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Case Report

A CASE OF PORPHIRIC NEUROPATHY ASSOCIATED WITH PERIPHERIAL, CENTRAL AND AUTONOMOUS NEUROPATHY

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Abstract

Acute Intermittent Porphyria (AIP) is a disease associated with a partial deficiency of biosynthesis enzymes caused by genetic anomalies and is characterized by several functional disorders, which are mainly neurologic. Our case is a 19 years old woman, who has been initially admitted with stomach pain and anemia. A couple of days after her arrival, she developed certain neurologic disorders (epileptic seizures, autonomous and peripheral motor neuropathy) as well as other system involvements (hyponatremia caused by inappropriate ADH syndrome, an increase in liver enzymes etc.). All these findings and symptoms pointed to the possibility AIP. After implementing central venous catheter, she was treated with intravenous infusions of Haem arginate and antiepileptic, antihypertensive and antiarrhythmic medications as well. Her urinary excretion of δ-aminolevulinic acid (ALA) was markedly increased being (81,70 mg/l). When analyzed, HMBS genes were found to be a heterozygote. The neurologic involvement in AIP generally has a proximal motor neuropathic character. Since distal neuropathy is a rare finding in porphyric neuropathy, we report this case which presented with the additional association of autonomous neuropathy and central nerves system involvement.

Keywords: Porphyric neuropathy, acute intermittent porphyria.

Introduction

Acute Intermittent Porphyria (AIP) is a hereditary disease during which neurovisceral crisis can be observed. The patients mostly present with stomach pain [1]. The cases can even lead to diagnostic laparotomy, depending on the severity of pain. The patients genetically tend to have a deficiency of PBDG (porphobilinogen deaminase) enzymes. Due to this defect, an increase is observed in porphirine precursors that are produced and secreted by the liver such as δ-aminolevulinic acid (ALA) and porphobilinogen (PBG). This increased production of precursors can be held responsible for several acute episodes during

AIP [2,3]. AIP is more likely to be observed in women compared to men (60-75%), and the severity and the frequency of the acute attacks are higher in women than men. Characteristics symptoms begin to occur between the ages of 20 and 30 for women, and 30 and 40 for men [4,5]. The facts that the disease rarely occurs at pre-puberty and that it occurs more frequently amongst women lead us to the idea that hormones may be the cause acute exacerbations. Besides, certain drugs, pregnancy, menstruation, infection or fasting can trigger the attacks as well [6]. Neurologic findings, hyponatremia caused by inappropriate ADH syndrome, arrhythmia, and hypertension are several other findings. Proximal motor neuropathy is an expected finding in AIP as a neurologic manifestation. In our case, there was an unexpected involvement of central nervous system presented with distal motor neuropathy, autonomous neuropathy, and epilepsy. We want to present this case due to the co-occurrence of these rarely seen neuropathies.

Case Report

An 18-year-old female patient (height cm; weight kg) was admitted to our hospital with abdominal pain which she had been suffering for the past month. She reported that occasionally she had a fever during abdominal pain. She had no prior complaints so she had not seen a doctor because the pain resolved at a short time. She visited our emergency room when the pain increased in the past couple of days. Once evaluated for an acute abdominal incident in the emergency room, she was admitted to the department of internal medicine for further evaluation and treatment. She did not any have any underlying disease and family history of any disease. She did not report any drug or substance abuse. Her physical examination revealed a good state overall. Upon arrival her blood pressure was 110/70 mmHg, heart rate was 96 beats/min which was disturbing her and the body temperature was 37.8°C. Examination of the pulmonary system and other systems revealed normal yet abdomen was sensitive at palpation. Other biochemical examinations revealed blood glucose 88 mg/dl, BUN 34 mg/dl, creatinine 0.5 mg/dl, ALT 40 IU/L, AST 42 IU/L, alkaline phosphatase 66 IU/L, sodium 134 mmol/L, potassium 4.4mmol/L, gamma glutamyl transferase 80 IU/L, microscopy of urine: normal, erythrocyte sedimentation rate 18mm/h, CRP:0.3 mg/dl, hemoglobin 8.7 g/dl, thrombocytes 253.000/mm^3.

