MEDICINE SOUTHEAST ASIA

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Case report

Atypical mononuclear cell in Immune Thrombocytopenia Purpura (ITP) with massive bleeding

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ABSTRACT

Background: Immune thrombocytopenic purpura (ITP) is a disorder that can lead to mild or severe bruising and bleeding. The bleeding results from unusually low platelet counts. Atypical mononuclear cells (AMC) in thrombocytopenia and anemia may raise doubt about the diagnosis of ITP. Furthermore, it warrants investigation.

Case report: A 50-year-old woman who came for investigation of melena and cutaneous bleeding (haemoglobin level 4.1-5.5 g/dl) for about 2-3 days. Thrombocyte count showed thrombocytopenia (2–6 × 10^3/µl), and she had a normal leucocyte count. Her peripheral blood film was anemia, normocytic, normochromic, thrombocytopenia, and normal leukocyte count with AMC. We evaluated the patient with another laboratory parameter, the antiplatelet antibody. It was positive, showing that there was an autoantibody against thrombocytes in her circulation, and we could exclude haematological cancer. AMC correlated with the activity of the mononuclear phagocyte.

Conclusion: Anti-platelet antibodies play an important role in unexplained thrombocytopenia, with or without anemia, and this parameter can exclude haematological cancer in the diagnostic process.

Keywords: Atypical mononuclear cell, ITP, bleeding

1. Introduction

Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by thrombocytopenia due to antibodies that bind platelet antigens, ultimately leading to platelet destruction in the reticuloendothelial system, particularly the spleen [1]. The antiplatelet antibodies opsonize platelets and then bind to antigen-presenting cells via Fcγ receptors. Platelet aggregation occurs, and macrophages subsequently phagocytose the platelets. Lymphocytes are another cell type that contributes to thrombocyte destruction. These processes, known as humoral and cellular responses, cause thrombocytopenia [2, 3].

Clinical manifestations of the major ITP are bleeding with varying degrees ranging from mild to severe in the mucocutaneous and mucous membranes, and also internal bleeding such as intracerebral and gastrointestinal bleeding. Mild splenomegaly can be

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found. ITP in the peripheral blood smear shows thrombocytopenia, with normal erythrocyte and leukocyte features. But if the bleeding is massive, it can show anemia. Antibody antiplatelet may show positive results [4-6].

We describe here the thrombocytopenia condition with massive bleeding that resulted in moderate to severe anemia. Additionally, we identified an atypical mononuclear cell on the peripheral blood smear, raising doubts about the patient's diagnosis. ITP or another condition like leukemia could be the diagnosis, so we needed laboratory parameters, such as antiplatelet antibodies, that could exclude leukemia. It has the advantage that the sample was obtained via an easy procedure with minimal risk and pain, rather than by bone marrow aspiration or biopsy.

2. Case Report

A 50-year-old woman came to the hospital with a complaint of black feces for five days. This complaint was felt increasingly heavier every day, and she let it go without medical treatment. She felt weak and lethargic with the complaint. The complaint was not accompanied by fever, nausea, vomiting, or abnormal urination. The woman claimed to have never suffered a similar disease, and the disease she had experienced was just a common fever. No family member suffers from the same illness as the patient. She is a mother of two children and a housewife.

Table 1. Results of complete hematological examination of the patient

Parameters (unit)	Days of Treatment						
	1	**3**	**5**	**6**	**7**	**8**	**10**
Haemoglobin (g/dL)	4,1	6,0	6,6	7,2	6,3	4,8	6,6
Hematocrit (%)	13,8	19,3	21,2	21,4	20,4	16	21,2
Erythrocytes count ($x10^6/\mu l$)	1,45	1,96	2,26	2,47	2,18	1,66	2,36
MCV (Fl)	95,2	98,5	93,8	93,5	93,6	96,4	89,8
MCH (Pg)	28,3	30,6	29,2	29,1	28,9	28,9	28,0
MCHC (%)	29,7	31,1	31,1	31,2	30,9	30,0	31,1
Leukocyte count ($x10^3/\mu l$)	7,12	4,71	5,13	4,38	4,2	6,6	7,4
Thrombocyte count ($x10^3/\mu l$)	10	6	11	2	1	1	8

The patient appeared generally conscious and weak, with typical vital signs. Eye examination revealed conjunctival anemia and no jaundice on the sclerae. There was no abnormality or bleeding in the nose, mouth, or ear. There was ecchymosis and petechiae on the right cheek (**Figure 1**). Examination of the heart and lungs was within normal limits. There was no organometallic, supple, or tender area in the abdominal examination. There was no lymphadenopathy. Right and left lower extremities appeared with petechiae (**Figure 2**), as well as on the upper extremities.

