Case Reports

Acute attack of AIP (acute intermittent porphyria) with severe vivax malaria associated with convulsions: a case report

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Acute intermittent porphyria (AIP) is a hereditary hepatic porphyria inherited as autosomal dominant with low penetrance resulting from mutation in the gene encoding the enzyme, porphobilinogen deaminase (PBG-D) [hydroxymethylbilane synthase, uroporphyrinogen I synthase]. The diagnosis is often obscured by the variable presentation, viz. abdominal pain (commonest), constipation, vomiting, convulsions, and peripheral neuropathy and further complicated by the variable course of illness. Incidence of convulsions is 10–20% but there may be presenting symptom of an acute relapse. Although *Plasmodium vivax* usually causes benign uncomplicated malaria, it can occasionally result in severe disease with life-threatening, end-organ involvement including cerebral malaria manifesting as convulsions. This case is a rare presentation of severe vivax malaria and exemplifies the dilemma associated with diagnosis and treatment of convulsions when it occurs in a case of AIP. This case underscores the importance of considering the safety profile of antimalarials and anticonvulsants in a case of AIP.

Case report: A 19-year-old unmarried female patient presented with low grade continuous fever associated with chills and rigors of two weeks duration and altered consciousness (EMV score – 6/15) for the last three hours following an attack of generalized tonic clonic convulsions. There was no history of headache, pain in the abdomen, decreased appetite or vomiting, however, the patient was passing red colour urine and having severe constipation. She was having past history of recurrent attacks of abdominal pain and passing red colour urine since last five years for which she was diagnosed as a case of AIP. The clinical examination revealed palpable liver and spleen. The detailed neurological examination did not reveal any finding except unarousable coma and bilateral extensor planter response.

The routine blood examination revealed Hemoglobin – 10 g/dL, TLC – 10200/mm³ with 88% neutrophils, platelet count – 2.46 lacs/mm³. Serum Na⁺ levels – 124.98 mmol/L, Serum potassium levels, liver function tests, renal function tests, widal test and blood culture were normal. The tests for leptospirosis and dengue fever are negative. The examination of thick and thin peripheral blood smear showed the evidence of *P. vivax* ring stage and trophozoites (density – 9600/mm³). The rapid diagnostic test (RDT; pLDH based) and PCR also demonstrated evidence of *P. vivax* and absence of *P. falciparum* infection. Urine complete and microscopic examination was normal with no evidence of haematuria. Urine Watson-Schwartz test was positive for porphobilinogen, Urine PBG level was 24.93 mg/day (normal 0–4), Urine ALA level was 47.28 mg/day (normal 1–7). Abdominal ultra sonography,
skiagram chest and non-contrast CT scan of head was normal.

Regarding specific antimalarial treatment, she was not given chloroquine as she was a known case of AIP in remission for the last five years but received an intramuscular injection of 80 mg artemether. After reaching to the emergency room she was treated with intravenous quinine along with dextrose and oral Gabapentin 300 mg three times per day through Ryle’s tube for management of seizures, the dose of which was increased to 600 mg thrice a day later on. She regained consciousness on third day of admission. Her urine output and colour also improved and was negative for porphobilinogen. At the end of fifth day, she was fully conscious, taking food and drugs by mouth and passing stools regularly. The blood smear for malarial parasite was negative. She was discharged after seven days of asymptomatic stay in the hospital.

Discussion

This case reaffirms the clinical course of AIP that is represented by acute attacks or ‘crisis’ occurring after puberty and is much common in females with highest incidence in the second and third decades. The attacks are usually precipitated by endogenous sex hormone changes, dietary restriction, alcoholic drinks, severe infection, fever, ‘stress’ or the administration of drugs4. Thus, it may truly be called a ‘pharmacogenetic’ disease5.

The causation of unconsciousness and convulsions in this patient could be complex including acute porphyric crisis1, cerebral malaria due to *P. vivax*3,6 and/or the use of artemether that has been associated with prolongation of coma and more incidence of seizures7.

Quinine and artemisinin derivatives are the recommended treatment options for severe vivax malaria8 but quinine is also a known experimentally porphyrogenic drug5 whereas there are no data available for the artemisinin derivatives. This challenges the justification of extrapolation of animal models to humans in case of porphyria hence evidence should be based on both clinical and experimental safety5. Further, artemisinin derivatives need evaluation with regard to their phophyrogenic status.

The treatment of convulsions in cerebral malaria with intravenous (or, if not possible, rectal) benzodiazepines or intramuscular paraldehyde is similar to that for repeated seizures from any cause8. On the other hand all first line antiepileptic drugs including benzodiazepines have been implicated in the precipitation of acute attack of AIP, leaving only magnesium sulphate and bromides as safe options. Nevertheless, clinically diazepam has been safely used for treatment of status epilepticus and clonazepam for the prophylaxis of convulsions in AIP5. Encouraging results with gabapentin, which is not significantly metabolized in the human liver, have been reported9. Similar observation has also been reported earlier in a clinical study from north-western India10. This case also had significant improvement in convulsions with gabapentin. Therapeutic success reports with carbamazepine are also emerging. At large, treatment of convulsions in a case of AIP with severe *P. vivax* infection is a challenging situation and remains a diagnostic and therapeutic dilemma as has been justifiably raised by this case report.

References


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