CLINICAL IMAGE

Multiple skin lesions caused by imatinib mesylate treatment of chronic myeloid leukemia

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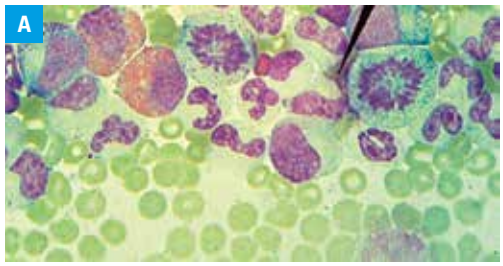
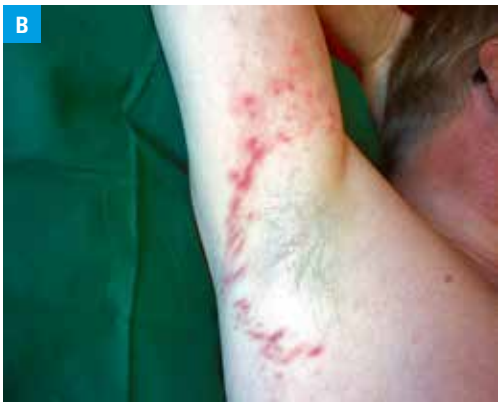
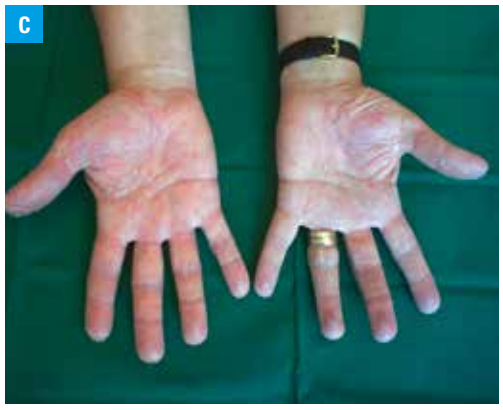
Chronic myeloid leukemia (CML) is a myeloproliferative disorder, caused by the clonal malignant transformation of a single pluripotent stem cell.[1] It results in excessive proliferation of myeloid cells in all stages of maturation in the bone marrow (FIGURE 1A), leukocytosis with a "left shift" in the peripheral blood, and often splenomegaly. CML is a rare disease constituting from 15% to 20% of all newly diagnosed adult leukemias with an average incidence of 1 to 2 cases/100,000 people. The underlying molecular abnormality of CML is the reciprocal translocation t(9;22)(q34;q11), widely known as the Philadelphia chromosome, which produces the chimeric *bcr-abl* oncogene that encodes a constitutively activated tyrosine kinase.[1,2]







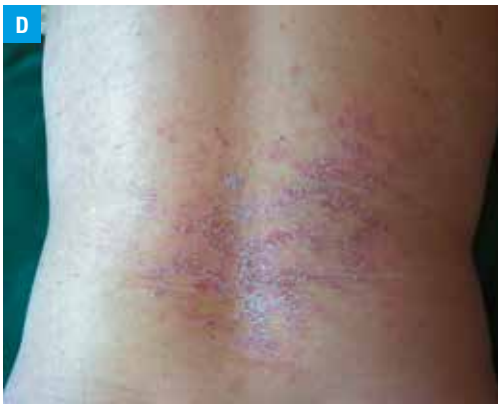


FIGURE 1 Chronic myeloid leukemia (CML) in chronic phase; bone marrow aspirate smears show excessive proliferation of different myeloid cells in all stages of maturation with the presence of frequent mitotic figures; May-Grünwald-Giemsa staining (magnification ×400) (**A**); skin lesions of the lichenoid dermatitis appearance caused by imatinib therapy 400 mg/d for newly diagnosed CML (**B–D**)

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The introduction of imatinib mesylate, the first tyrosine kinase inhibitor (TKI), at the end of 1990s has revolutionized CML therapy.[1,2] Its mechanism of action targets the BCR-ABL protein in CML, c-Kit, and platelet-derived growth factor receptors. Nowadays, TKIs represent the gold standard of CML therapy and are used as a front-line treatment in non-palliative patients.[1]

A 48-year-old, previously healthy man was diagnosed with chronic-phase CML, with the presence of the t(9;22)(q34;q11) karyotype. At diagnosis, he had moderate leukocytosis with 8% basophils, 2% eosinophils, and 0% blasts in the peripheral blood, a platelet count of 254×10^9/l, and no splenomegaly. His CML was classified as low-risk according to both the Hasford score (287) and the Sokal score (0.62). Imatinib mesylate (Glivec®, Novartis, Basel, Switzerland) was started at a standard dose of 400 mg/d with a prompt hematological response. However, after 2 months of treatment, the patient developed multiple erythematous skin lesions with severe peeling located on the fingertips and palms bilaterally, erythematous lesions in the armpits and on the sides, and confluent bright-red maculopapular lesions with lichenoid features on the back, penis, and groins (**FIGURE 1B–D**). The lesions were macroscopically assessed as lichenoid dermatitis caused by Glivec®. Dose reduction of imatinib to 300 mg/d was not helpful. However, the lesions subsided after discontinuation of treatment. The CML therapy was switched to dasatinib, a second-generation TKI, and new cutaneous lesions did not develop.

Usually, imatinib is a well-tolerated drug.[3-5] Nonhematological adverse events in CML appear in less than 10% of the patients and consist mostly of edema, weight gain, nausea, vomiting, diarrhea, fatigue, musculoskeletal pain and cramps, joint pain, and headache.[3,5] Cutaneous adverse events have been mostly reported as mild-to-moderate atypical rashes and occur mostly in patients treated with higher imatinib doses (i.e., ≥600 mg/d), accounting for 7% to 21% of all nonhematological adverse events of imantinib in CML.[3-5] Of note, severe skin reactions in the course of CML treatment with imatinib are rare.

Serious cutaneous adverse events may lead to discontinuation of TKI therapy in CML. However, this type of treatment in CML is of high priority due to its potentially curative properties. Thus, the use of second-generation TKIs (e.g., dasatinib, nilotinib) is recommended since cutaneous cross-sensitivity between these drugs and imatnib must not occur.

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