Reversible cholestatic hepatitis due to carbamazepine in an adolescent

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We report a 13-year-old boy who developed fever, rash and hepatitis with cholestasis (on biochemistry and liver histology) after 10 weeks’ use of carbamazepine. Recovery of liver biochemistry occurred 4 months after discontinuing the drug. [Indian J Gastroenterol 2005;24:172-173]

Carbamazepine (CBZ), an established antiepileptic drug, has clinical efficacy in the treatment of acute mania, stress disorders and neuropathic pain. It produces dose-related neurotoxicity; manifestations of idiosyncratic hypersensitivity include rashes, photosensitivity, hepatitis and, rarely, agranulocytopenia/aplastic anemia.

Hepatotoxicity is rare in children, and usually manifests as hepatitis with or without hypersensitivity syndrome. Fatal fulminant hepatic failure has been described with CBZ in children. There are no reports of cholestatic injury due to CBZ in children.

A 13-year-old boy presented with recurrent transient ischaemic attacks, and was diagnosed to have left internal capsule infarct on CT imaging. He was started on carbamazepine empirically in a dose of 200 mg BD. After 10 weeks of use he developed fever with generalized skin rash associated with itching. These improved promptly after withdrawal of CBZ, but the patient noticed yellowing of urine and sclera with worsening of pruritus. Examination revealed deep icterus, macular pigmented rash, and hepatosplenomegaly.

**Investigations:** WBC 11,300/cmm; total bilirubin 14 mg/dL (conjugated 9.6), AST/ALT 106/156 U/L, alkaline phosphatase 1414 IU/L (normal <280) and GGTP 159 IU/L (normal <35), serum albumin 3.8 g/dL, PT 14/12 s. Viral markers (HBsAg, IgM anti HBc, anti HCV, IgM anti HEV, IgM anti HAV) were negative, as were markers of immune-mediated liver disorders (ANA, AMA, ASMA). Serum ceruloplasmin was normal; KF ring was absent at slit-lamp examination. Ultrasonography showed hepatosplenomegaly with normal portal vein and no free fluid. ERCP was normal. Liver biopsy showed maintained echotexture, focal hepatocytic and canalicular cholestasis, and mixed inflammatory infiltrate consisting of lymphocytes and neutrophils and foci of lobular inflammation (Fig). Bile ductular proliferation was also noted. A diagnosis of CBZ-induced cholestatic injury was made and the patient was managed with ursodeoxycholic acid along with anti-histaminic drugs.

His jaundice improved and pruritus disappeared. However, over the next 12 weeks his liver function profile showed a progressively increasing GGT, which peaked at 3 months after stopping CBZ (Table). After 3 months there was an abrupt fall in GGT and normalization occurred at 4 months. The bilirubin and ALT values on the other hand showed a gradual decline 4 weeks after cessation of CBZ and normalization occurred at 3 months.

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<th>Date</th>
<th>Bilirubin (mg/dL)</th>
<th>ALT (IU/L)</th>
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<th>ALP (IU/L)</th>
<th>GGTP (IU/L)</th>
<th>Protein (g/dL)</th>
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Carbamazepine-induced hepatotoxicity is uncommon, occurring in 16 per 10,000 treatment years. It may occur in the first 6 weeks of treatment, although presentation may be delayed for as long as 6 years after starting the drug. Most reports are in adults more than 40 years old. The condition has two manifestations: two-thirds have granulomatous hepatitis with severe cholestasis induced by drug hypersensitivity. Others have direct toxic effect of CBZ metabolites causing acute hepatitis and hepatocytic necrosis without cholestasis. Rarely, patients may develop the vanishing bile duct syndrome. Most patients, with the exception of those with the vanishing bile duct syndrome, have uneventful recovery on withdrawal of drug.

Our patient seemed to have the hypersensitivity type of toxicity, with rash and fever. Previous descriptions of CBZ-induced hepatotoxicity in children describe the hepatic pattern of disease with or without hypersensitivity symptoms. Severe hepatotoxicity in children in the form of progressive liver failure and death has been documented before. However, cholestatic hepatitis as seen in our case has not been previously reported in children.
References


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Infiltrating Strongyloides stercoralis presenting as duodenal obstruction

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Small intestinal obstruction due to Strongyloides stercoralis is rare and has not been reported in an immunocompetent patient. We describe a 70-year-old immunocompetent man presenting with duodenal obstruction secondary to severe S. stercoralis infestation, as documented on duodenal biopsy. He was treated with ivermectin, with which he recovered remarkably. [Indian J Gastroenterol 2005;24:173-174]

The gastrointestinal manifestations of Strongyloides stercoralis infection include abdominal pain, diarrhea, nausea, vomiting and rarely malabsorption; many patients are asymptomatic. Chronic infestation is usually limited to the duodenum and jejunum. Disseminated infection occurs in the immunocompromised host.

A 70-year-old man presented with recurrent bilious vomiting and anorexia since 2 months. Vomiting was preceded by abdominal distension and pain. There was no history of GI bleeding. He had lost 12 Kg weight since 2 months. The patient did not give history of any significant illness in the past and was not on any medication. On examination, he was emaciated; abdominal examination was normal.

Routine blood tests showed hemoglobin 12 g/dL, serum albumin 2.9 g/dL, total WBC count 11,000/µL, neutrophils 65% and absolute eosinophil count 220/µL. Stool examination done twice was normal. Serology for human immunodeficiency virus was negative. Plain X-ray abdomen was normal. Upper GI endoscopy showed effacement of the duodenal folds, narrowing in the third part of duodenum, with food residue in the stomach. Bariumstudy revealed narrowing of the third part of duodenum with mucusal ulcerations; rest of the small bowel was normal. CT scan showed dilated stomach and proximal duodenum. Duodenal biopsy revealed S. stercoralis in the submucosa with inflammatory infiltrates (Fig).

The patient was treated initially with albendazole 400 mg twice daily for 2 days but he did not have relief of symptoms even after 2 weeks. He was then put on ivermectin 6 mg twice daily for 2 days. Within 2 months, his abdominal symptoms resolved, and he had gained 8 Kg weight. Upper GI endoscopy and barium study repeated after the treatment was normal.

Small bowel obstruction due to S. stercoralis infestation is rare. Duodenal obstruction due to enteritis has been described in an HTLV-1-infected patient. Small bowel obstruction in secondary to intense infestation and mucusal edema. Duodenal entrapment at the level of the enlarged superior mesenteric artery has also been reported.

Treatment consists of either albendazole 400 mg/day or ivermectin 200 µg/Kg/day twice daily for two days. Our patient responded to ivermectin.

References