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Case Study

CML- A IMPOSTER WITH MANY FACES

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ABSTRACT

Objective: The classification of chronic myeloproliferative diseases by the World Health Organisation includes eight forms of bone marrow neoplasms, including polycythaemia vera and Breakpoint cluster region-ABL viral oncogene homolog 1(BCR-ABL)-positive CML. Polycythaemia vera is diagnosed in the majority of cases (95%) only when the Janus kinase-2 mutation is present and the Breakpoint cluster region-Abelson murine (BCR-ABL) leukaemia viral oncogene homolog-1 rearrangement is negative.

Methods: Methods are not explicitly stated in the abstract; however, the study seems to have involved genetic testing and diagnostic evaluation to identify specific mutations and rearrangements associated with the conditions.

Results: With no Janus kinase-2 mutation, the presence of the Philadelphia chromosome, and the BCR-ABL leukaemia viral oncogene homolog one fusion gene, we report a case with erythrocytosis as the main feature of chronic myeloid leukaemia.

Conclusion: The case highlights a rare occurrence in the diagnosis of chronic myeloid leukaemia where typical genetic markers of polycythaemia vera are absent, indicating the complexity and variability in the genetic landscape of myeloproliferative diseases.

Keywords: Chronic myeloproliferative diseases, Polycythaemia vera, Chronic myeloid leukaemia, Janus kinase-2, BCR-ABL, Philadelphia chromosome

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INTRODUCTION

The World Health Organization classifies several chronic myeloproliferative neoplasms (MPNs), including Polycythemia Vera (PV) and Chronic Myeloid Leukemia (CML) characterized by specific genetic mutations. PV is predominantly diagnosed with Janus kinase 2 (JAK2) mutations, while BCR-ABL1 fusion genes hallmark CML. This case report describes a rare presentation of BCR-ABL1 positive CML initially presenting with isolated erythrocytosis, traditionally seen in PV, without the typical JAK2 mutations. This unexpected clinical presentation underscores the importance of comprehensive cytogenetic and molecular analyses in atypical cases of MPNs.

Chronic Myeloproliferative Neoplasms (MPNs) encompass a variety of disorders characterized by clonal proliferation of hematopoietic stem cells. According to the World Health Organization, these include Polycythemia Vera (PV), typically marked by JAK2 V617F mutations and BCR-ABL1 positive Chronic Myeloid Leukemia (CML). The coexistence or misdiagnosis between PV and CML can pose significant diagnostic challenges due to overlapping clinical features [1]. While PV primarily exhibits erythrocytosis, CML is commonly associated with leukocytosis and sometimes, unusual presentations like isolated erythrocytosis can occur, complicating the differential diagnosis [2]. Moreover, the genetic landscape of MPNs has been expanding with the identification of other mutations impacting diagnosis and treatment strategies [3].

CASE PRESENTATION

A 41 y old male, without significant medical history, presented with persistently elevated hemoglobin levels identified during routine checks. The patient exhibited no additional symptoms such as headaches, itching, presyncope, or dyspnoea, nor any history of exposure to high altitudes or radiation. Physical examinations were unremarkable, with no signs of hepatosplenomegaly. Laboratory findings revealed a hemoglobin level of 17.6 g/dl and a hematocrit of 51%, with mildly elevated erythrocyte counts. Secondary causes of erythrocytosis were ruled out through normal erythropoietin levels and lack of JAK2 mutations. Further diagnostic workup included bone marrow biopsy and cytogenetic analysis, which unexpectedly confirmed the presence of the BCR-ABL1 fusion gene, leading to a diagnosis of chronic myeloid leukemia [4, 5].

DISCUSSION

The five categories of stem cell diseases-primary myelofibrosis, essential thrombocythemia, polycythemia vera, CML, and erythroleukemia-were initially identified and described by William Dameshek [6]. After more than 50 y, the updated World Health Organisation categorisation [7] of MPN includes eight entities, including polycythemia vera and CML harbouring the BCR-ABL1 translocation, which has different phenotypes but shares a common stem cell-derived clonal heritage (leukocytosis with myelemia in polycythemia vera, whereas polycythemia in CML). Mutations in genes encoding tyrosine kinase proteins or related molecules (BCR-ABL1 fusion gene in CML and JAK2 V617F in polycythemia vera) cause aberrant signal transmission, which results in these changes [8]. An elevated mass of red blood cells is the definition of polycythemia in polycythemia vera. It could be assessed by lab results (Hb or HCT>99th percentile of method-specific reference range for age, sex, and altitude of residence) [9] or red cell volume measurement using radio-isotopic techniques, which enables the distinction between pseudo-erythrocytosis, which is found in a state of dehydration, and true polycythemia, as in paraneoplastic syndromes, chronic obstructive pulmonary illness, and polycythemia vera. Various diagnostic algorithms are used to investigate newly diagnosed (acquired) erythrocytosis. These algorithms rely on the measurement of erythropoietin levels to differentiate between primary erythrocytosis (which is caused by gene alterations and has low erythropoietin levels) and secondary erythrocytosis (which is caused by other factors and has high erythropoietin levels). In our case, measuring erythropoietin levels helped us avoid misdiagnosing a patient who had been clinically diagnosed with secondary erythrocytosis. Thus, other nonspecific markers-such as splenomegaly, which is lacking in this case, but as the patient we

treated had elevated lactate dehydrogenase and normal vitamin B12 levels, which are helpful in the diagnosis of MPN [10]. Additional research is recommended. Bone marrow cytogenetic analysis demonstrated the presence of the Philadelphia chromosome, which is found in CML; molecular analysis identified the presence of the BCR-ABL1 fusion gene, present in CML and the JAK2 V617F mutation, found in polycythemia vera, indicating panmyelosis (hypercellularity with tri-lineage growth). It is true that a small number of patients have been found to carry both the BCR-ABL1 fusion gene and the JAK2 V617F mutation. Nevertheless, the coexistence of the two mutations emerged as the illness developed [11]. To the best of our knowledge, the uncommon case presenting polycythemia is associated with a mutation-negative in JAK2 V617F; yet, it also carries the pathognomonic BCR-ABL1 fusion gene for the diagnosis of CML. Thus, we believe that polycythemia without a high neutrophil count may also be a hallmark of CML based on the normal erythropoietin level, the BCR-ABL1 positive status, which supports the monoclonality of red stem cells, and the massive evolution of erythrocytosis.

CONCLUSION

This instance represents a rare description of a CML in which erythrocytosis presents as the primary symptom, emulating a polycythemia vera with JAK2 V617F-negative status. Therefore, to conclude, we advise performing bone marrow cytogenetic analysis and examining such patients for BCR-ABL1 fusion transcripts, JAK2 V617F mutations, and exon 12 mutations.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally

CONFLICT OF INTERESTS

Declared none

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