

Severe Haemophagocytic Syndrome in Falciparum Malaria

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Malaria is responsible for 0.5-1.2 million deaths each year¹. The majority of fatal cases are due to Plasmodium falciparum infection which is known for its severity, complications and drug resistance^{1,2}. Most of the fatalities occur in children and non-immune travellers to the endemic areas¹. A number of complications have been described in falciparum malaria² but, to the best of our knowledge, haemophagocytic syndrome has not been described in this condition. We report a case of Chloroquine resistant falciparum malaria which was complicated with severe haemophagocytic syndrome.

Case Report

A young German tourist reported on 30 August, 1993 with fever, generalized weakness and yellow discoloration of eyes for seven days. He had been in Pakistan for the last 20 days and was not having chemoprophylaxis for malaria. He was non-addict and gave no history of risk factors for HIV infection. On examination, he was pale and jaundiced, temperature was 39.2°F. The positive findings, on systemic examination, were hepato (2'cm) splenomegaly (3 cm). His blood counts (Table) revealed mild anaemia with normal leucocyte and platelet counts. Peripheral blood smear showed numerous trophozoites and gametocytes of Plasmodium falciparum. Urine examination revealed increased urobilinogen but no haemoglobinuria and liver function tests showed hypethilirubinemia (168 umol/L) with normal hepatic enzymes. The screening tests for viral hepatitis and HIV infection were negative. The patient was put on standard doses of Chloroquine, to which he did not respond. Repeat blood counts on 3rd September (Table), showed a fall in Hb, leucocyte count and platelet count and malarial parasites were still present in almost the same numbers in the peripheral blood. Serum bilirubin raised further (340 umol/L). The patient was then put on standard doses of Fansidar with which his fever subsided and by 7th September the bilirubin level came down to 59.5 umol/L. At this stage, however, his blood counts showed a persistent fall in Hb, TLC and platelet count although the malarial parasites had disappeared from the peripheral blood (Table): Because of pancytopenia a bone marrow aspiration biopsy was performed on 9th September. The examination of Leishman stained bone marrow smears revealed marked proliferation of mature looking histiocytes, the majority of which showed active haemophagocytosis. Almost all types of blood cells were being phagocytosed by these macrophages (Figure).

