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**Case Report**

# Secondary immune thrombocytopenic purpura in a child with acute lymphoblastic leukemia on maintenance chemotherapy with 6-mercaptopurine: a rare case report

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## ABSTRACT

In patients with acute lymphoblastic leukemia (ALL), thrombocytopenia is most commonly attributed to chemotherapy-induced myelosuppression or disease relapse. We report the case of a 6 years young girl who developed isolated thrombocytopenia during the 12th week of maintenance therapy with 6-mercaptopurine and methotrexate. Despite discontinuation of chemotherapy for two weeks, her platelet counts did not improve. Multiple platelet transfusions were administered without response. Bone marrow examination revealed a hypercellular marrow with adequate megakaryocytes, suggesting peripheral platelet destruction, possibly secondary to chemotherapy. She was subsequently treated with a short course of steroids, as per her COG maintenance protocol, to which she responded well. This case underscores the importance of considering secondary immune thrombocytopenia (ITP) as a differential diagnosis in ALL patients on maintenance chemotherapy who present with persistent isolated thrombocytopenia.

**Keywords:** Secondary immune thrombocytopenic purpura, Acute lymphoblastic leukemia, 6-mercaptopurine

## INTRODUCTION

Immune thrombocytopenic purpura is a rare complication in children undergoing chemotherapy for ALL.[1,2] Differentiating it from bone marrow suppression due to toxicities or relapse is crucial for appropriate management.[3] We report a case of 6-year-old girl with B cell ALL who completed induction chemotherapy and undergoing maintenance developed isolated thrombocytopenia. Bone marrow examination ruled out relapse or suppression, and clinical profile favoured immune mediated thrombocytopenia. She responded well to the short course of oral corticosteroids and dose adjustment of chemotherapy drugs was done. This report signifies the importance of considering possibility of immune thrombocytopenic purpura in a case of the leukemia.

## CASE REPORT

A 6-year-old girl, presented with complaints fever, bleeding manifestations and swelling over neck and inguinal region. On investigations, she had bicytopenia with leucocytosis, peripheral smear was suggestive of blast cells, flow cytometry was positive for B cell markers. Patient was diagnosed as B cell ALL intermediate risk, she was started on ICICLE protocol. After completion of intensive chemotherapy for 6 months she was started on the maintenance chemotherapy according to COG protocol. Her maintenance protocol included 6 mercaptopurine 75 mg/m$^2$, methotrexate 20 mg/m$^2$, vincristine 1.5 mg/m$^2$ on every 28$^{th}$ day, oral prednisolone 60 mg/m$^2$ for 5 days every 28$^{th}$ day. After completion of 12 weeks, during second cycle of maintenance she developed petechiae and purpura all

over the body, without any life-threatening bleeding manifestations. Investigations were suggestive of isolated thrombocytopenia, initially bone marrow suppression was suspected and received multiple platelets transfusions. Despite of receiving multiple platelets transfusion, and cessation of chemotherapy for 2 weeks her platelet count was not improved. Bone marrow aspiration was performed which was suggestive of hypercellular marrow (Figure 1), with normal erythropoiesis, myelopoiesis and thrombopoiesis with presence of megakaryocytic forms (hypolobated forms) (Figure 2).[4] Blast count was 4% which indicated M1 status of marrow. Peripheral destruction of platelets was suspected and patient was given short course of monthly steroids in accordance to her COG chemotherapy maintenance protocol. Following short course of steroids her platelet counts improved to normal levels affirming diagnosis of immune mediated peripheral destruction of platelets. An attempt to normalise the dose of 6 mp was done which resulted in rapid fall of platelet counts confirming secondary ITP to 6-mercaptopurine (6 mp). She was diagnosed as the case of secondary ITP to 6-mercaptopurine (6 mp). Her 6mp dosage was reduced to 25% of initial dose and was given once a day. She is receiving monthly short course of steroids, oral prednisolone 60 mg/m$^2$ for 5 days and her platelets count is maintained between 80,000-1,00,000 and absolute neutrophilic count between 1000-2000. Currently patient is ongoing her remaining maintenance therapy without any complications.

