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Case Report

CASE REPORT

The dilemma in a case of immune thrombocytopenia in a patient with human immunodeficiency virus on antituberculosis treatment for miliary pulmonary tuberculosis

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Abstract

The multifactorial mechanisms of immune thrombocytopenia (ITP) in patients with human immunodeficiency virus (HIV) and tuberculosis (TB) could be caused by HIV, TB or anti-TB drugs. No patients with HIV and opportunistic infection of miliary pulmonary TB who developed thrombocytopenia after treatment with anti-TB drugs have been reported. A 47-year-old woman with HIV/acquired immunodeficiency syndrome and miliary TB with normal platelet count (229 000/μL) started anti-TB drugs (rifampicin, isoniazid, pyrazinamide and ethambutol). After 10 days of treatment, her platelet count was low (17 000/μL). As rifampicin and isoniazid were stopped and intravenous methylprednisolone was given, her platelet count began to increase. After more than a month, her platelet count was normal (192 000/μL) and she started antiretrovirals. This improved platelet count after high-dose methylprednisolone is suggestive of ITP; however, the dilemma is whether it was rifampicin alone that caused ITP or did HIV and disseminated TB infection also play a role?

INTRODUCTION

Thrombocytopenia in patients with human immunodeficiency virus (HIV) is associated with increased morbidity and mortality in addition to HIV infection or opportunistic infections, such as tuberculosis (TB) [1]. Thrombocytopenia in a patient with TB might be caused by various mechanisms, such as immune thrombocytopenia (ITP) or anti-TB drug-induced thrombocytopenia, among other things [2]. To our knowledge, no patients with HIV and opportunistic miliary pulmonary TB infection who developed ITP after treatment with anti-TB drugs have been reported.

CASE REPORT

A 47-year-old woman was admitted to the hospital with a 1-day-old fever. Bruises and rashes were observed on her upper extremities. She was diagnosed with HIV infection and miliary TB 10 days prior. Her CD4 count was 96/μL. She was given

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Table 1: Laboratory results of the patient

Laboratory	Reference values	Day −10	1	3	5	6	7	8	9	10	11	12	13	22	37	51
Hemoglobin (g/dl)	12.0–15.0	9.8	9.5	9.2	9.3	8.3	8.7	8.1	8.4	7.9	8.0	8.6	7.9	8.7	10.6	11.3
Hematocrite (%)	36.0–47.0	29.0	27.8	28.4	29.1	26.6	26.6	24.9	24.6	24.1	23.3	25.0	24.1	27.6	33.3	33.0
Erythrocyte ($\times 10^6$/µl)	4.20–5.90	3.58	3.43	3.38	3.40	3.01	3.16	2.95	2.96	2.87	2.78	2.95	2.77	2.84	3.18	3.47
Leucocyte (/µl)	4.00–10.00	4.13	4.23	2.95	3.25	2.27	2.59	2.58	1.88	2.06	2.26	3.23	2.90	5.72	5.28	3.65
Platelet ($\times 10^3$/µl)	150–350	229	17	8	7	13	4	6	7	17	18	42	84	99	192	201
Total bilirubin (mg/dl)	0.30–1.20		9.53		7.24			6.38				3.28				
Direct bilirubin (mg/dl)	0.00–0.30		8.69		7.12			6.12				2.83				
Indirect bilirubin (mg/dl)	0.30–0.90		0.84		0.12			0.26				0.45				
AST (U/l)	0–35		117		67			82				69				
ALT (U/l)	0–35		141		90			62				81				

AST: Aspartate Aminotransferase; ALT: Alanine Animotransferase

anti-TB therapy (rifampicin 450 mg/day, isoniazid 300 mg/day, pyrazinamide 1000 mg/day and ethambutol 1000 mg/day) and trimethoprim/sulfamethoxazole 960 mg/day. Her initial hematology test showed a normal platelet count. Her vital signs were within the normal range when she was admitted. A physical examination showed icteric sclerae, no hepatomegaly or splenomegaly, generalized multiple erythematous papules and excoriation and multiple purpuric lesions on her upper extremities. Hematology results were similar to the initial result but with a low platelet count (17 000/µL). Peripheral blood smear morphology showed hypochromic microcytic erythrocyte, with polychromation and target cells, but no nucleated erythrocytes. Her leucocyte count was within the normal range, but the platelet count was low with no giant thrombocytes. She also had increased transaminases and bilirubin levels.

