



### Human immunodeficiency virus Associated with Haemophagocytic Syndrome in Pregnancy: A Case Report

*Syndrome Hemophagocytaire Associe Au Vih Au Cours De La Grossesse : A Propos D'un Cas*

O. P. Arewa\*, A. A. Ajadi†

#### ABSTRACT

**BACKGROUND:** Haemophagocytic syndrome (HPS) is a rare condition that has been documented in association with viral, bacterial, fungal and parasitic infections as well as a wide spectrum of malignant neoplasms and autoimmune diseases. Whereas HPS is a known cause of anaemia in HIV infection, its occurrence is uncommon. Its occurrence in pregnancy is even rarer and very few such cases have been reported.

**METHODS:** Full clinical evaluation and investigations including bone marrow aspiration cytology were done to elucidate the cause of the anaemia.

**RESULTS:** Evaluation revealed severe anaemia, increased serum bilirubin HIV positivity and a low CD4 count. The final diagnosis confirmed the case to be haemophagocytic syndrome in pregnancy. A 31-year-old primigravida presented at 21 weeks of gestation with a two-week history of fever, jaundice and abdominal pain. She responded to treatment.

**CONCLUSION:** Although a rare condition, this case highlights the importance of a high index of suspicion for the syndrome in HIV positive pregnant women with persistent Coombs negative haemolytic anaemia. Full recovery could be expected following prompt institution of HAART and delivery. *WAJM* 2011; 30(1): 66–68.

**Keywords:** HIV/AIDS; Haemophagocytic syndrome; Pregnancy

#### RÉSUMÉ

**CONTEXTE:** Le syndrome hemophagocytaire est une affection rare pouvant être lié aussi bien aux infections virale, bactérienne, parasitaire, qu'à diverses pathologies néoplasiques, ou auto-immunes. Bien qu'étant une cause bien connue d'anémie au cours de l'infection à VIH, sa survenue est rare ; et encore plus rare au cours de la grossesse. Très peu de cas en ont été rapportés.

**METHODES:** Une évaluation clinique complète avec des explorations paracliniques comprenant le medullogramme étaient effectuées pour déterminer la cause de l'anémie

**RESULTATS:** L'exploration a fait état d'une anémie sévère, d'une augmentation de la bilirubinémie, une sérologie VIH positive, et un taux de CD4 bas. Le diagnostic retenu était un syndrome d'Activation macrophagique au cours de la grossesse. Une primigeste âgée de 31 ans, reçue à 21 Semaines d'aménorrhée, pour une fièvre ayant évolué pendant deux semaines avec une douleur abdominale et un ictère. Sous traitement l'évolution fut favorable

**CONCLUSION:** Bien qu'étant rare, cette observation met en évidence la pertinence de suspecter un syndrome hémophagocytaire pour une patiente enceinte, vivant avec le VIH, et avec une anémie hémolytique persistante avec test de Coombs négatif. Une guérison complète est possible avec la prompte mise en route d'un traitement antirétroviral hautement actif et l'accouchement. *WAJM* 2011; 30(1): 66–68.

**Mots -cles:** Vih, Syndrome Hemaphagocytaire, Grossesse.

## INTRODUCTION

Haemophagocytic syndrome (HPS) is a clinico-pathological entity characterized by systemic proliferation of benign macrophages in the bone marrow, spleen, liver and lymph nodes with inappropriate phagocytosis of erythroid precursors, granulocytes and platelets.<sup>1</sup> Its occurrence has been documented in association with viral, bacterial, fungal and parasitic infections as well as a wide spectrum of malignant neoplasms, autoimmune diseases and drugs.<sup>1</sup> Clinically, patients present with fever, multilineage or unilineage cytopenias, jaundice and evidence of liver dysfunction while diagnosis is confirmed with evidence of active haemophagocytosis by cells of the monocyte-macrophage system.<sup>2</sup>

Whereas HPS is a known cause of anaemia in HIV infection,<sup>3,4</sup> the occurrence of the syndrome in pregnancy is a rare event.

## Case Report

A 31-year-old unbooked blood group O+ primigravida, presented at gestational age of 21 weeks with two weeks history of intermittent high grade fever, jaundice, abdominal, and back pains and generalized weakness. She also had complaints of palpitations, generalized pruritus, loss of appetite and vomiting. There was no history of diarrhoea or significant weight loss. She received two units of packed cell transfusion at the referral peripheral hospital on account of severe anaemia two weeks earlier. She had no respiratory or neurological symptoms. Her past medical and drug history was unremarkable. She was married in a monogamous setting.

On examination, she was pale, febrile (admitting temperature 38.4°C) and jaundiced. The integument was normal and there was no peripheral lymph node enlargement. Her liver and spleen were not palpably enlarged. The symphysio-fundal height of the gravid uterus was 20cm. The laboratory investigations requested included a complete blood count with reticulocyte count, direct Coombs test, serum bilirubin, haemoglobin electrophoresis, malaria parasite screen, liver enzymes assay, urinalysis, viral screening for Hepatitis B and C.

Screening for Human Immunodeficiency Virus (HIV) was later requested after pretest counseling.

A CD4 cell count and bone marrow aspiration studies were subsequently performed. An abdominal ultrasound scan for foetal well-being assessment was also done.

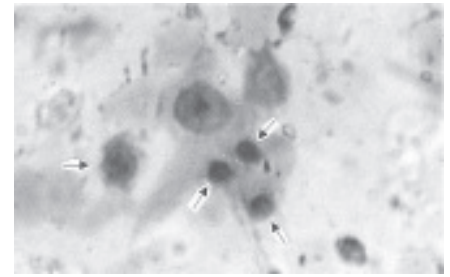
## PATIENT MANAGEMENT AND OUTCOME

The preliminary working diagnosis was haemolytic anemia in pregnancy with the differential diagnosis of malaria-induced haemolysis in pregnancy, to rule out autoimmune haemolytic anaemia. The platelet count was within acceptable value. The liver aspartate transaminase (AST) and alanine transaminase (ALT) were within normal limits. However the alkaline phosphatase (ALP) was elevated, (Table 1).

