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Case Report

Reactivation of Herpes zoster in an adult with *Plasmodium* infection

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People with malaria have a reduced immune response not only to the malaria parasite, but also to other organisms and antigens. Clinical studies and animal models have shown that plasmodia can temporarily suppress a host's humoral and cellular immune response, predisposing the host to super infections with other microorganisms. *Plasmodium* infections have been shown to induce alterations in immune reactivity and acute malaria has been associated with reactivation of chronic and latent viral infections such as Herpes zoster[1], Herpes simplex and Epstein-Barr virus, most of these commonly seen in children. There are no case reports of *Plasmodium* infections in adults with reactivations of chronic latent viral infections. An adult with *Plasmodium falciparum* infection, who had developed Herpes zoster in the course of illness is reported here. The case illustrates the need for considering the immunosuppressive effect of acute malaria, especially due to *P. falciparum* when latent viral infections manifest during the course of illness.

Case report: A 44-year old man was admitted with five days history of high grade fever associated with chills and rigors. On the second day of fever, he developed multiple vesicular skin lesions in the anterolateral part of left thigh also extending in continuity to the back above the gluteal region. He did not have any significant medical illness in the past. Bedsides examination, disclosed a regular pulse of 76/min, blood pressure 126/76 mm Hg, conjuctival pallor, scleral icterus (Fig. 1a), liver enlarged four centimeters below right costal margin, mild splenomegaly and multiple vesicular eruptions in L_1 and L_2 dermatomes (Figs. 1b & c).

Laboratory investigations revealed anaemia (Hb 6.8 g/dL), indirect hyperbilirubinemia (total bilirubin 3.1 mg/dL, direct bilirubin of 0.5 mg/dL), aspartate aminotransferase 122 IU/L, alanine aminotransferase 97 IU/L and alkaline phosphatase 216 IU/L. Peripheral blood showed normal leukocyte counts, schizonts and ring forms of *P. falciparum* and *P. vivax*. Blood sugar, renal parameters and serum electrolytes were within normal range. Blood ELISA for HIV was negative. Chest roentgenogram and ECG were normal. Dermatologist was consulted for the skin lesions. He opined that such vesicular eruptions were typical of Herpes zoster and confirmed it with Tzanck smear which showed characteristic multinucleated syncitial giant cell (Fig. 2).

In view of mixed plasmodial infection, treatment was started with oral chloroquine (IPCA Laboratories, Mumbai, Maharashtra, India) 10 mg base/kg followed by 5 mg of base/kg at 12, 24 and 36 h, oral primaquine (Nestor Pharmaceuticals, Goa, India) 0.25 mg/kg for 14 days, intramuscular arteether (Themis Medicare Ltd, Vapi, Gujarat, India)150 mg im for three days, doxycycline (Elegant Drugs Pvt. Ltd., Chalmatti village, Karnataka, India) 100 mg twice

