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Hepatic dysfunction in falciparum malaria

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HEPATIC DYSFUNCTION IN FALCIPARUM MALARIA

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Mild jaundice due to haemolysis[1] is common in severe falciparum malaria. Severe jaundice with bilirubin above 250umol/L has rarely been reported. We describe two cases of severe jaundice resulting from hepatocellular dysfunction induced by falciparum malaria. Both responded to treatment and liver functions returned to normal following treatment.

CASE I

A 30 year old lady, 10th gravida of eight months gestation presented with complaints of high grade fever for 10 days and progressive jaundice for 6 days.

11cr past medical history was unremarkable and there was no history of jaundice in her previous pregnancies.

On examination, she was very ill with temperature of 38°C, had severe jaundice and was anaemic. Her abdominal examination revealed pregnancy of 8 months gestation with normal foetal heart sounds. There was epigastric and right hypochondrial tenderness. Liver and spleen could not be palpated because of abdominal distension. The rest of her examination was normal.

Investigations

Blood film showed falciparum trophozoites and gametocytes, count was reported as high. Other investigations were Hb 6.6 gm/dl, WBC 7.1 x 10^9/L, platelets 91 x 10^9/L, reticulocytes 0.2.%, creatinine 327,umol/L, BUN 24 mmol/L, serum electrolytes were normal, haptoglobulin less than 0.38 gm/L (0.6 - 3.0), LDH = 2082 lu/L (253. 548). Bilirubin 510 1umol/L, with direct 323 umol/L, alkaline phosphatase 125 IU/L (29 - 132), ALT 81 lu/L (3-33), gamma GT 260 IU/L(3 -50), albumin 35 G/L. HBsAg, anti-HAV (1gM), anti-HBc (1gM) were all negative. Following diagnosis of falciparum malaria, she was started on quinine sulphate 600 mg three times daily.

The day after admission, she went into spontaneous labour and delivered a healthy child. She improved following delivery, and her fever and jaundice progressively settled. She was transfused 3 units of blood to correct her anaemia. Clinical examination following delivery showed that liver was enlarged 6 cm below right costa! margin. Ultrasound of abdomen after delivery confirmed that the liver was significantly enlarged but there was no intra or extrahepatic biliary dilatation. She was discharged after 10 days in a satisfactory condition.

Repeat liver function tests at 4 weeks showed bilirubin was 22 1urnol/L, ALT 377 lU/L, alkaline phosphatase 551 IU/L (29 - 132). Repeat ultrasound was normal. Liver biopsy at this stage showed preserved lobular architecture, with swelling of hepatocytcs, kupifer cells showed brownish black malarial pigment. Portal tracts were mildly dilated with inflammatory cell infiltrate (Figure).

