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Pediatric chronic myeloid leukemia with B-cell lymphoid blast crisis at presentation

TO THE EDITOR: Chronic Myeloid Leukemia (CML) is a rare hematological malignancy accounting for less than 3% of pediatric and adolescent leukemias, with an annual incidence of approximately 1 per million children and young people aged <20 years [1]. The natural history and biology of pediatric CML is similar to those of adult CML and follows a tri-phasic pattern. Approximately 95% of children present with chronic phase CML (CML-CP) and the remainder present in the accelerated phase CML (CML-AP) or in blast crisis (CML-BC) [2]. CML-BC is defined by >20% blasts in the marrow or the presence of extra-medullary blast proliferation [3, 4]. Blast transformation of CML is lymphoid in 30% of cases and myeloid in the remaining 70%. We report the case of a 10-year-old boy who presented with a 6-week history of weight loss and left-sided upper abdominal pain. On examination, he was found to have substantial splenomegaly extending into the right iliac fossa. His full blood count showed a hemoglobin level of 6.6 g/dL, a platelet count of 148×10^9/L, and a total white cell count of 575×10^9/L. A differential count showed the following: blasts, 30%; promyelocytes, 6%; myelocytes, 24%; metamyelocytes, 11%; neutrophils, 7%; eosinophils, 9%; basophils, 3%; monocytes, 1%; and lymphocytes, 10% (Fig. 1). Flow cytometry of the blast population showed that the blasts expressed CD19, cyCD79a, CD10, HLA-DR, CD34, and TdT surface antigens. Chromosome analysis showed a t(9;22)(q34;q11) translocation consistent with a Philadelphia chromosome (Fig. 2A). Interphase fluorescence in situ hybridization (FISH) showed *BCR-ABL1* fusion signals in 90% of the nuclei (Fig. 2B). A minor breakpoint cluster region (210 kDa) was confirmed using RT-PCR. In the absence of a documented CML-CP, distinguishing between lymphoid blast crisis of CML and a Philadelphia chromosome-positive ALL can be difficult. A diagnosis of CML in B-cell lymphoid blast crisis rather than *de novo* precursor B-cell ALL was made because of the concurrent presence of basophilia, a predominance of metamyelocytes and myelocytes, and the p210 *BCR-ABL* transcript. The patient did not have any additional chromosomal anomalies associated with advanced phase CML and was negative for IgH rearrangement on FISH analysis.

The patient achieved a complete hematological response and a minor cytogenetic response following induction therapy comprising dexamethasone, vincristine, daunorubicin, asparaginase, and imatinib. Nonetheless, he subsequently died of idiopathic pneumonitis after allogeneic stem-cell transplantation.

The progression from CML-CP to CML-BC in the pre-tyrosine kinase era is well described, but CML-BC at presentation in children is extremely rare. The case reported here adds to the literature on the simultaneous presence of features of both lymphoblastic transformation and CML at presentation in the absence of cytogenetic clonal evolution. Further research into the biology of the aggressive phase of CML is required to develop novel targets to improve outcomes.

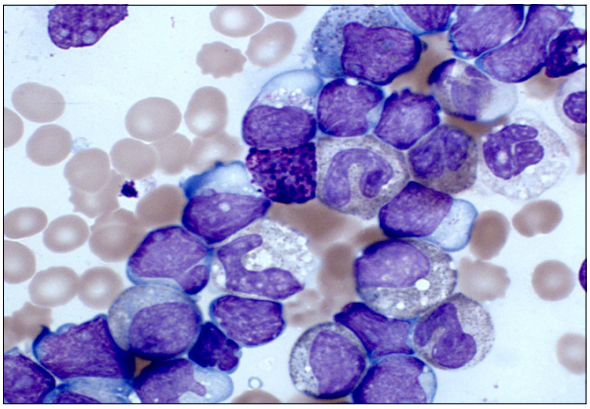

Fig. 1. Blood film demonstrating chronic myeloid leukemia in lymphoid blast transformation.

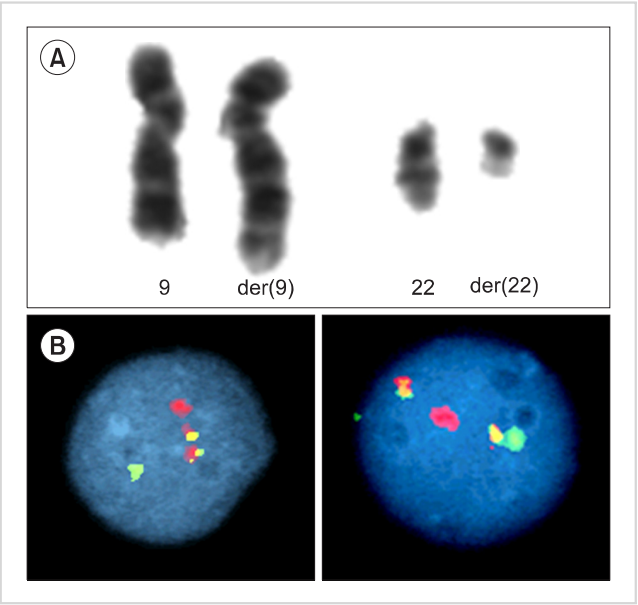

Fig. 2. **(A)** Karyotype showing t(9;22)(q34;q11) Philadelphia translocation. **(B)** Interphase FISH, Vysis dual-fusion probe set. Green: BCR; red: ABL1; yellow: fused BCR and ABL signals corresponding to der(9) and der(22) translocation products.

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Evolution of chronic myelomonocytic leukemia from refractory anemia: the unusual course of a myelodysplastic syndrome

TO THE EDITOR: Transformation from myelodysplastic syndrome (MDS) to chronic myelomonocytic leukemia (CMML) is rarely observed. However, this has been reported in cases of refractory anemia with ring sideroblasts or excess of blasts [1-4]. Moreover, MDS patients may present with monocytosis that does not meet the diagnostic criteria of CMML, which makes diagnosis and classification of these atypical mixed disorders a challenge [5, 6]. These difficulties in diagnostic classification and prognostic stratification may be concerning with regard to decision-making, particularly in this new era of effective disease-modifying therapies, such as hypomethylating agents [6, 7]. Recently, we faced such concerns during the management of a patient who developed CMML 7 years after having been diagnosed with refractory anemia (RA). The full clinical onset of CMML was preceded by progressive loss of response to ongoing treatment with an erythropoiesis-stimulating agent (ESA), worsening anemia, thrombocytopenia, leukocytosis, and increasing monocytosis. A morphological study of the peripheral blood (PB) and bone marrow (BM) revealed the coexistence of myelodysplastic and myeloproliferative syndromes. A cytogenetic alteration (45, X0,-Y), which was not present at diagnosis of RA 7 years earlier, was also detected during the CMML phase. The patient received azacitidine and showed a good response. Here, we describe this rare case and its implications in disease classification and management.

On January 2005, a 74-year-old man presented with moderately macrocytic slight thrombocytopenia. Five years earlier (in 2000), he had received postoperative radiotherapy after radical prostatectomy for prostate cancer. Apart from this prostatic neoplasm, for which a regular oncological follow-up had confirmed a persistent complete remission until then, he mentioned one previously cured gastric ulcer and well-controlled hypertension. He complained of fatigue and general unease for the past few weeks. A complete blood count prescribed by his general practitioner had revealed macrocytic anemia with a low reticulocyte count, mild thrombocytopenia, and slight neutropenia. On admission, he appeared pale and fatigued. A comprehensive laboratory evaluation did not reveal any remarkable abnormalities. His coagulative profile and renal and hepatic func-