Extramedullary blast crisis occurring in a ph+ cml patient with major cytogenetic response to imatinib

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Treatment of chronic myeloid leukaemia (CML) has been currently improved by the use of imatinib mesylate, a potent inhibitor of tyrosine kinase. This drug has been shown to induce a complete hematologic response (CHR) and major cytogenetic response (MCR) in over 80% and 60% respectively of patients who were resistant to other therapies1. However the long-term effects of imatinib are still unknown. We report here the occurrence of an extramedullary blast crisis in a patient who was treated with imatinib and had obtained a MCR.

A 71-year-old man was admitted to our Hospital in October 2002 for leukocytosis (WBC 56×10^9/L) and thrombocytosis (Plts 795×10^9/L). Physical examination revealed splenomegaly and cytogenetic analysis showed the presence of the Philadelphia t(9;22) translocation on 20 examined metaphases. No del 9q was evidenced. The patient was initially cytoreduced with hydroxyurea and was then started on interferon therapy. After 3 months, IFN? was stopped for intolerance (fever, anorexia, bone pains); at that time a karyotype analysis showed the persistence of 100% Ph^+ cells (20/20). Imatinib was then started and a CHR was obtained after 2 weeks; at 12 weeks a bone marrow examination revealed a MCR with 13% (2/20) Ph^+ cells. At week 20th of therapy, the patient experienced fever and chest pain. A CT scan revealed a pleural effusion and patient was treated with empiric antibiotic therapy. At that time CBC revealed only mild anaemia, with no evidence of blast cells in the peripheral blood. For the persistence of the chest pain the patient was admitted to our Emergency Unit where a thoracentesis was performed.

Cytological examination of the pleural effusion showed numerous myeloid blast cells (immunophenotype: $CD117^+$, $CD34^+$, $CD13^+$, $CD15^+$, $CD33^+$, MPO^+) (Figure 1); conventional cytogenetic analysis and FISH (Figure 2) showed a double Ph chromosome on all observed metaphases and interphases. A bone marrow examination, 1 week later, showed an infiltration by 25% blasts with similar cytological and karyotypic characteristics.

The patient received cytarabine and vindesine, but 2 weeks later he died for progression of disease.

This is the first report of an extramedullary blast crisis developed in Ph+ CML patient who was responsive to imatinib. The occurrence of abnormal Ph- clones as well as clonal evolution of Ph+ cells, has been reported in CML patients under imatinib treatment 2-5. It has been suggested that abnormal clones may arise from a Ph- stem cell in a preleukemic stage or may represent the clonal selection by imatinib in Ph- or in Ph+ stem cells with accumulated genetic lesions, occurring also in extramedullary tissues. Our case suggests that a careful monitoring in CML patients receiving imatinib must be made, in order to evaluate symptoms which can be not related to expected side effects of imatinib therapy. This case also indicates that long-term follow up of patients on imatinib trials is needed, in order to determine how this drug modifies CML natural history.

Figure 1. Myeloid blast cells in the pleural effusion.

Figure 2. FISH analysis on myeloid blast cells from pleural effusion.

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