Her abdominal ultrasonography was normal. Viral hepatitis markers (surface antigen of the hepatitis B virus and antibodies to hepatitis C virus) and dengue serology were negative. Rifampicin, isoniazid and pyrazinamide were stopped, ethambutol was continued and streptomycin was started (1000 mg/day). She was also given oral methylprednisolone 16 mg twice/day for the skin lesions. On the eighth day, intravenous methylprednisolone 125 mg/day was given for 3 days and tapered down to 62.5 mg/day for the next 3 days. On the 13th day, her platelet count was 84 000/µL and she was discharged with oral methylprednisolone 16 mg thrice/day. She returned to the outpatient clinic on the 22nd day, and the methylprednisolone was tapered to 4 mg twice/day. On the 37th day, her platelet count was normal, methylprednisolone was stopped and antiretrovirals were started with tenofovir (300 mg/-day), lamivudine (300 mg/day) and efavirenz (600 mg/day). On the 51st day, her platelet count was still normal. Table 1 presents the laboratory results, while the platelet count curve is shown in Fig. 1.

DISCUSSION

Thrombocytopenia is defined as a platelet count below 150 000/µL, while ITP is defined as a platelet count below 100 000/µL caused by the immune destruction of platelets. Secondary ITP is associated with infectious and noninfectious diseases, such as autoimmune disease, TB, HIV, hepatitis C virus, *Helicobacter pylori* or immune dysregulation syndromes [3].

Around 40% of patients with HIV develop thrombocytopenia during the disease course [1]. Thrombocytopenia in patients with HIV could be caused primarily by HIV or secondarily by opportunistic infections, such as TB [2]. In primary thrombocytopenia, the causes differ in different stages of HIV, where autoimmune destruction predominates in early stages, while defective thrombopoiesis predominates in the late stages [1]. In secondary thrombocytopenia, opportunistic infections are important causes and TB is the most common [2,4,5].

Thrombocytopenia in a patient with TB was caused by various mechanisms, including immune-mediated platelet destruction and anti-TB drug-induced thrombocytopenia, among other mechanisms. Thrombocytopenia is most commonly seen in pulmonary and disseminated TB [6] and responds well to anti-TB drugs [2]. Isolated thrombocytopenia in patients with TB is rare and hypothesized to be a secondary ITP. One review identified only 50 cases of secondary ITP associated with TB between 1964 and 2016 [7]. Anti-TB drug-induced thrombocytopenia could be caused by isoniazid, rifampicin or both, where autoimmune-mediated rifampicin is the most common [8,9]. The exact mechanism of isoniazid-induced thrombocytopenia is not known [9], and thrombocytopenia caused by isoniazid and rifampicin was reported only once previously [8].

A systematic review defined standard criteria to determine that a drug induces thrombocytopenia [10], but they were not applicable in this case because there were multiple drugs prior to the onset of thrombocytopenia. For example, two drugs could cause thrombocytopenia: isoniazid and rifampicin. Many etiologies of thrombocytopenia were present in this patient, including HIV and TB infections. Isoniazid and rifampicin could not be reintroduced because of the suspicion of drug-induced liver injury. Only one criterion could be fulfilled in this patient, which was that the suspected drugs preceded her thrombocytopenia, and her recovery was complete and sustained after both drugs were withdrawn.

