Recurrent acute hepatitis in patient receiving pulsed methylprednisolone for multiple sclerosis

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We report clinically significant, recurrent acute hepatitis in a 48-year-old woman receiving pulsed treatment with methylprednisolone for multiple sclerosis. No other cause was found for the episodes and the temporal and histological correlations were consistent with immune-allergic type drug-induced hepatitis. [Indian J Gastroenterol 2006;25:314-316]

Abnormalities of liver function following steroid use are well recognized and have a number of mechanisms. Transient rise in transaminases without clinical consequence after repeated courses, steatosis and steatohepatitis, reactivation of latent hepatitis B and C infection, and autoimmune hepatitis in patients with multiple sclerosis have been reported.

A 48 year-old Caucasian lady presented with seven days’ history of nausea, vomiting and jaundice. She had no fever or pain. She had no previous history of jaundice, denied alcohol consumption, and had no risk factors for viral hepatitis. She had been generally healthy, apart from neurological problems secondary to multiple sclerosis diagnosed 30 months earlier. She was taking no regular medication. She was neither overweight nor diabetic. Her sister had autoimmune thyroid disease.

She had been treated six weeks ago with the third course of intravenous methylprednisolone (Solupred®; Pharmacia, Surrey, UK) for exacerbation of multiple sclerosis. She denied any problems with the previous two courses. All available previous liver function test results were normal; however there were no results of such tests temporally related to her previous injections eight and twenty months ago.

On examination she was icteric. There were no features of chronic liver disease. The liver was just palpable but not tender. There was no clinical ascites, splenomegaly or encephalopathy. There was pallor of the left optic disk, impaired pain and touch sensation in the left lower limb, and dysdiadochokinesia on the left side, compatible with demyelinating disease.

Hematological and biochemical test results including serum immunoelectrophoresis, renal and thyroid function, and C-reactive protein were normal. Liver function tests at presentation and subsequent trend are shown in the Figure. Serological tests for hepatotropic viruses (HAV, HBV, HCV, HEV, CMV and EBV) and antibodies against mitochondria, smooth muscle and nuclear antigens were negative, neither was there increased immunoglobulin G levels or hypergammaglobulinemia. Tests for ferritin, transferrin saturation, ceruloplasmin and alpha-1 anti-trypsin levels were normal. Abdominal ultrasonography was normal.

Liver biopsy showed the architecture to be preserved, but there was striking infiltration of the parenchyma by lymphocytes, eosinophils and occasional plasma cells, most apparent in the perivenous area of acinar zone 3. The cell plate structure was disturbed, with ballooning degeneration and presence of Councilman-type bodies.

There was no interface hepatitis, cholestasis or fatty change.

Without specific treatment the liver function tests slowly improved. One year later she again presented with two days’ history of nausea and vomiting and abnormal liver function tests. Once again there was no evidence of risk factors for viral hepatitis and there was no pain, fever or drug usage other than having had the fourth course of intravenous methylprednisolone three weeks previously for relapse of multiple sclerosis. Apart from mild icterus there were no new findings. As previously, an extensive workup for causes of liver disease was negative. The liver function tests at presentation and their subsequent course were similar to the previous episode but the interval between steroid injection and onset of the illness was shorter and the abnormalities more severe and prolonged.

The patient has not required any further courses of steroids and there has been no recurrence of hepatitis. She has not developed any features of chronic liver disease, and liver function tests over the next 24 months have been normal.

The features in this patient are consistent with immuno-allergic drug-induced hepatitis, which is rare after first exposure, has a delayed onset that is shorter on rechallenge, and has characteristic biopsy findings of infiltration with activated lymphocytes and eosinophils and absence of interface hepatitis and steatosis.

Acute allergic hepatitis due to sodium saccharinate used as the excipient in a parenteral methylprednisolone preparation (Solupred®; Laboratoire Houdé, Puteaux, France) has been reported. The excipients in Solu-Medrone® are sodium hydrogen phosphate and sodium phosphate.

An extensive literature search suggests that immune-allergic reaction resulting in clinically significant and histologically proven acute hepatitis has not previously been reported for methylprednisolone. There has been one case report of subclinical, recurrent, transient transaminasemia with temporal relation to high-dose methylprednisolone injection for multiple sclerosis but there was no mention of exact
formulation used, neither was any biopsy done to elucidate the nature of hepatic damage.\textsuperscript{1}

\textbf{References}


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