-year-old Algerian female which was diagnosed with AIP associated with dyslipidemia, iron and copper disorder.

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female was referred to our daily hospital for a recurrent digestif disorder which has been evolving for 4 months, consisting of attacks of abdominal pain associated with a sub-occlusive syndrome a vomiting, in conjunction with electrolyte disorders. Abdominal CT scan and gastrointestinal endoscopy came back negative. Eventually the symptoms were linked to a psychiatric origin and she was put under antidepression drugs.

On clinical examination, in-addition to the symptoms described above, we noted tachycardia with heart rate of 110 bpm, high blood-pressure of 160/95 mmHg, accompanied by resting tremor of the right upper limb. Laboratory tests showed a moderate liver cytolysis (Aspartate Aminotransferase: 107 U/L, Alanine Aminotransferase: 115U/l) , hyponatremia (113 mEq/l), acute renal failure (creatininemia: 16 mg/l), hypercholesterolemia (total cholesterolemia: 3.03g/l, High density cholesterol: 0.94g/l, low density cholesterol: 1.93 g/l), slightly low ceruloplasmin (1.6µmol/l), and high urinary copper levels (51.98 µmol/24h). Urinary porphobilinogen (PBG) and acid delta aminolevulinic (ADA) levels came back very high (urinary PBG :180.8, ADA: 83.5µmol/l), fecal coproporphyrin was normal (23.5%). Hepatic-MRI identified slight hepatic iron overload. While on cerebral-MRI there was a discrete T2-hyposignal of the red nuclei and substantia nigra which can be related to a Wilson disease. The diagnosis of AIP associated with hepatic iron overload, copper overload, and dyslipidemia was made.

She was put on dextrose solutions, opioids antalgics, zinc supplement, and low-cholesterol diet. We were unable to use Haemin because it is not available in our country. Symptoms have resolved within a week. Three months later, she has another attack due to exposure to a solvent eventually resolved under symptomatic treatment.

Discussion

AIP is a rare metabolic disorder (European prevalence: 1/2000), it ranks as the most common and severe form of acute porphyria that appears between the age of 18 to 40, and affects women to a greater degree than men (ratio: 1.5 - 2) [1, 2]. In Our case, it is a female patient that had develops the first symptoms of the disease at the age of 18.

Inducers of acute attacks are alcohol, infections, low caloric intake, reproductive hormones change, and high-risk porphyrogenic drugs [1, 2]. In our case, it has been observed that the attacks are mainly triggered during the menstrual period, an exposure to a solvent; and also, the patient before the diagnosis were put under antidepressant drugs that might major the attacks.

AIP characteristically demonstrate acute episodes of neuro-visceral symptoms [1]. In this case, the abdominal pain was the first symptom; the neurological disorders were both related to the autonomic neuropathy (tachycardia, hypertension) and peripheral neuropathy (limb tremor).

Owing to the broad-spectrum neuro-visceral clinical presentation of AIP, and the non-specificity of its symptoms; the diagnosis can be delayed for mean of 15 years (an observational study about 90 patients with AIP) [1, 2]. It results from finding elevated PBG in urine in a random sample kept protected from light. Diagnostic confirmation should include quantitative measurement of PBG, ALA, and total porphyrins from the same urine sample [1]. In this case, it took eight months to reach a diagnosis of AIP, the non-specificity of the symptoms and the normality of the initial investigation misled practicians into concluding to a psychiatric origin of the episodes. it was the intensity and recurrence of the abdominal symptoms, the episodes of blood pressure peaks and tacchycardia, and the repetition of additional examinations revealing other disorders such as disturbed liver and kidney function tests and ionic disorders, together with the normality of the morphological and endoscopic examinations, that led us to consider the diagnosis of porphyria, which was confirmed by urinary assays of PBG, ALA, and total porphyrins.

Iron overload in AIP is usually related to hemenic treatment.

Non iatrogenic hepatic iron over load is extremely rare, one case has been reported in the literature [3, 4] were an excessive concentration of iron in the liver, spleen and marrow were objected in 50 years old patient with AIP [1].

Despite the fact that copper plays a role in heme synthesis, the association between copper overload and AIP is exceptionally observed [5, 6] and no case has been yet reported in the literature to our knowledge.

Hypercholesterolemia, although inconstant, is of common occurrence in the AIP (review of the records n=51), yet the exact mechanism of this disorder remains unclear [7].

Acute intermittent porphyria (AIP) is an inherited disorder caused by a mutation in the porphobilinogen deaminase gene. Since porphyria, dyslipidemia, and iron and copper overload are all metabolic disorders, their potential association may suggest a genetic link. It could also be explained by a cause-and-effect relationship. Further investigation is needed to explore this potential connection and to elucidate its mechanism.

Conclusion

In conclusion, this case report highlights that AIP is a rare and often misdiagnosed condition due to its non-specific symptoms, which can inadvertently lead to exposure to acute attack triggers such as antidepressants. It also serves as a reminder of the potential associations between porphyria and other metabolic disorders, such as dyslipidemia. Describing for the first time in the literature the unusual association between AIP and copper and iron overload-independent of haem treatment, it warrants further investigation to explore this potential link. We recommend investigating and screening for metabolic abnormalities in individuals with porphyria to assess potential associations and enable appropriate management. Further research is essential to explore this potential connection and improve our understanding of AIP's complexities and management strategies.

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