Development of Multiple Myeloma in a Patient with Chronic Myeloid Leukemia After Treatment with Imatinib Mesylate

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The co-occurrence of chronic myeloid leukemia (CML) and multiple myeloma (MM) is an extremely rare event and is considered to be coincidental [1, 2]. Imatinib mesylate (Gleevec®; Novartis Pharmaceuticals Corporation, East Hanover, NJ, http://www.pharma.us.novartis.com) is the new gold standard for the treatment of CML, particularly in patients who are not candidates for transplantation [3]. We report the case of a patient who was initially diagnosed with CML and developed MM after 7 months of treatment with imatinib mesylate.

A 68-year-old male was diagnosed with CML in December of 2001. Cytogenetic analysis revealed the presence of the Philadelphia (Ph) chromosome: 46, XY, t(9;14;22)(q34;q24;q11). BCR/ABL mRNA transcripts were detected with reverse transcription polymerase chain reaction (RT-PCR). The patient received interferon alpha, and after 10 months, a bone marrow smear revealed normal cellularity, normal maturation of all series, 2% mature plasma cells, and no increase in blast cells. Nevertheless, cytogenetic analysis showed no cytogenetic response. Therefore, on January of 2003, therapy was switched to imatinib mesylate (400 mg once daily), and after 7 months, a bone marrow smear revealed normal cellularity, normal maturation of all series, 2% mature plasma cells, and no increase in blast cells. Nevertheless, cytogenetic analysis showed no cytogenetic response. Therefore, on January of 2003, therapy was switched to imatinib mesylate (400 mg once daily), and after 7 months, a bone marrow smear revealed normal cellularity, normal maturation of all series, 2% mature plasma cells, and no increase in blast cells. Nevertheless, cytogenetic analysis showed no cytogenetic response. Therefore, on January of 2003, therapy was switched to imatinib mesylate (400 mg once daily), and after 7 months, a bone marrow smear revealed normal cellularity, normal maturation of all series, 2% mature plasma cells, and no increase in blast cells. Nevertheless, cytogenetic analysis showed no cytogenetic response. Therefore, on January of 2003, therapy was switched to imatinib mesylate (400 mg once daily), and after 7 months, a bone marrow smear revealed normal cellularity, normal maturation of all series, 2% mature plasma cells, and no increase in blast cells. Nevertheless, cytogenetic analysis showed no cytogenetic response. Therefore, on January of 2003, therapy was switched to imatinib mesylate (400 mg once daily), and after 7 months, a bone marrow smear revealed normal cellularity, normal maturation of all series, 2% mature plasma cells, and no increase in blast cells. Nevertheless, cytogenetic analysis showed no cytogenetic response. Therefore, on January of 2003, therapy was switched to imatinib mesylate (400 mg once daily), and after 7 months, a bone marrow smear revealed normal cellularity, normal maturation of all series, 2% mature plasma cells, and no increase in blast cells.

RT-PCR did not detect any BCR/ABL mRNA transcripts. Cytogenetic analysis revealed the absence of the Ph chromosome and no additional abnormalities. Laboratory values were within normal limits and a skeletal survey showed no lytic lesions. Using nephelometry, IgG levels were 2,340 mg/dl (normal range, 751–1,560 mg/dl) and λ light chains levels were 2,450 mg/dl (normal range, 313–723 mg/dl), without depression of the other immunoglobulins. One month later, examination of a new bone marrow smear revealed that mature plasma cells rose to 45%, while a bone marrow aspirate disclosed diffuse bone marrow infiltration by plasma cells that were shown to be λ light chain positive with immunoperoxidase staining. The patient was treated with melphalan (Alkeran®; GlaxoSmithKline, Philadelphia, http://www.gsk.com) and prednisone (Deltasone®; Pfizer Pharmaceuticals, New York, http://www.pfizer.com); imatinib was continued. Eight months later, a bone marrow aspirate showed normal findings (plasma cells 1.5%) and so did nephelometry.

The chromosomal abnormality detected in our patient is a complex Ph1 chromosome containing translocations between chromosomes 9, 14, and 22 and involves the locus of the λ light chain (22q11). This abnormality might have triggered the development of the two distinct hematologic malignancies: CML and IgGλ MM.

Our patient developed MM after 7 months of treatment with imatinib mesylate. Whether the development of MM was spontaneous or accelerated by imatinib is difficult to prove. Recently, imatinib has been shown to inhibit proliferation of MM cells in vitro by arresting cell-cycle...
progression; furthermore, it inhibited the proliferation of MM cells resistant to dexamethasone (Decadron®; Merck and Co., Inc., Whitehouse Station, NJ, http://www.merck.com) or melphalan and had an additive effect when combined with dexamethasone. Nevertheless, imatinib also exhibited a small stimulatory effect on the proliferation of MM cells through activation of the Erk1/2 mitogen-activated protein kinases route [4]. Existence of causality between the treatment with imatinib and development of MM cannot be ruled out.

Imatinib has revolutionized the treatment of CML, but experience with its use is still limited. Even though there is no evidence that administration of imatinib could result in the development of MM, vigilance should be shown in order to promptly identify potential side effects of this novel agent.

DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST
The authors have indicated no potential conflicts of interest.

REFERENCES


