CASE STUDY

FULMINATING VIRAL HEPATITIS ASSOCIATED WITH ACUTE FALCIPARUM MALARIA

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SUMMARY

After 6 months residence in Ghana, a 41-year old non-Ghanaian developed a febrile illness which proved at the outset to be malaria with heavy falciparum parasitaemia. Despite prompt treatment with adequate doses of parenteral chloroquine, the illness and fever persisted. Jaundice was noticed within one week of onset of the illness. Liver function tests revealed evidence of severe hepatitis with positive hepatitis-B surface antigen. Clinical evidence of hepato-cellular failure manifested by hepatic flap, rapidly accumulating ascites, in addition to the jaundice was followed by confusion coma and death within 48 hours of onset of jaundice. Post mortem examination showed an enlarged liver with fulminating necrotic hepatitis, ascites, and an enlarged fluffy and friable spleen which disintegrated on handling. The hypothesis that the fulminating nature of the hepatitis was facilitated by malaria-induced immuno-suppression referable to splenic disruption is discussed.

Key Words: Viral hepatitis *falciparum malaria*, immunity, Ghana

INTRODUCTION

Malaria and viral hepatitis are both endemic in this country. Although large numbers of both conditions are seen throughout the year, their simultaneous occurence has not been well documented, nor has the nature of such association been investigated. The clinical and public health significance of such an association is therefore unknown. The bulk of the cases of hepatitis in this country present as mild infections, and full recovery is the rule. The predominant clinical impression is that the few cases which turn out to be fulminating and/or end fatally were associated with pregnancy, alcoholism, malnutrition and poor general health, all of which have in common a lowered resistance to infection most probably of immunological nature. It has therefore been our practice to look for the above factors in all cases of hepatitis in order to anticipate the fulminant ones. The occurrence of fulminating hepatitis in a robust well-nourished caucasian with none of the factors enumerated above apart from severe malaria provoked this case study which provided some clinico-pathological evidence in support of the hypothesis that malaria induced immuno-suppression could be a factor in fulminating viral hepatitis.

It is well documented that malaria is capable of reducing immunological response to various antigens. Malaria-induced immuno-suppression in relation to bacterial infections has been reported by several authors.[1-4] Greenwood et al[5] using standard immunological tests demonstrated that children with malaria were deficient in humoral antibody response, while animal experiments have revealed immuno-suppression in malaria-infected mice.[6]

In 1979 Michel et al[7] reported depression of induction of T-lymphocyte delayed hypersensitivity by malaria. Immuno-suppression in relation to various viral antigens by murine malaria has also been reported by various authors.[8,9]

METHODS

Case History:

The patient was a 41-year old Caucasian of German extraction who had come to Ghana to work 6 months prior to the illness. He presented with a short (4-day) history of febrile rapidly progressive illness, associated with anorexia, nausea, vomiting, abdominal pain and diarrhoea. In the past he had enjoyed good health, and claimed to have taken malaria prophylaxis regularly for the 6 months he had been in the country. He was working in the hinterland as project manager for a bore-hole water company.

On examination, he was found to be drowsy and disoriented, deeply jaundiced, febrile (temperature 38.2^0C) with cold clammy extremeties. There was no lymphadenopathy. Radial pulse was 72 per minute, small volume, blood pressure was 100/70 mm Hg. No significant findings were made upon further examination of the cardio-pulmonary systems. The abdomen was distended with fluid, the liver was enlarged (2cm below the right costal margin) and so was the spleen which was palpable 4cm below the left costal margin. There was no neck stiffness, and no neurological deficits apart from the drowsiness.

Investigation revealed haemoglobin; of 110g/l, total white cells; 4.5×10^9/l with 71% neutrophils and 27% lymphocytes. Blood film examination showed numerous malarial (P. falciparum) parasites. On admission, liver function tests revealed total bilirubin of 279umol/l (normal 3-20), direct bilirubin 200umol/l indirect 79umol/l; SGOT 160iu/l (normal 1-28), SGPT 120iu/l (normal 1-21) all pointing to severe liver damage. 12 hours after admission, total bilirubin had risen to 400umol/l, and direct and indirect bilirubin to 280 and 120umol/l respectively. Hepatitis B surface antigen (HBs Ag) was positive. His condition deteriorated rapidly and within 16 hours of admission the jaundice had deepened further and he was unconscious. The regime for liver failure was started. Ascites which had been minimal on admission progressed rapidly and the abdomen became tensely distended. When no urine had been passed 12 hours after admission, a catheter was passed into the bladder and 30ml of urine collected suggesting oliguric renal failure. He was being prepared for haemodialysis when he died, 24 hours after admission. Post mortem examination revealed the body of a well nourished middle-aged caucasian who was deeply jaundiced. The liver was enlarged but flabby due to necrosis. Spleen was swollen, soft and fluffy and its normal architecture was disrupted. The brain was swollen but contained no malarial pigment. Heart, lungs, kidneys, stomach, pancreas, intestines and lymph nodes were normal. Death was due to liver necrosis from hepatitis and severe malaria with splenic destruction.

DISCUSSION

The patient being non-immune for malaria, and working under primitive camp conditions in the bush, not surprisingly, developed rapidly progressive malaria. The patient had been in the country for only 6 months, so he either contracted the hepatitis virus shortly after arrival in the country or harboured the virus before arrival in Ghana. In Ghana fulminant hepatitis has been known to be a function of immuno-suppression especially that of pregnancy and malnutrition. In this patient, it was suspected that the fulminant hepatitis was related or facilitated by the heavy falciparum parasitaemia in view of the well-documented phenomenon of malaria-induced immuno-suppression referred to in the introduction of this paper. Although the bulk of the clinical and experimental evidence for malaria-induced immuno-suppression deals with bacterial infections, recent studies in man and experimental mice have shown that severity of viral infection is exaggerated by malarial infection.[8, 9, 10.] More specifically Nickel et al[11] working with mice infected with *Plasmodium yoeli* and *berghei* were able to demonstrate impairment of virus specific cytotoxic T-lymphocyte responses to viral antigens. They concluded that the inhibiting effect of malaria on the above responses was due to splenic disruption involving macrophage function impairment by the parasitaemia as suggested by the work of Loose et al[12], Warren and Weindanz[13] and Brown et al[14]. It is interesting to note in the light of the conclusion drawn by Nickel et al that, the spleen of the patient under discussion had been completely destroyed by the heavy falciparum parasitaemia, thus giving credence to the suspicion that, there was immuno-suppression of the type described by the authors.

The case history apart from providing clinico-pathological evidence of malaria-induced T-cell immuno-suppression for a viral infection, is significant in other respects. It shows clearly that in endemic malarious zones jaundice in malaria is not necessarily haemolytic, i.e. clinical and biochemical assessment must be thorough, since viral hepatitis is a real possibility in severe malaria. Secondly this case suggests that control of malaria might definitely reduce the incidence and/or severity of hepatitis in our environment.

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