

Case Report:**HIV associated thrombocytopenia**N. Chandra,¹ P. Bhavnadhar,¹ Y. Satyanarayana Raju,¹ Uppin Shanthveer²*Departments of ¹General Medicine, ²Pathology, Nizam's Institute of Medical Sciences, Hyderabad***ABSTRACT**

We report the case of 47-year-old male who presented with fever, cough and expectoration since 4 months and diarrhoea, malaise and dysphagia since 3 months. He was known to have diabetes mellitus and hypothyroidism and was receiving insulin and thyroxine supplementation. He was evaluated outside and was found to be co-infected with human immunodeficiency virus (HIV 1) and pulmonary tuberculosis and was receiving antituberculous treatment. He had hyperpigmented macular and non pruritic rash over his body. Oral thrush was present. Laboratory evaluation showed thrombocytopenia (20,000/ μ L) with giant platelets; bone marrow aspiration and biopsy revealed normocellular marrow with increased and hypolobated megakaryocytes. The patient was treated with tenofovir, emtricitabine and efavirenz, antituberculosis drugs and oral fluconazole. Insulin and thyroxine replacement therapy were continued. He was diagnosed to have HIV associated thrombocytopenia and was started on dapsone treatment. Two months later, his platelet count had become normal. The present case highlights the importance of being aware of HIV associated thrombocytopenia so as to facilitate the prompt recognition and treatment of this condition.

Key words: *Human Immunodeficiency Virus, Thrombocytopenia, Haematological manifestations*

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INTRODUCTION

Haematological manifestations of human immunodeficiency virus (HIV) infection have a broad spectrum, ranging from mild disturbances to life threatening conditions. Thrombocytopenia is one of the haematological manifestations that alerts clinicians.¹ It is a common finding in individuals infected with HIV, affecting approximately 40% of patients during the course of their illness.² Approximately 3% of patients with untreated HIV with CD4+ count greater than 400/uL have platelet count less than 150,000/uL and this incidence increases to 10% in HIV-seropositive patients with CD4+ count <400/uL. Clinically, this entity resembles thrombocytopenia seen in patients with idiopathic thrombocytopenic purpura (ITP). While several reports on HIV-related thrombocytopenia have been documented in the world literature,³ there are few reports on this topic from India.⁴⁻⁶ Recognizing the need to create an awareness regarding asymptomatic thrombocytopenia in patients presenting HIV infection we document

this case and discuss the therapeutic options that are available in this scenario.

CASE REPORT

A 47-year-old male patient presented with fever, cough with expectoration since 4 months, diarrhoea, malaise and dysphagia since 3 months. He was known to have diabetes mellitus and hypothyroidism and was on insulin therapy and thyroxine supplementation for the same. He was evaluated elsewhere for these symptoms and was diagnosed to have HIV-1 infection and was suspected to have pulmonary tuberculosis. His CD4+ count was 94 cells/mm³. There was evidence of right upper lobe infiltrates in chest radiograph, his sputum tested positive for acid-fast bacilli and he was initiated on antituberculosis treatment. He then reported to our out-patient department for further evaluation and management.

He was moderately built and nourished and was afebrile. He had hyperpigmented macular and non pruritic rash over his body. Oral thrush was present. His respiratory, cardiovascular and neurological examination was unremarkable.

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Complete blood count (Table 1) showed thrombocytopenia (20,000/ μ L) with giant platelets; haemoglobin, total and differential leucocyte count and erythrocyte sedimentation rate (ESR) were within normal limits. Serum aspartate aminotransferase [(AST) 45 U/L] and serum alanine aminotransferase [(ALT) 48 U/L] were mildly elevated. Serum bilirubin was 1 mg/dL. Renal parameters were normal. Upper gastrointestinal endoscopy (UGIE) revealed oro-oesophageal candidiasis. Bone marrow aspiration and biopsy revealed normocellular marrow with increased and hypolobated megakaryocytes (Figures 1, 2 and 3).

