Imatinib for secondary Ph+ acute lymphoblastic leukemia induces response in concomitant GBM

Imatinib is an inhibitor of tyrosine kinase currently employed for the treatment of chronic myelogenous leukemia and inoperable gastrointestinal stromal tumor (GIST).

Several trials [1, 2] have been conducted recently with imatinib as monotherapy for treatment of glioblastoma multiforme (GBM) and preliminary results suggest a good level of efficacy in this setting. According to these observations, Dresemann [3] has reported a series of 30 patients with grade IV progressive GBM refractory to chemotherapy and radiotherapy treated with a combination of imatinib 400 mg once daily and hydroxyurea 500 mg twice daily. The response rate in these patients was 20%, including complete and partial responses. Clinical benefit rate was 57% and median time to progression was 10 weeks, with a median overall survival of 19 weeks.

We here report the case of a 40-year-old man affected since June 2004 by grade IV GBM. He was treated with surgical resection of a left parietal lesion and from August 2004 he started a combination treatment with radiotherapy and temozolomide. Temozolomide was administered orally at 140 mg/daily (70 mg/m²/daily) for five consecutive days every week, for 6 weeks. Simultaneously radiotherapy was administered at a whole dose of 60 Gy in 30 fractions of

Figure 1. (A) Focal relapse of GBM during induction therapy. (B) Reduction of the size of GBM after 7 months of imatinib treatment.
2 Gy limited to the parietal region. After combined therapy on October 2004 the patient started planned maintenance treatment with temozolomide at 400 mg/daily (200 mg/m² daily) for 5 days every month. One month later temozolomide was discontinued for hematological toxicity as the patient developed persistent neutropenia and thrombocytopenia. Fifty-three days from the last dose of temozolomide, blasts cells appeared in peripheral blood and the patient was referred to our Department of Hematology, where we made diagnosis of Ph+ ALL FAB L1 subtype [4].

The patient started induction therapy according to the GIMEMA LAL 2000 protocol, including prednisone, vincristine, daunoblastine and asparaginase. Imatinib 800 mg/daily was added to standard induction therapy according to the presence of Philadelphia chromosome. At the end of induction therapy he was in complete hematological and cytogenetic remission. CNS prophylaxis was administered with intrathecal methotrexate and prednisone. Restaging of GBM was conducted during induction therapy with brain nuclear magnetic resonance, which documented focal relapse of disease (see Figure 1A).

The patient is now in continuous complete remission of the hematological disease. Blast cells did not ever appear in cerebrospinal fluid. Although an HLA-identical donor was available in the family, the progression of GBM was considered as an exclusion criteria for stem cell allogeneic transplantation and the patient was kept on imatinib. Eighth months after starting imatinib the patient remains in continuous complete remission confirmed at cytogenetic and molecular level. Unexpectedly, the last MRI performed at 7 months of imatinib showed a reduction of the size of GBM (see Figure 1B) diagnosed 11 months ago. This report seems to confirm the importance of imatinib as monotherapy for the maintenance of grade IV GBM previously treated with surgical resection and temozolomide. Furthermore, in our patient imatinib administration allowed him to reach stable disease both of GBM and ALL Ph+.


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