Laboratory examination revealed hemoglobin levels ranging from 4.1 to 7.2 g/dL, consistent with the decrease in hematocrit and normal MCV and MCH. It showed normochromic normocytic anemia. Further, the examination revealed thrombocytopenia, with platelet counts ranging from 1,000 to 10,000/μl. The number of leukocytes was normal. Reticulocyte count increased by 2.1%. The results of a complete hematological examination of the patients are shown in **Table 1**.

The other PT and aPTT examinations were regular. Liver function tests, kidney function tests, and blood glucose levels were within normal limits. HBsAg, anti-HCV, IgG, and IgM anti-Dengue parameters were non-reactive. The subsequent examination for antiplatelet antibodies was positive, indicating the presence of autoantibodies against platelets (**Table 2**).

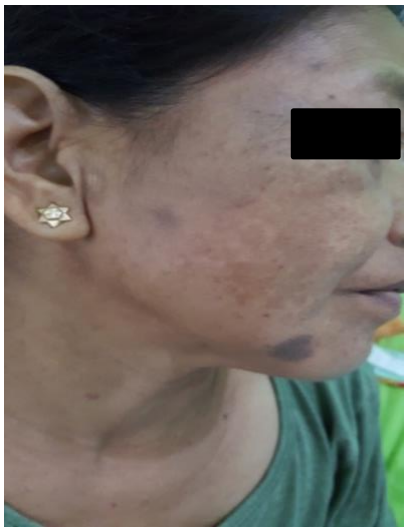

Figure 1. Ecchymosis and petechiae on the right cheek

Evaluation of blood morphology revealed normochromic, normocytic anemia with polychromatous and nucleated erythrocytes. The estimated leukocyte count was normal, with relative lymphocytosis and some atypical mononuclear cells (AMC) (**Figure 3**). Platelet count estimation decreases with the size of large platelets and platelet giants.

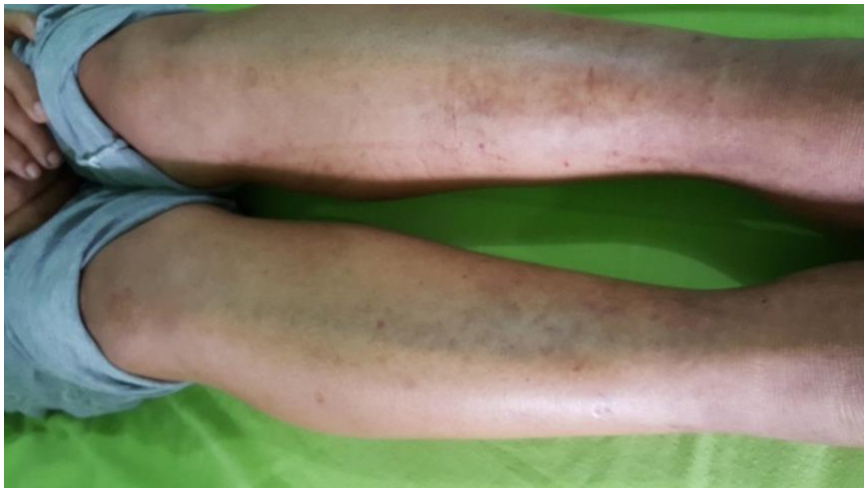

Figure 2. Petechiae on right and left lower extremities

3. Discussion

The cases described above showed normochromic normocytic anemia with thrombocytopenia, relative lymphocytosis, and AMC. Reticulocyte count increased, indicating a favorable spinal cord response to bleeding (blood loss). Clinical chemistry results for hepatic and renal function were normal.

Table 2. Results of other laboratory parameters

Parameters (unit)	Results
PT (seconds)	13
aPTT (seconds)	20
AST (U/L)	27
ALT (U/L)	30
Ureum (mg/dl)	25
Kreatinin (mg/dl)	0,9
Blood glucose level (mg/dl)	130
HBsAg	Non-reactive
Anti-HCV	Non-reactive
IgG anti-Dengue	Non-reactive
IgM anti-Dengue	Non-reactive
Antibody antiplatelet	Positive

The diagnosis was ITP with suspected malignant blood, based on laboratory results. The differential diagnosis of blood malignancy was based on findings of bisitopenia with the presence of AMC. The diagnosis of ITP remained a major concern, as the laboratory results were consistent with clinical findings of melena, bleeding from the skin surface and the upper and lower extremities, and the absence of organomegaly.