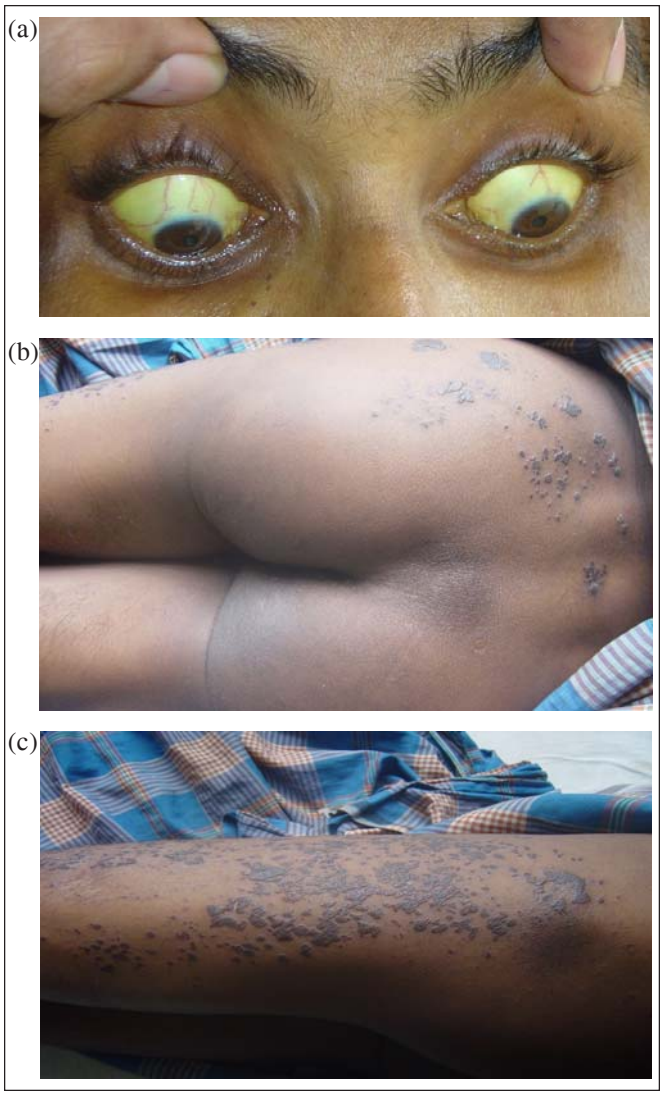

Fig. 1: Patient showing (a) scleral icterus; (b) multiple vesicular eruptions in L_1; and (c) multiple vesicular eruptions in L_2

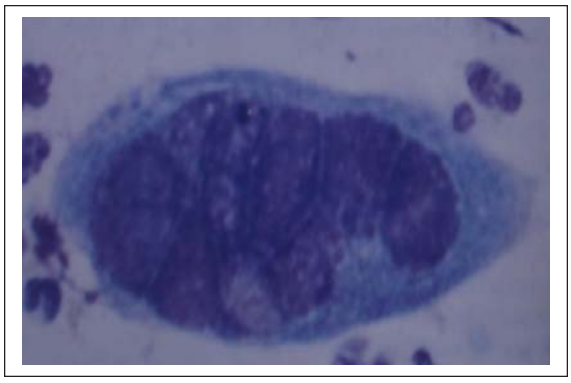

Fig. 2: Tzanck smear showing multinucleated syncitial giant cell

daily for seven days and oral acyclovir 800 mg five times a day for seven days. Adequate hydration was ensured and renal parameters were monitored frequently. The patient improved slowly, became afebrile on the second day of treatment and repeat blood smear on the third day was negative for *P. falciparum* and *P. vivax*. Zoster showed signs of healing on the fourth day. There was no secondary infection of the vesicles, crusting started on the seventh day and the patient was discharged on the tenth day. On follow-up after one week, zoster had completely healed and fever had not recurred.

To survive their hosts' immunological defenses, microorganisms manage to fine-tune their hosts' immune responses—they suppress these responses enough to allow their own survival, but leave some immune surveillance to prevent uncontrolled growth (which would kill the host). In this way, the microorganism can be passed to another host, so continuing the species. In malaria such parasite induced diminished immune response helps not only to evade the immune mechanisms, but also leaves the host more susceptible to reactivations of latent viral infections[1] and secondary infections like *Salmonella* (non-typhoidal)[2]. Moreover responses to other heterologous antigens including vaccines are also down regulated, thus interfering with large vaccine regimes[3,4].

Earlier studies reported that falciparum malaria is associated with decreased T-lymphocyte response[4]. Recently, *in vitro*[5] and *in vivo*[6] studies have shown that suppression of dendritic cells (DCs) by the parasitized erythrocytes (pRBCs) is the key event. DCs are antigen presenting cells (APCs) essential for innate and adaptive immune responses[7]. DCs' activation is dynamically altered by pRBCs, partly because of deposition of the malarial pigment hemozoin within these cells and also other yet unknown parasite components which would down regulate the immune response[8]. Following presentation of heterologous antigen by pRBCs — exposed DCs, there is less expansion of CD4+ 'helper' T-cells and CD8+ T-

cells that are essential for the induction of adaptive immunity[9]. This annuls the migration of T-cells to the destination site or lymphoid follicles resulting in diminished B-cell differentiation and a resultant failure of the humoral response[10]. By suppressing the CD 8+ T-cell responses which are protective against the liver stage of disease, the host becomes vulnerable for next infection. All these effects are the end result of abnormal DCs maturation and release of inappropriate cytokines following exposure to pRBCs. Also *in vitro* studies have observed that such abnormal DCs fail to undergo apoptotic cell death after antigen stimulation, resulting in prolonged immunomodulatory effects[9].

Thus, the immunocompromised state during acute malaria, especially due to *P. falciparum* predisposes the host to reactivation of latent viral infection as in the present case where Herpes zoster developed during the course of illness. Such reactivations have been observed mostly in children from endemic areas[1] and rarely in adults, which needs to be identified with strict vigilance as it may even prove fatal[11]. This case is being reported to emphasize the significance of malaria associated immuno incompetence in an endemic area, which would compound to the overall morbidity if not identified as part of the illness and treated promptly.

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