He was managed with tenofovir, emtricitabine, efavirenz; antituberculosis treatment with rifampicin, isoniazid, pyrazinamide, ethambutol, and oral fluconazole. Insulin treatment and thyroxine replacement therapy were continued. He was diagnosed to have HIV-associated thrombocytopenia and was started on oral dapsone. At 2-months follow-up, his platelet count increased to 150,000/ mm^3 (Table 1) and he remained free of any haematological symptoms.

DISCUSSION

Reduction in all major blood cell lines has been recognized among patients infected with HIV, shortly after the first description of the acquired immunodeficiency syndrome (AIDS). Thrombocytopenia is a common finding in individuals infected with HIV.⁷ It occurs in patients from all major risk groups and may present with at any time during the course of HIV infection, from asymptomatic infection to advanced acquired immunodeficiency syndrome (AIDS). The incidence of platelet abnormalities appears to increase with progressive immunosuppression.⁸ In the current era of combination antiretroviral therapy, it is more commonly encountered among patients with uncontrolled HIV replication and hepatitis C virus (HCV) co-infection.⁹

The causes of thrombocytopenia in HIV-infected patients can be divided into two groups: primary HIV-associated thrombocytopenia (PHAT) and secondary thrombocytopenia.¹⁰ PHAT is the most common cause of low platelet counts encountered in HIV-infected patients. Clinically, PHAT is similar to classic ITP. Platelet counts are often higher in HIV-infected patients,

Table 1: Complete blood picture report at the time of initial presentation and at 2 months of follow-up

| Variable | At initial presentation | At 2 months follow-up |
|---|---|---|
| Haemoglobin (g/dL) | 13.6 | 12.8 |
| MCV (fL) | 84.3 | |
| MCH (pg) | 28.0 | |
| MCHC (mg/dL) | 33.2 | |
| Total leucocyte count(/ mm^3) | 4200 | 5800 |
| Differential count | Neutrophils 76%, lymphocytes 23%, eosinophils 2%, monocytes 1% | Neutrophils 75%, lymphocytes 21%, monocytes 1%, eosinophils 1% |
| Platelet count (/ mm^3) | 20,000 | 150,000 |
| Reticulocyte count (%) | 0.5 | |
| ESR mm (at the end of 1 st hour) | 15 | |

MCV = mean corpuscular volume; MCH = mean corpuscular haemoglobin;

MCHC = mean corpuscular haemoglobin concentration;

ESR = erythrocyte sedimentation rate

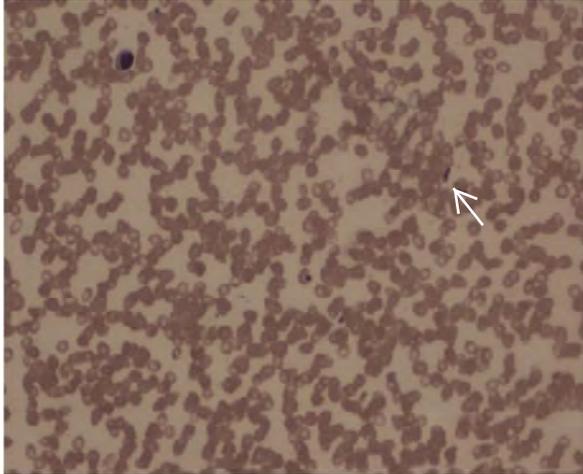


Figure 1: Photomicrograph of the peripheral smear showing giant platelets (arrow) (Geimsa, $\times 200$)

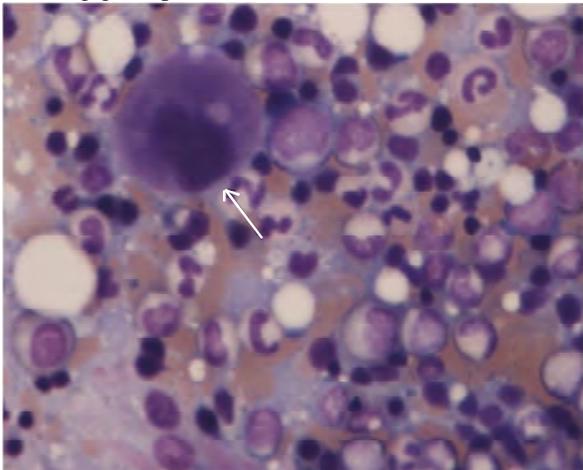


Figure 2: Photomicrograph of the bone marrow aspirate showing hypolobated megakaryocytes (arrow) (Geimsa, $\times 200$)