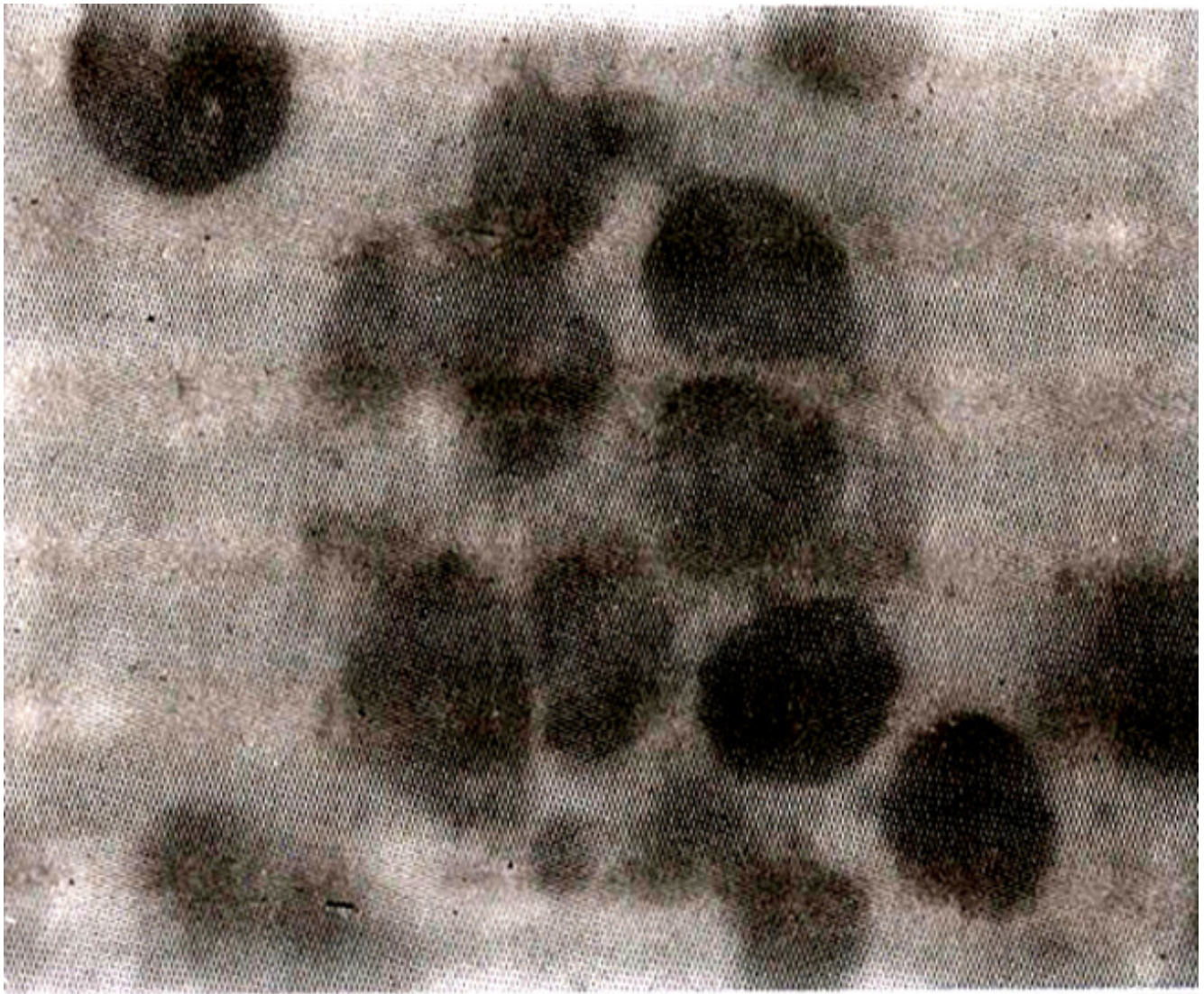


Figure. A histiocyte showing ingested mature and immature haemopoietic cells.

There was associated cry thyroid hyperplasia with normal mvelopoiesis and normal mega karyocytes. Few gametocytes and occasional trophozoite of *Plasmodium falciparum* were seen in the bone marrow. One week later, his blood counts had markedly improved and no malarial parasite could be seen in the peripheral blood (Table).

Table. Laboratory parameters.

Parameter	30 Aug	3 Sept.	7 Sept.	15 Sept.
Hb. (g/L)	120	110	93	118
TLC(x10⁹/L)	4.0	3.5	3.0	4.2
Platelets (x10⁹/L)	210	140	74	150
Serum Bilirubin (umol/L)	168	340	59.5	15.3
Malarial parasite in peripheral blood.	Present	Present	Absent	Absent

Discussion

Histiocytic hyperplasia with haemophagocytosis (HHH) was first recognized by Scott and Robb-Smith in 1939³ and was believed to be a malignant condition for a long time. In 1979 a similar benign and reversible condition was described in association with viral infections in immunosuppressed patients by Risdal et al⁴. Since then, reactive histiocytic hyperplasia with intense haemophagocytosis has been described in a number of benign and malignant disorders. These have been reviewed by Suster et al⁵. However, malaria has not been documented as a cause of HHH. Risdal et al⁴ proposed that this type of haemophagocytosis results due either to alteration in the phagocytic cells or in the ingested elements and probably represent an exaggeration of the normal function of the histiocytes. In our case a high antigen load, due to malarial parasites in a previously unexposed individual, might have resulted in an exaggerated macrophage response. It has also been suggested that increased production of macrophage colony stimulating factor probably could result in proliferation of histiocytes⁶. The marked stimulation of the immune system could also result in excessive production of phagocytosis inducing factor (PIF) by CD4⁺ T-lymphocytes⁷ and PIF could then cause histiocytic proliferation and haemophagocytosis. These mechanisms may also have been operative in this case. Besides the Tumour Necrosing Factor (TNF), which is produced in excess in falciparum malaria, also induce phagocytosis⁸. It is important to note that the benign haemophagocytosis can be differentiated from the malignant histiocytosis by the greater involvement of the bone marrow than other reticulo-endothelial tissue, the mature appearance of the proliferating phagocytic cells and by the improvement in the clinical condition after successful therapy⁴. However, even benign haemophagocytosis may prove fatal, because of the resulting pancytopenia. It can easily be reverted by treating the underlying cause and supporting the patient during pancytopenic phase.

References

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