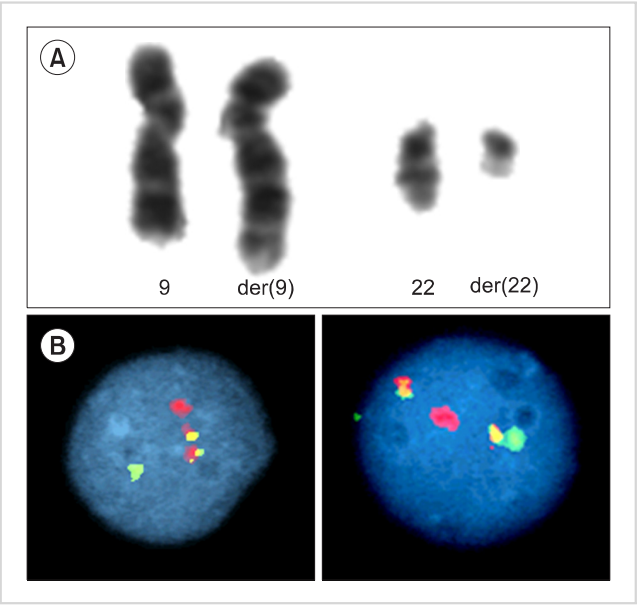

Fig. 2. **(A)** Karyotype showing t(9;22)(q34;q11) Philadelphia translocation. **(B)** Interphase FISH, Vysis dual-fusion probe set. Green: BCR; red: ABL1; yellow: fused BCR and ABL signals corresponding to der(9) and der(22) translocation products.

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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-

tion were normal. Suspicions of hemolytic disorders, virus infections, and iron and vitamin deficiencies were also dismissed. Morphological examination of PB smears showed isolated erythrocyte macrocytosis but did not provide any other diagnostic findings. BM aspiration and trephine biopsy were performed. BM examination revealed hypercellular BM with evident erythrodysplasia and 6% of blasts without fibrosis. Conventional karyotyping and fluorescence *in situ* hybridization analyses did not show abnormalities. Therefore, the patient was diagnosed with MDS, RA, according to the French-American-British classification. The patient had an International Prognostic Scoring System score of 1 (intermediate-1 risk). On admission and during the diagnostic phase, he received 4 units of red blood cell (RBC) concentrates. Thus, the patient was scheduled to receive ESA at a weekly dose of 40,000 units by subcutaneous injection (in January 2005). Since then, the patient was regularly followed-up at our clinic and continued to receive erythropoietin treatment. Normal PB values were maintained without the requirement for transfusion, clinical complications, or side effects until June 2012, when his hematologic status slowly began to deteriorate. Worsening anemia (requiring RBC transfusions), thrombocytopenia, and leukocytosis with absolute monocytosis became prominent. A comprehensive medical examination was performed. The examination of PB smears showed absolute monocitosis with 2% of circulating blasts. BM examination showed marked erythroid dysplasia and monocytosis with 15% blasts. A karyotype abnormality, such as 45, X0,-Y, which was not detected at initial diagnosis of RA 7 years earlier, was also found; however, the *JAK2* V617F mutation was absent. Therefore, the patient was diagnosed with RA, coexisting with type II CMML. The patient had a MD Anderson Prognostic Score of 3 (intermediate-2 risk) [8]. After a brief course of hydroxycarbamide, administered in order to reduce leukocytosis, the patient received 6 cycles of azacitidine (75 mg/m^2, schedule 5+2+2, each cycle every 4 weeks), according to approved indications [9]. After the second course, transfusion independence was achieved and the PB counts significantly improved with disappearance of monocytosis. Complete remission of CMML was achieved after 6 courses of hypomethylating therapy, without any adverse events. In conclusion, this case represents an atypical presentation of CMML secondary to MDS. In addition to its rarity and anecdotal interest, we believe that this report should be discussed with regard to several topics, such as the possible evolution of low-risk MDS in CMML, the existence of secondary CMML as a distinct disease, its absence in the current classification systems, and, finally, the efficacy of hypomethylating therapy [4, 10].

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