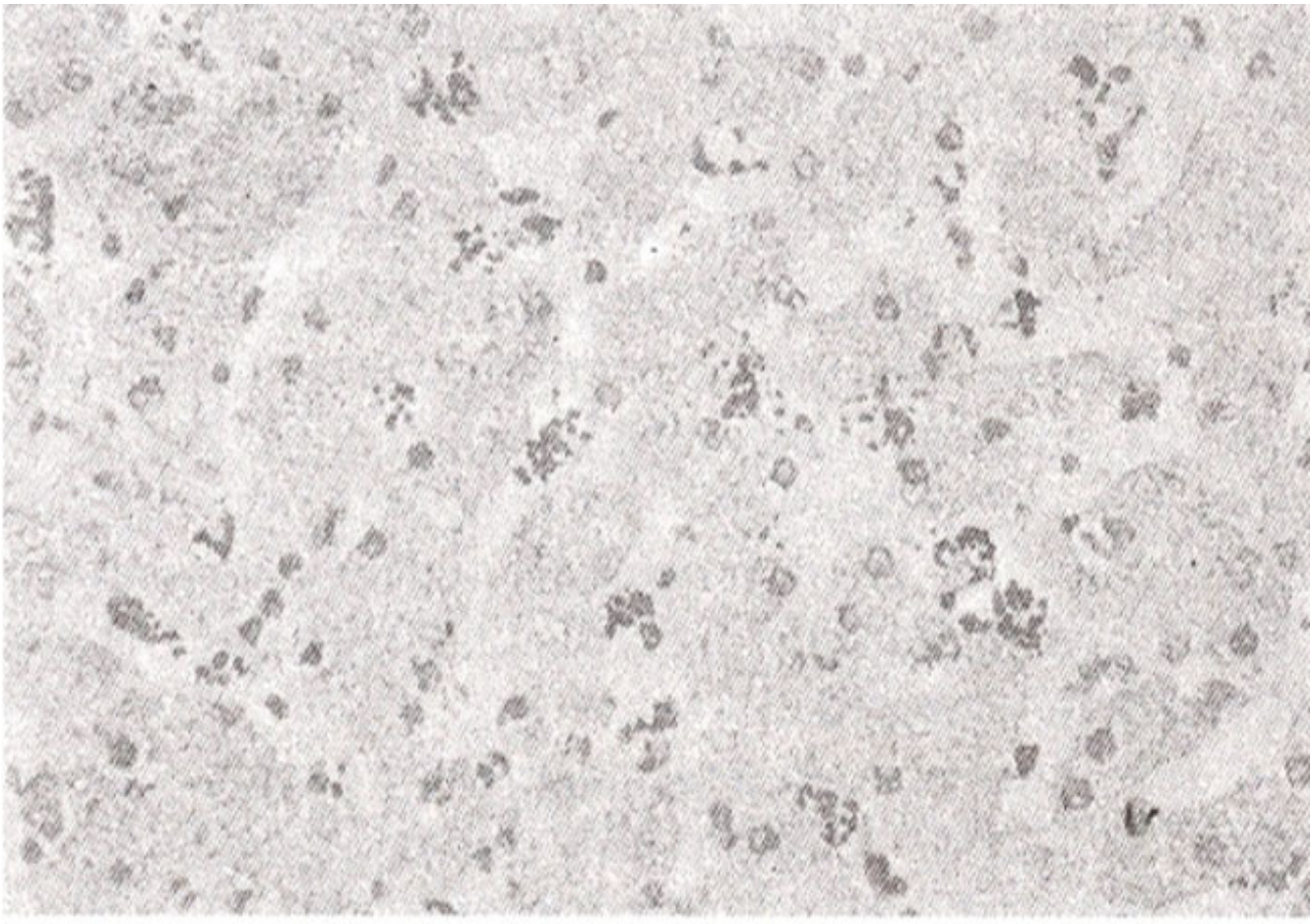

Figure. Liver biopsy showing malarial pigment (black colour) within the sinusoid. H & E x 400

She was seen again 3 months later. Her physical examination was normal and all her liver function tests had returned to normal.

CASE2

A 30 year oldAfghani residing in USA for past several years developed low grade fever during his trip to Karachi. Five days following the onset of fever he developed progressive jaundice.

On examination patient had severe jaundice. His temperature was 37.4 °C. His liver was enlarged 10 cm below right costal margin and it was tender to touch. Rest of his physical examination was normal. Spleen was not palpable.

Investigations

Blood film - falciparum malaria trophozoites and gametocytes were seen. Hb was 13.3-G/dl, WBC 13.5 x 109/L, platelets 38 x 109/L, creatinine 264 umol/L, BUN 21 mrnol/L, bilirubin - 290 Aumol/L, direct 180 uimol/L, gamma GT 210 lU/L (3-50), ALT 75 IU/L (3-33), alkaline phosphatase 110 Iu/L, albumin 27 G/L, LDH = 1345 lU/L (253 - 548).

HBsAg, anti-HAY (1gM), anti-HBc (1gM) were negative. Ultrasound abdomen - diffuse enlargement of liver.

Patient was treated with quinine sulphate 600 mg three times daily, and he responded well.

Seven days later his bilirubin decreased to 40.8 umol/L, ALT was 156 lU/L, alkaline phosphatase 166 lU/L. In 6 weeks time, his liver function tests were normal and liver had considerably decreased in size.

DISCUSSION

The incidence ofjaundice in falciparum malaria has been reported in various studies ranging from 2.5% to 20-30%[2]. In most instances it is mild in severity and caused by destruction of red blood cells both intravascularly and by sequestration of parasitized cells in the spleen and other parts of microcirculation.[3] In some hepatocellular dysfunction may contribute to jaundice. Whatever is the cause,it is generally considered to be mild and bilirubin level above 51.3 umoI/L has been reported to be rare[4]. In the study of Ramachandran regarding jaundice and hepatomegaly in primary malaria, maximum level of bilirubin reported was 8721 umol/L[5].

In our two patients jaundice was severe in intensity. Massive hepatomegaly and elevation of liver enzymes suggested hepatic injury. First paticnt's liver biopsy confirmed involvement by falciparum malaria.

Liver function tests in malaria were first studied in 1923 by MacCormac and Dodds[6], who observed an increase in urinary urobilinogen and urobilin. Maegraith reported liver damage in uncomplicated cases of falciparum malaria and described increased excretion of urobilin and reduction in excretion of azorubin-S[7]. In 1966 Sadun et al[8] first used liver enzymes to detect liver damage in malaria. They found elevation of ALT and low albumin in patient with falciparum malaria. Alkaline phosphatase has been reported to be either normal and there is moderate reduction[8]. In both of our patients, alkaline phosphatase was normal at presentation but rose later before falling back to normal in few weeks. The rise in alkaline phosphatase could be due to predominant cell wall injury and also suggests cholestatic contribution to jaundice.

Clinically hepatomegaly has been reported to occur in 70% cases of vivax and falciparum malaria[9]. In one study it was found to be more common than splenomegaly in malaria[4].

Various histopathological changes have been described which include reticuloendothelial cell hyper-plasia, pigmentation of kupifer cells, fatty changes, sinusoidal and portal infiltration and cholestasis[10]. Out of these, most consistent finding has been reported to be reticuloendothelial cell hyperplasia and pigmentation of kupffer cells.

Non-specific "reactive hepatitis" was the biopsy diagnosis given by Ramachandran in his review on hepatic biopsy in primary malaria from falciparum and vivax[4].

In our two cases severe jaundice was the result of combination of haemolysis and hepatic damage induced by falciparum malaria. Although the concept of "malarial hepatitis" has been challenged by some authors,[1] we feel that falciparum malaria did produce hepatic dysfunction causing severe jaundice in our patients as evidenced by the elevated transaminases and histopathology of the liver.

Due to common belief that malaria only causes mild jaundice, an error in the diagnosis may be made, unless falciparum malaria is considered in the differential diagnosis.

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