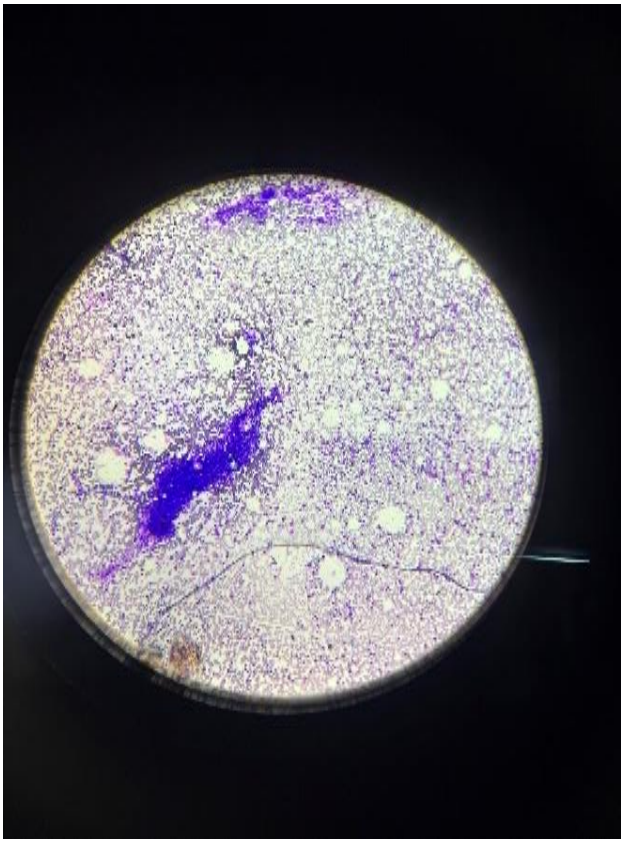

**Figure 1: Histopathological slide of bone marrow aspiration showing hypercellular bone marrow.**

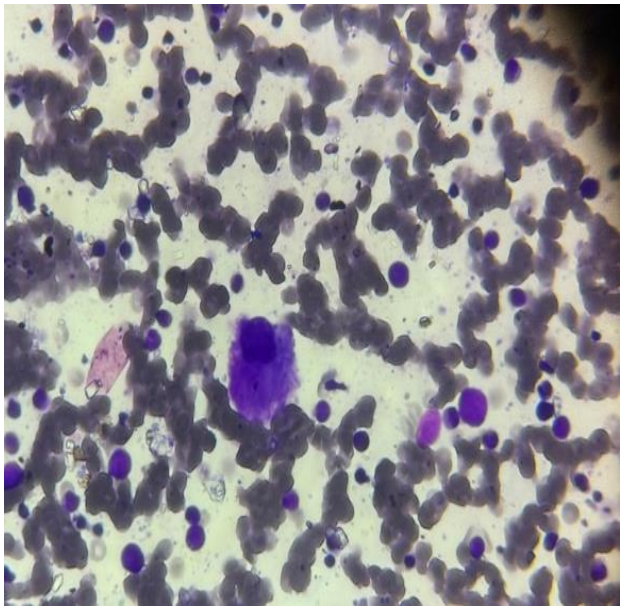

**Figure 2: Histopathological slide of bone marrow aspiration showing hypolobated megakaryocyte with blast cells.**

## DISCUSSION

Thrombocytopenia in a case of ALL is suspected due to disease relapse or secondary to chemotherapy, both these conditions present with reduced platelet production.[5] In general accelerated destruction of platelets results in the increased megakaryocytes in bone marrow as distinctive finding in ITP however impaired megakaryocytosis can also be seen in the case of ITP.[6,7] In our case we have done bone marrow study which was suggestive of normal platelets production with megakaryocytes and response to the short course of steroids was strongly suggestive to the diagnosis of ITP.

Classically ITP is caused by the opsonisation of platelets by IgG and then phagocytosis and destruction by macrophages in the reticuloendothelial system within the spleen.[6] T cell mediated immunity is also important in the pathogenesis of ITP, regulatory T cells marked by CD4+CD25+Foxp3+ have role in suppression of humoral and cellular immune response dysregulation of this cells is seen in cases of ITP.[7-10] Reduction in this regulatory T cells is shown in multiple case reports on ITP.[8-10] Purine analogues like 6-mercaptopurine causes the defects in DNA synthesis and induces apoptosis.[11] Purine nucleoside analogues cause profound depletion of T cells.[12] Regulatory T cells CD4+CD25+Foxp3+also reduce and cause immune dysregulation which subsequently lead to ITP in patients treated with 6-mercaptopurine.[11,12]

## CONCLUSION

Persistent isolated thrombocytopenia resistant to transfusions should alarm peripheral immune mediated

destruction of platelets in case of leukemia. This case highlights secondary ITP as an important differential diagnosis in the known cases of ALL on chemotherapy. High index suspicion must be maintained when there is isolated thrombocytopenia resistant to multiple transfusions. Timely diagnosis using bone marrow examination, along with interventions such as a short course of steroids every 28th day, can prevent unnecessary interruptions in chemotherapy and also contribute to the effective management of the underlying malignancy.

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