To the editor:

Severe skin reaction to imatinib in a case of Philadelphia-positive acute lymphoblastic leukemia

STI571 (imatinib) is increasingly being used in the treatment of different phases of chronic myeloid leukemia and metastatic gastrointestinal stromal tumors.[1,2] Philadelphia-positive acute lymphoblastic leukemia (Ph^+ALL) has a poor prognosis with the current treatment options.[3] Allogenic stem cell transplantation is the only curative management option available to date, the long-term survival being 35% to 65%[4] in first complete remission, and poorer in second and third remissions. In a phase 2 trial with relapsed or refractory Ph^+ALL, imatinib induced hematologic responses in 60% of cases.[5] In this journal, Rule et al[6] recently reported that imatinib treatment can be continued in patients with skin eruptions by using concomitant short-term steroid therapy or by reintroducing imatinib with gradual dose escalation. The present study describes a case of Ph^+ALL with a severe adverse cutaneous reaction to imatinib, and its course upon reintroducing imatinib.

A 72-year-old white woman with Ph^+ALL showed hematologic response with induction therapy (vincristine, daunorrubicine, cyclophosphamide, and prednisolone). Maintenance therapy was started with mercaptopurine, after which imatinib was continued at a dose of 400 mg/d. After 17 days of treatment, the patient developed an erythematous maculopapular and mildly pruritic rash, with erosive ulcers on the mouth. The rash affected the back, abdomen, and upper and lower limbs. Some papules had a vesiculated center whereas others were target lesions. A papule biopsy diagnosed drug-induced erythema multiforme with folliculitis. Imatinib was discontinued and prednisolone was introduced. The patient refused to restart imatinib and continued with mercaptopurine alone. ALL relapsed 3 months later, followed by second complete remission with reinduction chemotherapy. At this point the patient agreed to restart treatment with imatinib. We decided to start with a low imatinib dose (100 mg/d) associated to prednisolone (30 mg/d). There were no further recurrences in skin eruption and presently, 30 days later, the dose is well tolerated. As a result, the imatinib dosage has been increased to 400 mg/d, with continuation of prednisolone at 10 mg/d.

Erythema multiforme is a severe adverse cutaneous reaction producing important morbidity.[7,8] In patients treated with imatinib, 7% to 21% suffer adverse cutaneous reactions.[9] This incidence appears to be dose-dependent, and 5% of such reactions are severe or life-threatening.[9] In coincidence with Rule et al,[1] the present case shows that imatinib can be reintroduced when it is associated to steroids over the short-term, even in patients with severe adverse cutaneous reactions.

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To the editor:

No effect of fasting plasma total homocysteine on protein C activity in vitro

Although the association between the plasma levels of total homocysteine (tHcy) and the risk of atherosclerosis and thrombosis is well documented, the mechanism(s) by which hyperhomocysteinemia might contribute to atherogenesis and thrombogenesis are scarcely understood.[1] In vitro studies showed that homocysteine, among other effects, inhibits both protein C activation and the activity of activated protein C (APC).[1,2] The inhibition of APC activity in vitro apparently depends on the interaction of homocysteine with cysteine residues of factor V, which interferes with the proteolytic action of APC on factor Va, resulting in APC resistance, a very common and well-established risk factor for venous thromboembolism.[2] However, several in vitro findings have not been confirmed in in vivo studies. For instance, in a study of healthy individuals and patients with previous thrombotic events, Cattaneo et al[3] showed that neither the fasting plasma levels of tHcy nor their acute increase after an oral methionine load affects the plasma concentration of APC. These data, which suggest that hyperhomocysteinemia does not interfere with protein C activation