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Case report

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Colitis and chronic bleeding in patients treated with dasatinib

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Abstract

Dasatinib is a key therapeutic option in patients with chronic myeloid leukemia. Previous case reports associated it with acute colitis. This is another report that demonstrates a link between dasatinib and chronic colitis akin to inflammatory bowel disease, in patients undergoing therapy with dasatinib for a prolonged time.

Keywords: CML; dasatinib; colitis; toxicity

Introduction

Dasatinib is a tyrosine kinase inhibitor (TKI) approved for first and second line therapy in chronic myeloid leukemia (CML) and Philadelphia-positive acute lymphocytic leukemia.

The most common side effect of dasatinib is hematologic toxicity, while the most common non-hematologic side effects are pleural and pericardial effusions [1]. Few reports are available regarding gastrointestinal toxicity and a very few cases of dasatinib-related acute colitis have been reported [2-4].

Case report and discussion

Since 2009, we treated 14 patients affected by CML in chronic phase with dasatinib 100 mg per day. Five patients, all of them with a major molecular response, (BCR-ABL transcript level < 0.01% IS) developed abdominal pain and mild diarrhea (grade 1 or 2 according to CTCAE v4.0) at 13, 16, 18, 20 and 22 months from the start of therapy, associated with hypochromic microcytic anemia (grade 1 or 2 according to CTCAE v4.0) and low serum ferritin level in two cases. All symptomatic patients had fecal occult blood. A colonoscopy was performed, showing in all cases an erythematous colonic mucosa, associated in three cases with diffuse small aphthous ulceration.

Colonic mapping was performed in all of the patients; colonic mucosa appeared erythematous but substantial macroscopic differences were not found between the colonic tracts.

Microscopic examination of bioptic samples demonstrated mild glandular distortion, focal mucus depletion and a dense inflammatory infiltrate with neutrophil, lymphocytes, plasma cells and macrophages. No cryptic abscesses were observed (Figure 1). *Clostridium difficile*, cytomegalovirus (CMV), bacterial and parasitic infections were ruled out with specific tests.

Dasatinib treatment was suspended in all cases. The three patients with macroscopic mucosal lesions also received prednisone 25 mg per day for one month and mesalazin 3 g per day for two months. A new colonoscopy was performed three months after the first one, showing the regression of macroscopic lesions: histology demonstrated a normal colonic mucosa in all cases. All patients restarted therapy with a reduced dose of dasatinib (i.e., 80 mg per day). In one case, clinical signs of colitis reappeared after one month and dasatinib was permanently changed with another TKI.

Conclusion

Our experience seems to indicate that gastrointestinal toxicity in patients affected by chronic myeloid leukemia in therapy with dasatinib is not uncommon (5/14). In all of our

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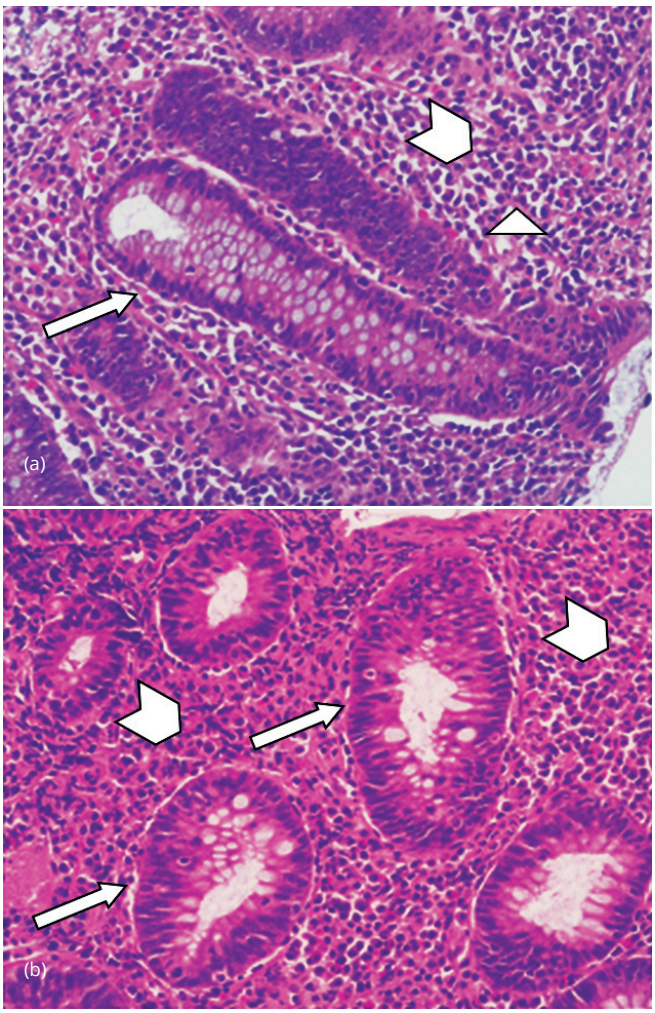

Figure 1a,b Bioptic samples of colonic mucosa in two different patients with CML treated with dasatinib. In both cases, there is a mild distortion and mucus depletion in colonic glands (arrows) and a dense polymorphic inflammatory infiltrate in the lamina propria with numerous eosinophils (arrowheads). Cryptic microabscesses are absent (Hematoxylin and eosin, x200).

patients who developed gastrointestinal toxicity we found occult colonic bleeding. We suggest to perform a fecal occult blood test periodically during chronic treatment with dasatinib. In selected cases with symptoms such as abdominal pain and diarrhea, or presence of fecal occult blood, a colonoscopy should be considered.

Conflict of interest

The authors declare that they have no conflict of interests.

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