The patient had no personal or family history of thrombocytopenia. Her hepatitis C serology was negative, although *H. pylori* was not examined. Her peripheral blood smear was suggestive of ITP. Antiplatelet antibody testing was not recommended in this case because of high interlaboratory variability and poor sensitivity [6]. HIV and disseminated TB could cause ITP in this patient, but her platelet count was normal when she was diagnosed with HIV and TB and antiretrovirals were not

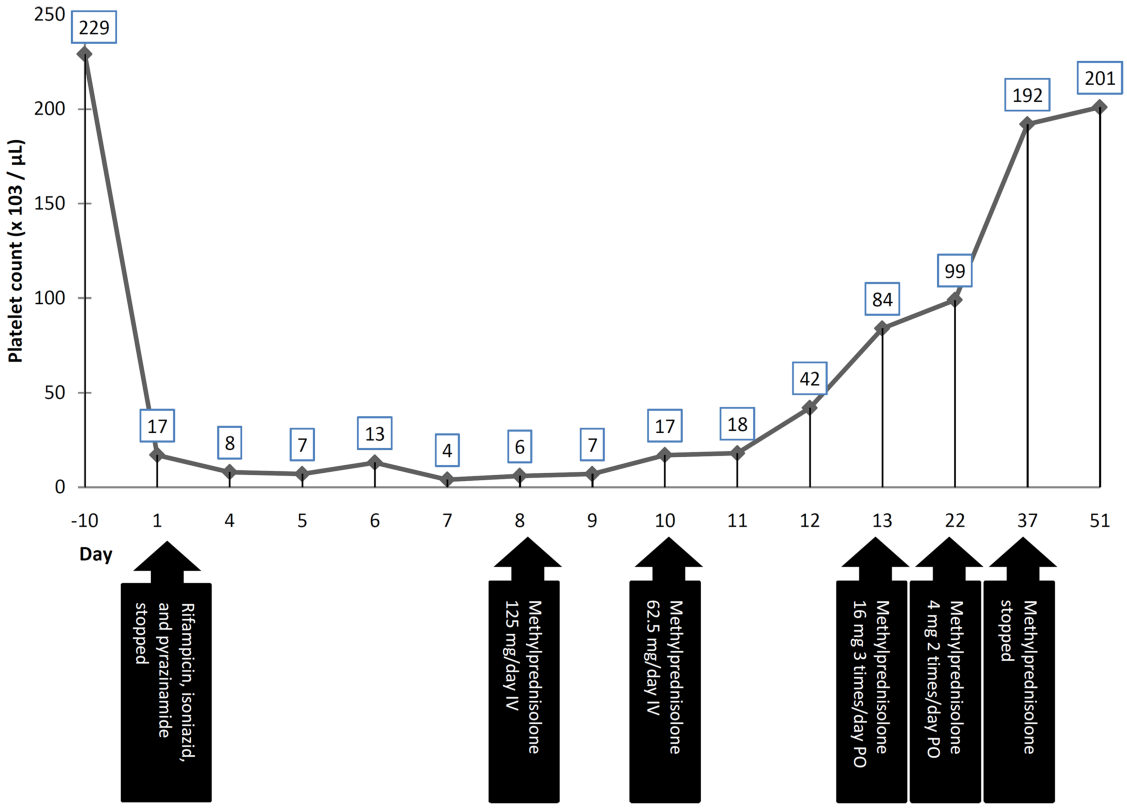

Figure 1: The platelet count curve of the patient.

given. The patient was on anti-TB treatment, which could have caused thrombocytopenia. Her platelet count began to decrease as the anti-TB treatment started. Her thrombocytopenia was suggestive of secondary ITP due to rifampicin. On the first day of admission, methylprednisolone was already given and both rifampicin and isoniazid discontinued. Although rifampicin was the most probable cause of ITP, HIV and TB could not be excluded convincingly. Although steroids have no benefit in the management of drug-induced thrombocytopenia, steroids could be given in severe thrombocytopenia where it is difficult to determine a cause of thrombocytopenia where multiple causes are present, such as in this case [8].

CONCLUSION

We reported a case of secondary ITP in a patient with HIV treated with isoniazid and rifampicin for miliary pulmonary TB. There was a dilemma in this case because rifampicin alone could have been the prime suspect for ITP, but HIV and disseminated TB infection were also not innocent bystanders.

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CONFLICT OF INTEREST STATEMENT

None declared.

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ETHICAL APPROVAL

No ethical approval was required.

CONSENT

Written informed consent was obtained from the patient for publication of this report.

GUARANTOR

N.P.H.L. is the guarantor of this article.

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