Case study

Insidious onset of Chronic Myeloid Leukemia in a longstanding case of chronic Immune Thrombocytopenia: A rare entity

Abstract:

*Aim:*To study the unusual association of development of chronic myeloid leukemia (CML) in a longstanding case of chronic immune thrombocytopenia with the help of lab investigations.

*Methodology:*The peripheral blood smear slides were stained by using Leishman stain and observed under microscope. BCR ABL 1 was done by quantitative real time polymerase chain reaction (RT-PCR).

Presentation of case: We present a peculiar case that forms a link between the two independent diagnoses. This case highlights a 51-year-old woman on treatment for chronic ITP who was subsequently diagnosed with CML during follow-up.

Discussion: The combination of series of events following the unresponsiveness of thrombocytopenia to Eltrombopag which was well-controlled over the years and a sudden uneventful rise in the total white blood cell count led to the suspicion of myeloproliferative disorder. Further bone marrow examination and molecular studies confirmed the diagnosis of chronic myeloid leukemia (CML).

*Conclusion:*Thereby, we emphasize that survival rate can be improved by early identification and by suspecting clonal disorders as a differential diagnosis along with timely management of the condition in an early stage.

Keywords: Immune thrombocytopenia, chronic myeloid leukemia, idiopathic thrombocytopenic purpura, Eltrombopag, BCR-ABL1.

INTRODUCTION:

Immune thrombocytopenia was previously called as idiopathic thrombocytopenic purpura and is considered as a diagnosis of exclusion. It is an acquired autoimmune disorder characterized by increased destruction of platelets secondary to an anomalous antibody response against the platelet glycoproteins Ib/IX or IIb/IIIa and megakaryocytes resulting in defective platelet production. [1, 2, 3]

Platelet count of $100x10^3$/µL or less can be a risk for bleeding. ITP is often linked with clonal disorders of myeloid or lymphoid origin and with many hematological malignancies. The latest literature indicates that ITP can occur before, after or be accompanied by the clonal disorders. [2]

The literature mentions disorders like myelodysplastic syndrome that are consistently associated with ITP whereas it is rare to see CML develop after chronic persistent ITP.[3, 4]

Case report:

We received a blood sample of a 51-year-old female for complete blood count test who was a known case of ITP for 20 years at Metropolis Healthcare Limited lab Mumbai. Her past history was unremarkable and diagnosis was made during her first pregnancy wherein after normal delivery she developed post-partum hemorrhage. She was given blood transfusion only once during this period. All the blood indices were within normal limits except the platelet count which was persistently low. A comprehensive autoimmune markers test panel was inconclusive. Prothrombin time and activated partial thromboplastin time were normal but her bleeding time was prolonged.

A bone marrow examination was done to rule out other causes of thrombocytopenia and displayed hyperplasia of megakaryocytes with increased proportion of immature megakaryocytes. The megakaryocytes had smooth borders which lacked budding indicating decreased platelet production. All the other cell lineages were normal. After ruling out all other autoimmune and secondary causes of thrombocytopenia a diagnosis of idiopathic thrombocytopenic purpura was made. The treatment initially included steroids followed byeltrombopag. She was following up at our lab since 30th March 2021 when she had persistent thrombocytopenia which was then unresponsive to Eltrombopag (Figure A).