The acute abdominal symptoms of the patient did not resolve yet increased after admission. A diagnostic workup including abdominal computerized tomography (CT) and consultations from Gynecology and Surgery Departments were held in order to rule any emergency. The CT was normal. Abdominal MR angiography was taken in order to rule out intra-abdominal vascular obliteration which also revealed normal. The day after admission, she presented epileptic seizures which were taken under control by antiepileptic agents following neurology consultation. Meanwhile, serum sodium level was markedly decreased (Na:114 mmol/L). Epileptic seizures and hyponatremia were suggestive of inappropriate ADY syndrome due to an intracerebral incident but cranial MR imaging revealed normal. However, sinusal tachycardia (140b/min) and hypertension (180/100 mmHg) were detected concurrently to which we interfered with a calcium channel blocker (Diltiazem). At the evening of the same day, she reported dark urine. Abdominal pain, epileptic attack, hyponatremia and associating hypertension and tachycardia was suggestive of AIP. A urine sample was further investigated for AIP and blood sample was taken for genetic evaluation.

Intravenous/oral glucose treatments were administered while any medicine that may have caused the attacks was discarded. Three days later the patient's liver enzymes

increased (ALT: 155 IU/L, AST: 129 IU/L). Following intensive IV glucose administration, abdominal pain relieved significantly and the epileptic attacks did not re-occur followed by the gradual decrease in liver enzymes day by day. However, three days later, the patient complained of an intense pain starting from distal muscles of the lower extremity which moved upwards and left her weak and limpy. This clinical expression was considered as peripheral neuropathy and treatment was initiated accordingly that focused directly and essentially on AIP. Human Haem has initiated 3 mg a day for 4 days. The patient improved rapidly. The 24 hour urine sample evaluation revealed the following: δ-aminolevulinic acid (ALA): 81,70 mg/day (Range (R): 0- 4,5mg/day), uroporphyrin I, III: 5971 µg/day (R: 0- 25 µg/day), copropophyrin I: 100 µg/day (R:0-25 µg/day), copropophyrin III: 70,2 µg/day (R:0-75 µg/day). Genetic analysis was focused on the HMBS gene in order to identify AIP, which revealed that the HMBS gene NM_000190.3, IVS10+2T>C (c.651+2T>C) was a heterozygote.

Discussion

Given the findings, our case was early diagnosed and appropriately treated for AIP. The initial complaint by the patient was abdominal pain whilst running fever. When she reported that she had had a fever and indefinite abdominal pain attacks before and that she was passing out in a few seconds, we considered the possibility of "Familial Mediterranean Fever" (FMF) which is widely seen in our region. However a few days later her complaints increased together with neurologic symptoms such as epileptic attacks and some others like hypertension and tachycardia which we do not expect in patients with FMF. Therefore the team found AIP a more plausible diagnosis than FMF. Neuropathic uptake in AIP occurs due to a mutation in the gene that encodes the porphobilinogen deaminase PBGD enzyme, and this involvement usually occurs as proximal motor neuropathies in upper extremities [7,8]. In our case, dextrose infusion and a high-calorie diet were initiated which in return relatively decreased the abdominal pain and hyponatremia but associated the patient suffered from weakness and an intense pain starting from the low extremities moving upwards. This situation was considered to be peripheric neuropathy. We expect proximal motor neuropathy at the upper extremities as the characteristics of porphyric neuropathy whereas in our case there was distal polyneuropathy that started from lower extremities. This neuropathy was associated with autonomic neuropathy presenting with hypertension and tachycardia.

Hypertension is present in 64% of acute porphyria attacks [9]. Additionally, in our case, there were epileptic attacks as an early finding, caused by central nervous system involvement. Even though distal motor neuropathy isn't an expected finding for porphyric neuropathy, although rarely it has been reported in some AIP cases [10]. Even though the physiopathology of porphyric neuropathy isn't known for certain, it may be caused by the neurotoxic effects of increased porphyrin precursors [11]. In severe cases of AIP, quadriparesis similar to Guillain-Barré syndrome can be observed as well [12]. If the patient's other clinic findings are indefinite, plasmapheresis may be done mistakenly by administering intravenous immunoglobulin. Moreover, antiviral treatment may even worsen the attacks. In severe attacks, respiratory paralysis can even lead to death. In our case, AIP-related findings such as abdominal pain, hyponatremia caused by inappropriate ADH, and convulsions occurred before peripheral neuropathy, hence we were able to diagnose the disease clinically in an early stage. Following the acute and painful presentation of peripheral neuropathy, Human Haem treatment was initiated before we achieved the results of

diagnostic tests and that helped to prevent fatal complications in time.

Conclusion

Porphyric neuropathy can manifest with various neurological involvements. Therefore, one must consider and rule out AIP in differential diagnosis at each neuropathic involvement by looking for the other symptoms and signs of this disease.

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