To the editor:

Dasatinib induces a response in chronic lymphocytic leukemia

Dasatinib is a novel oral multitargeted kinase inhibitor of Bcr-Abl and Src family widely used for the treatment of imatinib-resistant chronic myelogenous leukemia. Furthermore, preclinical studies by Shah et al[1] indicate that dasatinib may also inhibit gastrointestinal stromal tumor (GIST)–related mutations that result in resistance to imatinib. We describe the case of a dasatinib-responsive chronic lymphocytic leukemia (CLL) in a 61-year-old woman with coexisting relapsed GIST.

The patient was diagnosed with CLL in August 2007 (Binet stage B with unmutated IgV_H genes, del 17p13.1, and symptomatic disease). She was treated with fludarabine and rituximab and achieved a complete remission according to the International Workshop on Chronic Lymphocytic Leukemia criteria.[2] In January 2008 she underwent emergency laparotomy due to gastrointestinal bleeding. A jejunal GIST ($8 \times 10 \times 7$ cm) was completely resected and the patient was initiated on imatinib mesylate 400 mg daily until March 2008, when she developed unresectable metastases on the left hepatic lobe. Sunitinib 50 mg/day was administered for 4 consecutive weeks. In April 2008, computed tomography (CT) and magnetic resonance imaging (MRI) scans showed further tumor hepatic progression and numerous 2-cm lymph nodes in the anterior and posterior cervical chains as well as the supraclavicular, inguinal, and axillary regions. Her white blood cell count was 70.1×10^9/L with 96% lymphocytes with ZAP-70 and high CD38 expression in more than 20% of B cells by flow cytometric analysis; β_2 microglobulin was 4620 ng/mL (v.n. 1010-2150 ng/mL). Given the patient's poor performance status, no CLL therapy was initiated, she was prescribed oral dasatinib 140 mg daily after patient and institutional ethical board consensus.

After 3 months of dasatinib therapy the patient had normal complete blood counts. A new total body CT scan showed that all the lymph nodes had nearly completely resolved themselves. Bone marrow aspirate was free of CLL infiltration on cytologic and flow cytometric examinations, and hepatic MRI scans showed substantial tumor shrinkage. The most relevant aspect of our case is the powerful antineoplastic activity of dasatinib on CLL cells even if recent studies have revealed the in vitro capacity of dasatinib to induce apoptosis in CLL cells of patients with unmutated IgV_H genes[3] and the inhibition of antiapoptotic CD40 program in CLL cells with dysfunctional p53.[4]

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