Typically, ITP circumstances are thrombocytopenia with no abnormalities found in erythrocytes and leukocytes, but in cases with severe anemia, it may result from excessive bleeding [7]. This obscures the diagnosis of ITP with an amplified blood predilection by AMC in its leukocyte appearance.

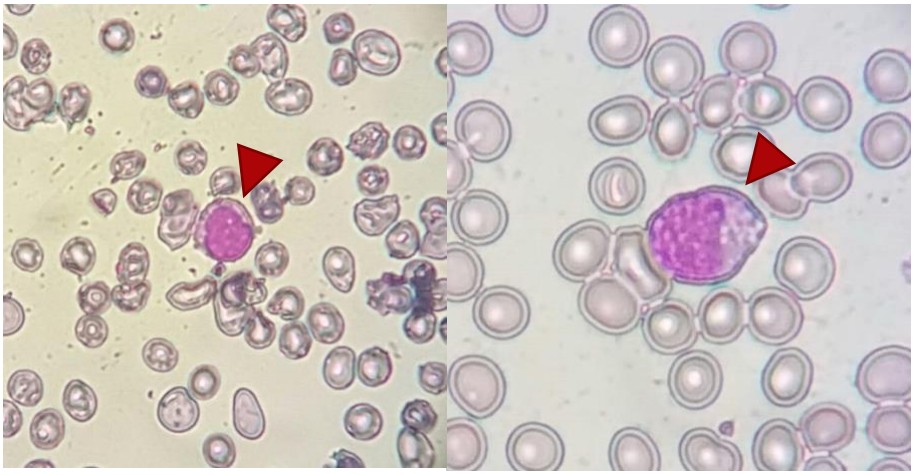

Figure 3. Atypical Mononuclear Cell (AMC) (red arrow) in peripheral blood smear (left: 40x objective lens with Giemsa staining; right: 100 x objective lens with Giemsa staining)

A positive laboratory test for antiplatelet antibodies confirmed the diagnosis of ITP. The presence of autoantibodies against platelets was clear evidence of ITP disease in this patient. Bone marrow aspiration was not performed on the patient. Invasive intervention can be avoided if there were other noninvasive interventions, such as laboratory findings, to make the diagnosis.

ITP is an autoimmune disorder characterized by platelet destruction that occurs through two processes. The process is a decrease in platelet production and an increase in platelet destruction [8]. The process is a complex condition with the participation of various cells and protein substances in it, including antibodies, cytokines, antigen-presenting cells, co-stimulatory molecules, T lymphocytes, and B lymphocytes [9].

Reactive autoantibodies are associated with abnormal T and B cells, leading to platelet destruction and impairment of thrombopoiesis and megakaryopoiesis. This pathological condition is exacerbated by increased proinflammatory cytokines, including IFN-γ, IL-2, and IL-17, and by decreased immunosuppressive cytokines, such as IL-10, TGF-β, and IL-4, thereby promoting autoantibody formation. The incidence resulted from a lack of immune tolerance due to abnormalities in Treg and Breg cells [7-9].

Autoantibodies from ITP patients were directly bound to Gp Ib/IX and Gp IIb/IIIa. The specificity of attachment of autoantibodies can still be expressed in other platelet antigens. Autoantibodies may be undetectable in patients with ITP at the time of examination. This can occur due to the limitations of laboratory and biological examination methods of ITP. Immune complexes containing platelet antibodies may be present at low levels, resulting in antibody titers below the detection limit. Strong antithrombocyte antibody binding can complicate dissociation during examination. Antibodies with low specificity or the presence of cryptic antigen on platelets make the examination undetectable. Additionally, antiplatelet antibodies are absent in some patients [4, 13].

The presence of AMC in ITP can obscure the diagnosis, so it should be investigated further to determine whether it is related or whether another disease, such as a blood malignancy, is present. This can be eliminated after positive results of antiplatelet antibodies. AMC can be found in ITP because one of the pathogeneses of ITP is increased activation of phagocytic mononuclear cells, resulting in platelet destruction [14]. Other features of leucocytes that can be found are atypical lymphocytes (Downey cells) that indicate suspicion of previous viral infections. An immunoserologic examination of the patient should be performed if this cell is present in HCV, HIV, CMV, and H. Pylori infection [15, 16].

4. Conclusion

Anemia and thrombocytopenia may occur in ITP patients with severe bleeding. The examination of antiplatelet antibodies is useful in cases of unclear thrombocytopenia to exclude the diagnosis of blood malignancy.

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