**Table 1: Laboratory Investigation Results**

Parameter	Result	Normal Range
<b>Full Blood Count</b>		
PCV (%)	18	30–44
WBC ( $\times 10^9/l$ )	4.2	2.5–11
Platelet ( $\times 10^9/l$ )	125	100–350
Reticulocytes (%)	< 1	1–3
<b>Plasma Electrolytes and Urea</b>		
Sodium (mmol/l)	132	128–142
Potassium (mmol/l)	5	3.5–4.8
Bicarbonate (mmol/l)	22	20–30
Urea	8	2.5–6
<b>Liver Function Test (Serum)</b>		
Total bilirubin ( $\mu\text{mol/l}$ )	39	5–17
Conjugated bilirubin ( $\mu\text{mol/l}$ )	6	<8
ALT iu/l	6	0–12
AST iu/l	4	0–12
ALP iu/l	132	0–32

Direct Coombs Test was negative, while microscopy showed scanty trophozoites of *P. falciparum*. Her haemoglobin electrophoresis pattern was AS while the CD4 count was 100cells/ $\mu\text{l}$ , (normal 400–1,200 cells/ $\mu\text{l}$ ) in addition to being positive for HIV. Bone marrow showed normocellular marrow fragment with a myeloid: erythroid ratio of 1:4. Marrow was hyperplastic and megaloblastic with plasma cells. Other cells included numerous activated macrophage-monocyte cells with phagocytosed erythroid cells (Fig. 1).



**Fig. 1: Photomicrograph of the bone marrow aspirate from the patient showing activated macrophage with phagocytosed erythroid cells (arrows). x 400. Numerous erythrophagocytic macrophages like this were seen in the aspirate.**

Initial management was with antimalaria (amodiaquine) and repeated packed cell transfusion on account of persistent drop in her packed cell volume with a nadir of 15% (Hb 5g/dl). The malaria parasitaemia cleared after the course of antimalaria therapy. The anaemia however persisted. As a result of seropositivity of HIV-1, she was commenced on HAART (zidovudine, lamivudine and nevirapine). Moderate anaemia with jaundice persisted till term in spite of transfusions. At term she was delivered of a live male infant weighing 3.2kg by emergency Caesarean section on account of failure to progress in labour due to malpositioning. The baby had oral Nevirapine administered at the dose of 2mg/kg at delivery. Her post delivery follow up has remained stable with complete resolution of symptoms and normalization of her haemogram and all other indices.

## DISCUSSION

Several pathogens including viruses (HIV, Herpesvirus and Human T cell Leukaemia Virus 1), Mycobacterium tuberculosis, atypical organisms (*Pneumocystis carinii*), and fungi have been found in association with HPS.<sup>5,6</sup> In addition, autoimmune disorders and a wide spectrum of malignant neoplasms and drugs have also been implicated. The central feature in the aetio-pathogenesis of the syndrome is immune dysregulation characterized by low or absent Natural Killer (NK) cell activity with hyperactivation of T lymphocytes and macrophages and consequent pro inflammatory storm.<sup>4</sup> The manifestations

may be acute or subacute with the patient exhibiting fever, malaise, weight loss, rapidly developing cytopenias, jaundice and evidence of liver dysfunction.<sup>1</sup> Bethume *et al*,<sup>4</sup> observed that jaundice in part is a result of the destruction of red cells and their precursors in the marrow, spleen and liver. A liver biopsy was contraindicated in this case as a result of her pregnant state. The human immunodeficiency virus (HIV-1) is the only previously documented aetiology associated with HPS identified in this case. Baraldes *et al*<sup>6</sup> observed that “superimposed immune suppression” is an added risk to the development of haemophagocytic syndrome in HIV/AIDS and indeed HPS development worsens prognosis in them. The relative state of immune suppression which exists in pregnancy is an additional risk on the pathogenesis of immune dysregulation that tipped the patient into developing the syndrome. Although some reports have suggested increased incidence of foetal loss and preeclampsia in pregnant women with sickle cell trait (AS), recent reports have concluded that AS carries no added risk to the outcome of pregnancy as compared to women with normal haemoglobin (AA).<sup>7,8</sup> While the condition has been recognized as a cause of fatality in patients with the diagnosis, HPS is a potentially treatable condition through adequate management of the underlying predisposing condition.<sup>9</sup> Moritaka *et al*,<sup>10</sup> reported successful recovery from HIV associated HPS on treatment with Highly Active Antiretroviral Therapy (HAART).

Disseminated infection with an unusual organism in a patient with haemophagocytic syndrome may represent secondary infection in an immunocompromised host; however, the resolution of the condition following treatment of infection suggests that, in

many cases, it is secondary to the underlying infection.<sup>11</sup>

Our patient was commenced on HAART and gained clinical improvement with resolution of most of the presenting symptoms. However, jaundice and moderate anaemia persisted till term when she was delivered by caesarean section. Full restoration of her haemogram parameters post delivery suggests that the pregnancy had a modulating effect on the condition. A recent report by Teng *et al*<sup>12</sup> similarly suggests a role for pregnancy in the aetiology of haemophagocytic lymphohistiocytosis (HLH). In the report, resolution of symptoms occurred only after termination of the pregnancy.

This case highlights the importance of a high index of suspicion for the couple of HPS in HIV positive pregnant women with Coombs negative haemolytic anaemia. Full recovery with resolution of symptoms can be expected following institution of HAART and delivery.

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