

Transformation of Polycythemia Vera into Acute Lymphoblastic Leukemia

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Abstract

Transformation of Polycythemia Rubra Vera to acute lymphoblastic leukemia is extremely rare. A case of 22 years old female is reported who developed acute lymphoblastic leukemia 17 years after the initial diagnosis of Polycythemia Vera {PV}. Analytical Immunocytochemistry confirmed Precursor B cell Acute Lymphoblastic Leukemia (BALL) with expression of CD13 and showed gated population of 86% and Blast/atypical population of weak CD45(92%), CD10+19(72%) and HLADR 87%. The rare occurrence of Acute Lymphoblastic Leukemia (ALL) in patients of Polycythemia Vera (PV) indicates clonal expansion of an abnormal uncommitted pleripotent, haemopoietic cell which results in polycythemia Vera (PV) disease phenotype.

Keywords: Polycythemia vera, Acute lymphoblastic leukemia.

Introduction

Myeloproliferative Neoplasms (MPN) refer to clonal disorders of haemopoiesis that lead to an increase in the number of one or more mature red cell progeny.¹ These diseases, classically identified as Chronic Myeloproliferative Disorders, have been recently re-named by the World Health Organization as Myeloproliferative Neoplasms (MPN).² The classical MPNs include Polycythemia (rubra) Vera (PV), essential thrombocythaemia (ET) and primary myelofibrosis (PMF). They share clinical, morphological and molecular features and can transform, in their course, into one another. They are clonal disorders of pleripotent haemopoietic cell and have, a varying degree of potential to transform into acute myeloid leukemia (AML).¹

Mutation and clonal expansion of a single hematopoietic stem cell leads to Polycythemia Vera³ The main features of PV is increased red-cell mass. Polycythemia Vera (PV) is one of the Philadelphia chromosomes (Ph)-negative chronic Myeloproliferative disorders (CMPDs). It is driven by oncogenic mutations that constitutively activate the JAK-STAT signal transduction pathway, such as JAK2 V617F, or exon 12 mutations or LNK mutations. Diagnosis of PV is based on the WHO criteria.⁴ The clinical course in most cases of Polycythemia Vera ends with thrombosis or hemor-

rhage, but a significant number of patients transform to myelofibrosis with myeloid metaphase, myelodysplasia, or acute myeloid leukemia.⁵ A few cases of transformation of Polycythemia Vera(PV) to Chronic Neutrophilic Leukemia have been described.⁶ A long-term study (At a median follow-up of 11 years) evaluated prognostic risk factors for survival and leukemia in 327 PV patients has shown that the risk of myeloid metaplasia is three percent.⁷ The transformation of Polycythemia Vera (PV) into Acute Lymphoblastic Leukemia is very rare (Only 5 cases have been reported so far).

Case Report

In July 2012, a female patient who was 22 years old, presented with history of headache and weakness. She was a known case of polycythemia which was diagnosed at the age of 05 years when she was referred to AFIP Rawalpindi from Azad Kashmir CMH Muzaffarabad in 1994 for complete investigations like hemoglobin studies including hemoglobin electrophoresis. Bone marrow Aspiration was done which turned out normal. She was investigated to exclude secondary causes of erythrocytosis. The patient was treated with regular phlebotomy every 4-6 wks along with occasional use of Aspirin. It was on 3rd July 2012 when she complained of headache and tinnitus and underwent routine phlebotomy. It was followed by blood complete picture which revealed anemia and thrombocytopenia.

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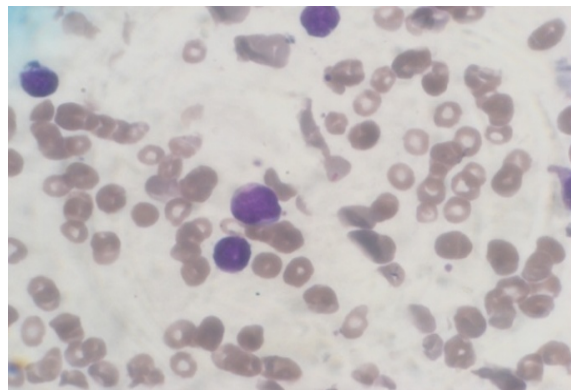


Figure 1.Peripheral blood picture showing Blast cells (Wright×1000)

Patient had moderate splenomegaly. Her TLC was $31.2 \times 1000/\mu\text{L}$, hemoglobin, 8.6g/dl, platelets, $45 \times 1000/\mu\text{L}$ and Blast cells of 73% on the peripheral smear. Bone marrow aspiration revealed markedly hyper cellular bone marrow with 96% blast cells which were large heterogeneous with low N:C ratio having irregular nuclear membrane and were occasionally PAS positive. A diagnosis of Acute Lymphoblastic Leukemia (FAB Type ALL-L2) was made, which turned out as Precursor B ALL with expression of CD13 on flow cytometry.