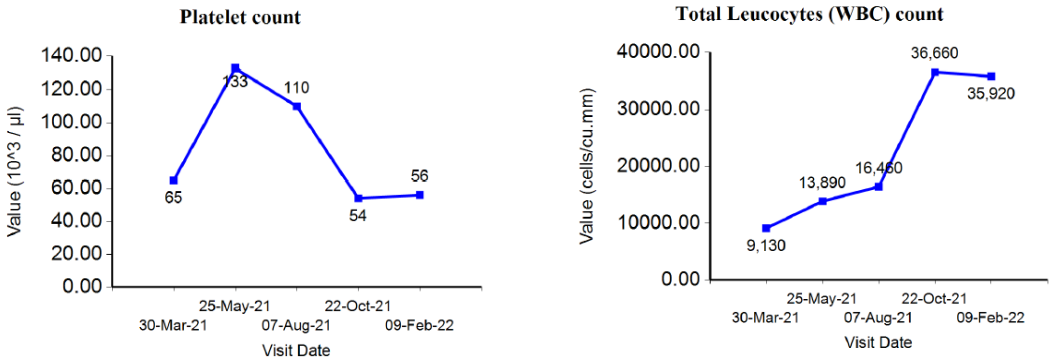

FIGURE A: Trend analysis of Platelet and WBC count

On 22nd October 2021,there was a sudden increase in the white blood cell (WBC) count without any shift to left. The patient had mild fever with myalgia for a day in the month of January 2022 which subsided subsequently without any medications. On 9th February 2022,neutrophilic leukocytosis with a total leukocyte count of 35,920 cells/cu.mm was noted. A shift to left was observed on the peripheral smear with 5% blasts, 7%promyelocytes, 14% myelocytes, 12 % metamyelocytes, 5% band forms, 27% neutrophils,10 % lymphocytes, 4% monocytes, 6% eosinophils and 10% basophils (Figure B). The hemoglobin level was 11.4 g/dl;the platelet count was $56x10^3$/ µL without any physical findings or hepatosplenomegaly.