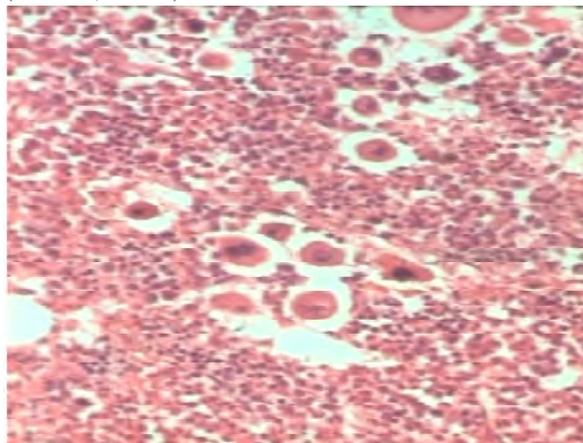


Figure 3: Photomicrograph of the bone marrow trephine biopsy section showing increased megakaryocytes (Haematoxylin and eosin, $\times 100$)

and mild thrombocytopenia occasionally resolves without therapy.¹¹ The aetiology of thrombocytopenia in PHAT is complex. The

combination of normal or increased numbers of megakaryocytes in the face of reduced numbers of circulating platelets in bone marrow examination is seen, as in our case. It suggests the presence of ineffective platelet production and/or increased peripheral destruction. Kinetic studies using radiolabelled autologous platelets from HIV-infected individuals have shown that both factors contribute i.e., there is reduction in platelet survival and platelet production.¹² Secondary causes of thrombocytopenia are generally the result of underlying opportunistic infections, hypersplenism, malignancy, drugs and other co-morbid conditions.¹³

After the exclusion of secondary causes of thrombocytopenia and discontinuation of potentially marrow-suppressing medications, there are many therapies available for the management of PHAT. Individual circumstances dictate the necessity and acuity of therapy. Spontaneous remission has been seen in as many as 18% of patients who have PHAT. In those who do not, therapy historically has consisted of institution of zidovudine (AZT).¹³ Recent studies¹⁴⁻¹⁶ indicate that highly active anti retroviral therapy (HAART) is equally effective. Other treatment modalities include glucocorticoids, intravenous IgG (IVIG), intravenous anti-D therapy, splenectomy, danazol, dapsone, interferon and vincristine. In our case we had chosen HAART which has minimal interactions with anti tubercular therapy.¹⁵⁻¹⁶

In the present patient, oral dapsone was administered as it has been shown to raise platelets with no major toxicity.¹⁷ Dapsone has shown to be effective in some patients with HIV-related thrombocytopenia.¹⁷ Some trials have shown that dapsone is a safe, inexpensive treatment. The studies have also confirmed the beneficial effect of dapsone in patients with chronic idiopathic autoimmune thrombocytopenic purpura.¹⁸⁻¹⁹ Glatt and Anand¹¹ propose that patients with symptomatic HIV associated thrombocytopenia be treated

with IVIG, without distinction between anti-Rh(D) and high-dose IVIG. The use of IVIG is hampered by its high cost and the need for hospitalization.

HIV-related thrombocytopenia is a complex and incompletely understood phenomenon. The ideal treatment for HIV-related thrombocytopenia has not yet been determined. Published data favours the use of AZT. Used by itself, AZT safely slows HIV infectiousness, but may not always stop it entirely. This may allow HIV to become AZT-resistant over time, and for this reason AZT is usually used in conjunction with the other nucleoside analogue reverse transcriptase inhibitors, zidovudine is mandated in the World Health Organization's "essential drugs list", which is a list of minimum medical needs for a basic medical health care system.^{12,20}

In addition, studies have shown that HAART is equally effective.¹⁴ As far as other treatments are concerned, most of the effects appear to be transient and risks and benefits should be weighed on a case-by-case basis. Treatment should be individualized and it is reasonable to accept chronic thrombocytopenia even with low platelet counts as long as there are no significant bleeding complications.

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