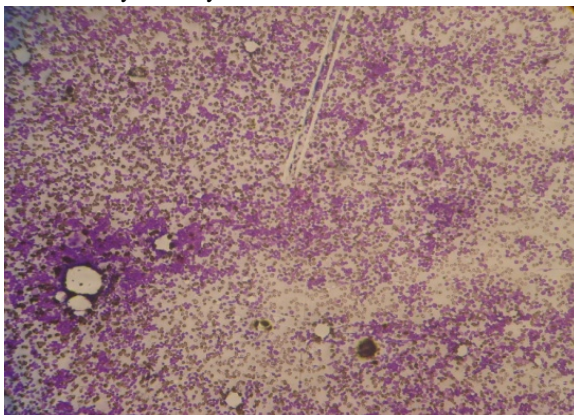


Figure 2. Bone marrow Aspirate smears showing hyperplastic marrow (Wright×40)

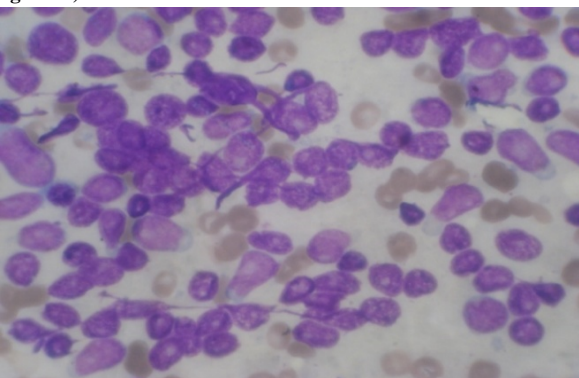


Figure 3. Bone marrow Aspirate smear showing Blast cells (Wright×1000)

Analytical Immunocytochemistry confirmed Precursor B ALL with expression of CD13 and showed gated population of 86% and Blast/atypical population of weak CD45(92%), CD10+19(72%) and HLADR 87%, CD20+34(46%), CD34(47%), CD13(44%), CD33(12%), CD3(3%), CD7(2%), CD5(3%). Histological section of Trephine Biopsy revealed diffuse infiltration by atypical lymphoid cells with mild degree of fibrosis in the section examined. Molecular genetic studies were done. PCR for JAK2-617F Mutation and bcr-abl gene re arrangement were negative. Patient is being treated as a case of ALL-L2 and is responding well.

Discussion

Polycythemia Vera (PV) is a Myeloproliferative disorder (MPD) characterized by clonal proliferation of myeloid progenitors leading to increased production of mature hematopoietic cells predominating on the erythroid lineage.⁸ The incidence (newly diagnosed cases) of PV for all races and ethnicities is approximately 2.8 per 100,000 population of men and approximately 1.3 per 100,000 population of women.⁹ The prevalence (estimated number of people alive on a certain date in a population with a diagnosis of the disease) is approximately 22 cases per 100,000 population.¹⁰

There have been reports previously of transformation of (PV) in to acute lymphoblastic leukemia in adults. Two of the reports have described “null” ALL.^{11, 12} One T cell ALL transformation¹¹ and one case was unclassified. All of the patients received previous treatment with radioactive phosphorus or Alkylating agents. These patients developed ALL 15-16 years after the initial diagnosis of polycythemia and died shortly after this development. Other report describes polycythemia Vera in a child in remission from ALL who subsequently relapsed with ALL.

In a previous report published in 2007, a case of 76 years old male with polycythemia rubra Vera was reported who at the time of diagnosis in 1974 had hemoglobin of 23g/dl. TLC of 11.2×10^9 and platelets of 260×10^9 with spleen of 3cm, while his red cell mass was 60.6ml/kg and he was initially treated with venesection and aspirin¹³

While in our case patient had TRBC of 9.37×10^{12} and hemoglobin of 19.3g/dl with PCV of 66 l/l. The MCV was 64.2fl, MCH=18.6pg and MCHC was 29.0g/dl. TLC and Platelets were within normal limits. She had mild splenomegaly initially, which regressed after wards, she was also treated with venesection on regular basis.

In the previous case report patient was given low dose busulphan for increasing splenomegaly in 1979 because of

development of pancytopenia (Hb=12g/dl, TLC=2.5×10⁹, PLT=26×10⁹). He also developed splenomegaly of 12cm.

In our case patient did not have any treatment except regular phlebotomy and occasional use of aspirin and it was after 17 years that she developed Acute Lymphoblastic Leukemia while in previous report patient developed acute Lymphoblastic Leukemia within 05 years and his bone marrow showed 98% blasts. These blasts were positive for PAS and negative for SBB, choleacetate and butyrate estrases.

Bone marrow aspirate of our case showed 96% blast cells which were large heterogeneous with low N: C ratio having irregular nuclear membrane and were occasionally PAS positive. A diagnosis of Acute Lymphoblastic Leukemia (FAB Type ALL-L2) was given which turned out as Precursor B ALL with expression of CD13 on flow cytometry Analytical Immunocytochemistry confirmed Precursor B ALL with expression of CD13 and showed gated population of 86% and Blast/atypical population of weak CD45(92%), CD10+19(72%) and HLADR 87%, CD20+34(46%), CD34(47%), CD13(44%), CD33(12%), CD3(3%) , CD7(2%), CD5(3%).

While the previous case had strongCD38(99%), HLADR (76%), CD19(63%), CD10(49%),but surface immunoglobulin was negative and expression of CD23(2%), CD3(2%), CD5(0%), CD7(14%), CD11b(11%), Cd13(4%), CD33(7%) & CD14(6%) antigens were all at low frequency. These features were consistent with common ALL. That patient was given Vincristin and prednisolone but at 14th day bone marrow revealed residual disease, so he was given cytaraine. He did not recover and died of infection on 26th day of induction.

The association of Polycythemia Vera with ALL is of interest. The extreme rarity of transformation of Polycythemia Vera (PV) indicates that in most cases target cell is plueripotent Myeloid committed cell, however the rare occurrence of ALL in patients of PV indicates clonal expansion of an abnormal uncommitted plueripotent haemopoietic cell results in polycythemia Vera (PV) disease phenotype.¹³

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