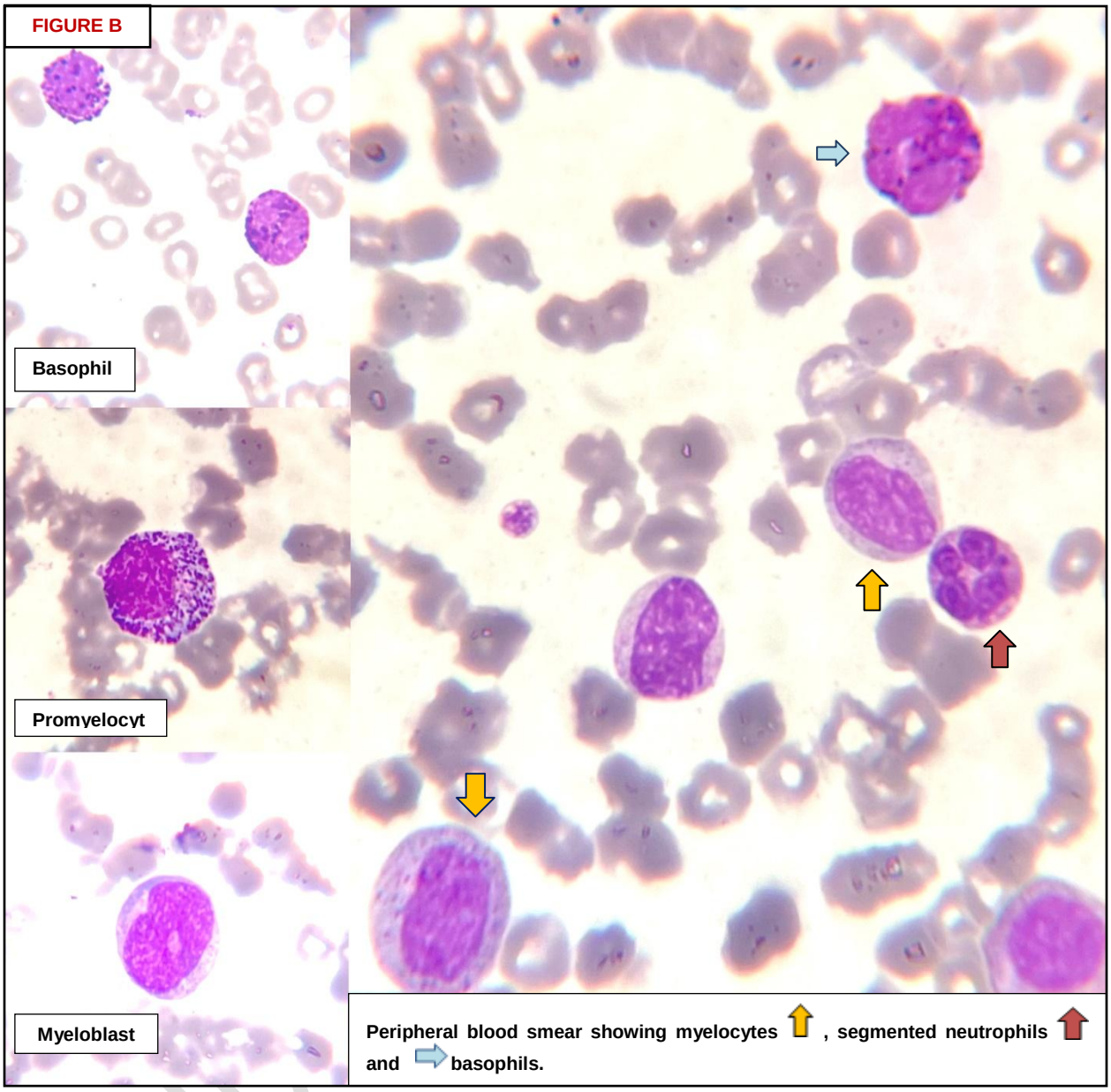

FIGURE B: Peripheral blood smear showing myelocytes

The bone marrow smear was hypercellular showing myeloid hyperplasia with less than 5% blasts and increased number of hypolobated megakaryocytes. Erythroid cells were decreased in number but were normal morphologically. Molecular analysis done by real time quantitative polymerase chain reaction (RTPCR) was positive for BCR-ABL 1 fusion oncogene found in Philadelphia chromosome. On the basis of these findings a diagnosis of chronic myeloid leukemia (CML) was made.

Discussion:

The pathological connection between ITP and clonal myeloid and lymphoid disorders is still unknown. The succession of events is not conclusive in determining the association of conditions with each other, whether the anomalous clonal multiplication causes the disturbance in the immune regulation or abnormality in immune regulation causes promotion of precursors of clonal hematological malignancy. [5-7]

The development of CML after chronic ITP is a very rare entity and is described only in two adult case reports and two pediatric age group case reports. [8] The first report was described in 2014; of a 77-year-old man on treatment for ITP who was treated with prednisolone and later with eltrombopag eventually developed CML and died following blast crisis.[9] The secondpublished report from the literature was narrated in 2021; wherein a 64-year-old male with ITPlater became unresponsive to steroids like dexamethasone and prednisone as well as eltrombopag and after 15 years was positive for p210 b3a2 transcript of BCRABL 1 fusion oncogene.[8] Similarly, our report described the case of a 51-year-old female on treatment with steroids and immunosuppressants who developed CML over a course of 20 years,when the thrombocytopenia became refractory to eltrombopag and revealed hyperleukosis in the complete blood count (CBC) hemogram profile. Molecular studies eventually confirmed BCR-ABL 1 positivity on RT PCR.

One pediatric case published in 1981; concerned an 8-year-old girl which was diagnosed with ITP which later became indolent to treatment when she developed pneumococcal meningitis and was treated for the same. In 7 years, she was diagnosed with Philadelphia chromosome positive CML and died within 3 years.[10] Other pediatric case was described in 2003; in this case report, a 32-year-old male with ITP since childhood was efficiently treated with steroids but had to undergo splenectomy when he became indolent to intravenous immunoglobulins. Meanwhile, he also contracted hepatitis C probably due to the immunoglobulins and was given interferon alpha. In 2001,his platelet count came to normal but there was an increase in the total leukocyte count which was confirmed as CML on BM findings, fluorescent insitu hybridization (FISH) and cytogenetics. [11]

In our case, the patient was consulting at a tertiary care hospital where BM aspiration was done by the consulting hematologist. The molecular analysis was done at Metropolis Labs Mumbai on the blood sample collected for CBC which revealed BCR ABL 1 positivity and subsequently a diagnosis of CML was made on bone marrow examination at the tertiary care center.

Our case report emphasizes on the significance of constant monitoring and timely diagnosis of any clonal disorder with regular follow up visits as well as the value of molecular analysis in early and specific diagnosis. This is beneficial for both the patient and the clinician in planning instantaneous targeted therapy and increasing the survival rate.

Nevertheless, the conundrum of association of ITP with clonal myeloid and lymphoid disorders remains obscure.

Conclusion:

In this case report we discussed a distinctive case of chronic persistent ITP insidiously developing CML that was diagnosed in time by advanced diagnostic tests like molecular analysis which can be treated promptly by targeted therapy and have a better chance at survival.

DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly used products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors

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Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

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Myeloblast

Peripheral blood smear showing myelocytes , segmented neutrophils and basophils.