CLINICAL IMAGE

Oral lesions in the course of myelofibrosis successfully treated using combination therapy with thalidomide, betamethasone, and cytarabine

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Myelofibrosis is a clonal proliferation of a pluripotent hematopoietic stem cell characterized by bone marrow fibrosis, extramedullary hemopoiesis, and leukoerythroblastic blood picture.[1] In myelofibrosis, the abnormal cell population releases different cytokines and growth factors, which leads to fibrosis and stromal changes in the bone marrow.[2] Extramedullary hemopoiesis in the spleen and liver is common but it is exceedingly rare in the mouth.[3]

A 67-year-old man presented with a several-day history of general weakness and sweats. The whole blood analysis revealed a hemoglobin concentration of 114 g/l (reference, 134–170), a platelet count of 413×10^9/l (145–348), and a white blood cell count of 32.8×10^9/l (3.5–8.8) with the presence of an apparent "left shift" (blast count, 0.32×10^9/l) and erythroblastosis. Moreover, his serum concentration of lactate dehydrogenase was elevated (40 μkat/l; 1.8–3.4) and computed tomography imaging disclosed splenomegaly (17 × 11 cm). A cytohistological examination of the bone marrow slides and trephine biopsy sections showed a picture of primary myelofibrosis with reticulin fibrosis (grade 3–4) and focal collagen fibrosis. Hydroxycarbamide was administered with a prompt improvement of the patient's general condition and normalization of peripheral blood picture.

Two years later, the patient developed painful lesions in the oral cavity (FIGURE 1A). The microbiological examination of one of the oral lesions revealed growth of *Candida albicans* and *Staphylococcus aureus*. Unfortunately, despite the administration of antimicrobial therapy (fluconazole, aciclovir) and local corticosteroids (clobetasol), the ulcerations grew progressively worse (FIGURE 1B) and the patient could not eat due to severe pain. He started to lose weight quickly and required opioids for pain control. A biopsy of oral lesions was performed and the histological examination showed a blastic infiltrate, which was immunohistochemically positive for CD45 (leukocyte common antigen) and myeloperoxidase. One month after the lesions appeared, the patient started injections with low-dose cytarabine s.c. without improvement. Two weeks later, the therapy was switched to high-dose cytarabine i.v. (1 g every 2–4 weeks) and betamethasone p.o., and the patient was started on total parenteral nutrition. After 1 month, the ulcerations almost healed and the patient could drink and eat again. Unfortunately, several weeks later, new mouth lesions appeared. The patient was started on thalidomide (50 mg/d, which was later increased to 100 mg/d) and betamethasone (4 mg twice a day) orally, in combination with high-dose cytarabine i.v. (1 g every 2–4 weeks). After 2 weeks of this therapy, the ulcerations healed (FIGURE 1C) and since have not reappeared.

Immunomodulatory drugs, such as thalidomide, lenalidomide, and pomalidomide, are a group of drugs that inhibit different cytokines and have antiangiogenic effects.[4,5] They are used in patients with myelofibrosis, alone or in combination with glucocorticoids, but the response is mostly seen with respect to anemia.[2] To our knowledge, this is the first report on severe oral blastic lesions in the course of myelofibrosis successfully treated using thalidomide,

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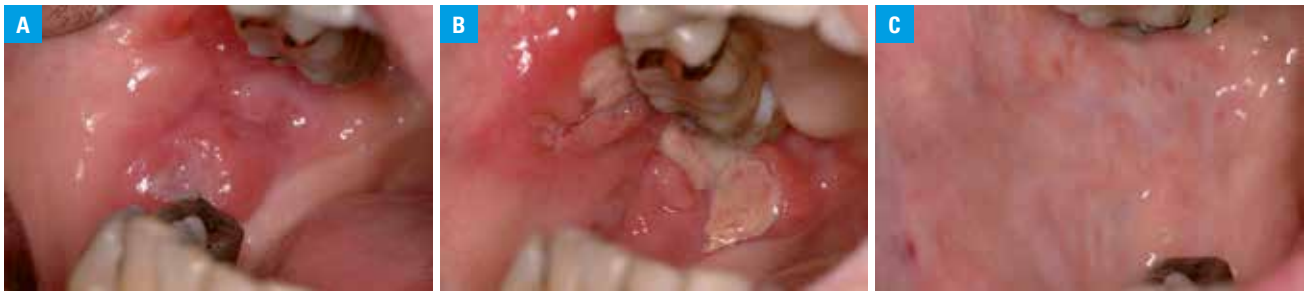

FIGURE 1 Oral lesions caused by blastic infiltrates in the course of myelofibrosis: (**A**) at diagnosis, (**B**) before, and (**C**) after thalidomide therapy

betamethasone, and cytarabine. We speculate that the addition of thalidomide to the therapy regimen had a key effect on the outcome.

REFERENCES

1 Barosi G. Myelofibrosis with myeloid metaplasia: diagnostic definition and prognostic classification for clinical studies and treatment guidelines. J Clin Oncol. 1999; 17: 2954-2970.

2 Cervantes F. How I treat splenomegaly in myelofibrosis. Blood Cancer J. 2011; 1: e37.

3 Jazieh AR, Kyasa MJ. A patient with myeloid metaplasia of the skin and mouth. N Engl J Med. 2000; 343: 1270-1271.

4 Jabbour E, Thomas D, Kantarjian H, et al. Comparison of thalidomide and lenalidomide as therapy for myelofibrosis. Blood. 2011; 118: 899-902.

5 Lacy MQ, Tefferi A. Pomalidomide therapy for multiple myeloma and myelofibrosis: an update. Leuk Lymphoma. 2011; 52: 560-566.