Cholestatic jaundice due to toxoplasma hepatitis

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Summary

A case of toxoplasma hepatitis presenting with cholestatic jaundice is described. The diagnosis was based on serological testing and evidence of hepatitis on biopsy.

Introduction

Acquired toxoplasmosis may present as acute hepatitis (Vischer, Bernheim and Engelbrecht, 1967; Weitberg *et al.*, 1979; Bars *et al.*, 1978; Kouba, Jira and Zitova, 1971). Bars *et al.* (1978) in a survey of the literature reported 11 such cases. Weitberg *et al.* (1979) reported a case of granulomatous hepatitis due to *Toxoplasma gondii* and suggested that the severity of hepatitis may be greater than previously described. In most patients the outcome is favourable without specific treatment (Weitberg *et al.*, 1979).

Case report

A 62-year-old farmer's wife was admitted with a history of anorexia, lassitude and exhaustion for 2 weeks and of jaundice for one week. On the day before admission a rash had developed. She had received a post partum blood transfusion 25 years previously. The patient had been to Portugal 2 years previously and had returned from a holiday in Oberammergau 2 days before admission. She took sherry occasionally and was receiving no medication.

On admission she was pyrexial (38°C) and deeply jaundiced with a generalized maculopapular rash and scratch marks. She did not have palpable lymph nodes or spider naevi. The liver and spleen were not enlarged and the remaining examination was normal.

The haemoglobin and haematocrit were normal. Total white cell count was $25.5 \times 10^9/l$ with 35% neutrophils, 62% lymphocytes (with many atypical lymphocytes) and 3% monocytes.

The prothrombin time was 15.5 sec with a control of 12.5 sec. The erythrocyte sedimentation rate was

2 mm/hr. The alkaline phosphatase was greatly elevated at 1024 i.u./l (normal 30–100), aspartate aminotransferase 243 i.u./l (normal 5–40), total bilirubin 200 $\mu\text{mol/l}$ and conjugated bilirubin 120 $\mu\text{mol/l}$. The total protein was 71 g/l, albumin 27 g/l, and electrophoresis showed a slight increase in gammaglobulin. The Paul Bunnell test and serology for adenovirus, hepatitis A, hepatitis B, mumps virus, herpes simplex, measles, varicella, cytomegalovirus, leptospira, mycoplasma, brucella and psittacosis were negative, in both acute and convalescent sera. The chest X-ray and abdominal ultrasound examination were unremarkable. An attempted transhepatic cholangiogram was unsuccessful.

Her temperature fell to normal after 2 days. The rash faded gradually over a week. After 2 weeks the stool became dark and her serum bilirubin started to fall. Liver function tests returned to normal after 10 weeks. The atypical lymphocytes persisted for a long time.

Three weeks after onset of symptoms the toxoplasma serology showed a positive dye test of 1 : 1024, haemagglutination test 1 : 4096, fluorescent IgM 1 : 40 and specific IgM (after fractionation) of 1 : 20, which was consistent with acute infection. Repeat serology after 10 weeks showed a positive haemagglutination test of 1 : 2048 and dye test of 1 : 1024. Fluorescent IgM was negative. A liver biopsy, performed 12 weeks after the onset of symptoms, showed infiltrations of portal tracts and sinusoids by mononuclear cells. Focal necrosis and degeneration of hepatocytes were seen. *Toxoplasma gondii* were not identified in the liver biopsy. The patient improved progressively without treatment and has been well subsequently.

Discussion

Vischer *et al.* (1967) reported two cases of toxoplasma hepatitis and demonstrated *Toxoplasma*

gondii in the liver in both. Two presentations of post-natally acquired hepatic toxoplasmosis were described by Kabelitz (1962). One is a late complication of cervical or generalized lymphadenitis (Vischer *et al.*, 1967, Geyer, 1966); the other is liver disease without preceding lymphadenopathy or lymphocytosis. Weitberg *et al.* (1979) described a third variety with a granulomatous hepatitis and generalized lymphadenopathy occurring concurrently. Their patient also had abnormal lymphocytes. Bars *et al.* (1978) described one patient with toxoplasma hepatitis in whom sub-maxillary glands were involved later in the illness without any abnormal lymphocytosis. Our patient presented with acute hepatitis and although she did not have any lymph node enlargement there was marked atypical lymphocytosis. Occasionally eosinophilia is observed (Jones, Kean and Kimball, 1969).

The majority of patients described hitherto have had mild hepatitis reflected principally in the serum transaminase levels with no evidence of cholestasis. In contrast our patient presented with the clinical and biochemical picture of cholestatic jaundice. Her alkaline phosphatase was markedly elevated at presentation and bile pigment was also absent from the stool, which suggests that hepatitis was severe (Weitberg *et al.*, 1979).

The principal method of diagnosis in general are the serological tests for specific toxoplasma antibodies. IgM antibodies may be detected by an indirect fluorescent antibody test, Sabin-Feldman dye test, indirect haemagglutination test and complement fixation test. IgM antibodies, detected by an indirect fluorescent antibody technique, appear in the first week and peak within a month. In most cases the IgM titre will then revert to negative within a matter of months and in a minority as early as 3 weeks after infection. Thus a single high IgM antibody titre establishes the diagnosis of recently acquired or reactivated infection (Krick & Remington, 1978).

In our patient the first serum specimen for toxoplasma antibodies was tested 3 weeks from the onset of her symptoms. This showed a titre of 1 : 40 of fluorescent IgM antibodies and very high titre in the dye and haemagglutination tests. The repeat test after 13 weeks showed a complete absence of fluorescent antibody which establishes diagnosis of recent infection by *T. gondii* beyond doubt.

The liver in toxoplasma hepatitis reportedly shows infiltration of portal tracts and sinusoids by mononuclear cells and foci of hepatic necrosis. These changes were identified in the liver biopsy from our patient. Some workers have demonstrated toxoplasma trophozoites in the areas of necrosis and

inside liver cells using the Giemsa stain and by a fluorescent antibody method (Vischer *et al.*, 1967; Weitberg *et al.*, 1979). Protozoa were not identified in our biopsy specimen, but this was taken 12 weeks after the onset of illness when the patient had improved and toxoplasma might be expected to have disappeared from the liver. The differential diagnosis includes cytomegalovirus infection, infectious mononucleosis and malignant lymphoma. In the absence of these and with positive serology for acute infection by *T. gondii*, it is reasonable to assume the hepatitis to be due to *T. gondii*.

The recommended treatment of toxoplasmosis consists of drugs including pyrimethamine and sulphadiazine although this has been questioned (Weitberg *et al.*, 1979; Kabelitz 1962; Beauvais *et al.*, 1974). Our patient was not treated with chemotherapy and recovered completely. This suggests that it may not be essential to treat these patients unless they remain unwell after several weeks. Furthermore this case reinforces the observations of others that *T. gondii* should be considered as a cause of acute hepatitis. We suggest that as the prognosis appears to be good in most patients, conservative treatment should be adopted initially with high likelihood of spontaneous recovery thereafter.

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