Letters to Editor

Anagrelide induced acute pancreatitis in a patient with unknown etiology of bicytopenia and thrombocytosis

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Dear Editor,

Drug-induced pancreatitis has no distinguishing clinical features. A high index of suspicion and careful drug history are therefore essential for making the diagnosis. Proving the association with a particular drug may not always be possible, even in suspected cases.

The prevalence of drug-induced pancreatitis is still unclear because most incidences have been documented only as isolated case reports. The overall incidence probably ranges from between 0.1 and 2% of pancreatitis cases. When pancreatitis is induced as an adverse drug event the disease course is usually mild or even subclinical [1]

Anagrelide hydrochloride is an antithrombotic agent indicated for the treatment of essential thrombocythemia (ET). Anagrelide acts on cyclic-AMP phosphodiesterase III activity, which inhibits platelet aggregation selectively [2]. However, patients treated with anagrelide might experience adverse effects. The prevalence of adverse events due to anagrelide has ranged from 8% to 28% in various clinical studies [3, 4]. Anagrelide Study Group's experience with anagrelide was associated with major adverse effects including neurologic, gastrointestinal and cardiac [5]. Mazzucconi et al. reported gastrointestinal distress with anagrelide at a ratio of 15% in 19 ET patients. A larger study with a total of 405 patients with ET who were at high risk for vascular events received aspirin plus anagrelide; 59 (14.5%) of them had gastrointestinal adverse events except pancreatitis [3].

A 44 year-old-man was admitted to our clinic with bicytopenia, thrombocytosis and recurrent urinary way infection. His medical history revealed no chronic diseases or alcohol intake. Previously, bicytopenia and splenomegaly were detected during medical examinations in March 2009. At that time, bone marrow biopsy was normocelular, and revealed a relative increase in eosinophilic precursors and significant myelosuppression. Megacaryocytes were normal in size, number and morphology. Splenectomy was than performed in September 2009. Pathologic examination of spleen was compatible with congested spleen.

Initial complete blood count was; Hb: 9.2 g/dL (normal range: 13.6-17.2), WBC: 2.3 × 10^3/μL (normal range: 4.3-10.3), PLT: 865 × 10^3/μL (normal range: 156-373). Sedimentation rate was 70 mm/hour (range: 0-20). Peripheral blood smear showed 2% neutrophils, 54% lymphocytes, 10% monocytes, 4% basophils and 30% eosinophils. Anemia markers were associated with chronic disease anemia. Liver function tests were in normal ranges, except a moderate increase in ALP level (164 U/L, normal range: <129). Anti-nuclear antibody and anti-ds-DNA were negative.

He had neutropenic fever and imipenem 4 × 500 mg/day intravenously was initiated. Bone marrow biopsy was normocellular and revealed an increment in eosinophils and lymphocytes. Noteworthy, some of these lymphocytes were as large granular lymphocytes. Flow cytometry of bone marrow was positive for CD2, CD3, CD5, CD7, CD8, CD45, HLA-DR; and negative for CD16, CD56 and CD57 (CD4/8=6/83%). Conventional cytogenetic examination was normal. T-cell clonality was found to be positive with PCR. His platelet count increased to 1168 × 10^3/μL during follow-up. Therefore, anagrelide (Thromboreductin) 0.5 mg capsule two times daily peroral was started. Three days later he had an acute abdomen pain, with rebound tenderness in his physical examination. His oral intake and anagrelide administration were stopped. Abdominal ultrasound revealed hepatomegaly. However, abdominal computed tomography showed diffuse contrast enhancement around pancreas, extending to the pararenal fascias which was compatible with acute pancreatitis. Amylase and pancreatic amylase levels were 98.70 U/L (normal range: 28-100) and 25.61 U/L (normal range: 17-115) respectively. Lipid panel was as follows: triglyceride: 84.73 mg/dL (normal range: <200); HDL: 37.99 mg/dL (normal range: 40-60), LDL: 109.35 mg/dL (normal range: <130). Liver function tests remained in normal ranges, but LDH levels were increased to 592 U/L (normal range: 240-480). His abdomen pain improved gradually in three days after withdrawal of anagrelide. Platelet count was monitored closely and he was quite good in his next outpatient visit with a platelet count of 1059 × 10^3/μL.

Physicians should be aware of this rare clinic entity in the course of anagrelide treatment. Thus, patients started on their medications should be closely monitored and the related drug promptly discontinued in case of anagrelide-induced pancreatitis.

References

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