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LETTER

Bortezomib-Induced Acute Pancreatitis

Bouraoui Elouni[1], Chaker Ben Salem[2], Michelle Zamy[1], Jaballah Sakhri[3], Kamel Bouraoui[2], Michel Biour[1]

[1]Pharmacovigilance Regional Center, Saint Antoine Hospital. Paris, France.
[2]Department of Clinical Pharmacology, Faculty of Medicine of Sousse; [3]Department of Surgery, Farhat Hached University Hospital. Sousse, Tunisia

Dear Sir:

Bortezomib is the first proteasome inhibitor approved by the Food and Drug Administration (FDA) and indicated for patients with multiple myeloma refractory to at least one prior therapy [1].

The most common adverse effects of bortezomib include hematological toxicities (especially transient thrombocytopenia), gastrointestinal disturbances, peripheral neuropathy, fatigue, fever, dyspnea, rash, and myalgia [2]. We herein present the first case of acute pancreatitis induced by bortezomib.

A 58-year-old female was treated with vincristine, doxorubicin, and dexamethasone for a myeloma. She had no history of dyslipidemia or alcohol abuse. In relation to the relapse of the myeloma, two doses of bortezomib (1.3 mg/m^2) were administered intravenously at a 4-day time interval. Concomitant medications in our patient included dexamethasone, levothyroxine for hypothyroidism, and paracetamol. Two days later, she presented because of abdominal pain of medium intensity localized in the epigastrium for which she was hospitalized. On admission, the patient had normal vital signs without fever. Abdominal examination revealed only mild epigastric tenderness. There was no rigidity or guarding. There were no palpable abdominal masses. The remainder of the examination was normal. A laboratory work-up showed a normal blood cell count and did not demonstrate hypertriglyceridemia, hypercholesterolemia or hypercalcemia. A liver test, renal function, serum electrolytes and blood sugars were all normal. The determination of pancreatic enzymes revealed that serum lipase was high at 493 IU/L (reference range: 0-200 IU/L) but serum amylase was normal at 67 IU/L (reference range: 0-110 IU/L). Serology of infectious agents (hepatitis A, B, C, varicella zoster virus, cytomegalovirus, Epstein-Barr virus, human immunodeficiency virus, echovirus and Coxsackie viruses) were negative. On such basis, pancreatitis was suspected. Abdominal ultrasonography revealed a morphologically normal pancreas; there were neither peripancreatic fluid collections and nor biliary dilatation. Abdominal computed tomography (CT) did not show cystic or tumor lesions. An MRI-cholangiopancreatography examination revealed no hepatobiliary abnormalities including stones, and confirmed the abdominal ultrasonography and CT findings. Her lipase level four days after the last bortezomib administration had dropped slightly to 419 IU/L, and it was close to the normal level (256 IU/L) after another four days. At this time, the patient became asymptomatic. All the biologic values were within the normal range. Concomitant medications including dexamethasone and levothyroxin had not been stopped. Ten days after the last administration, the patient received bortezomib again. A few hours later, she developed abdominal pain with hyperlipasemia at 477 IU/L. The bortezomib was stopped immediately with the diagnosis of acute pancreatitis. The patient improved quickly after bortezomib withdrawal and serum lipase levels decreased to normal (145 IU/L) six days after the last administration. According to the Naranjo probability scale, bortezomib-induced acute pancreatitis was probable [3].

Although many drugs have been suspected of causing pancreatitis, they are a relatively rare cause with an estimated incidence of only 0.1-2% [4]. The pathogenesis of drug-induced pancreatitis is not clear, but it may be caused by an allergic response or by a direct toxic effect [5]. In our case, the diagnosis was based on the exclusion of potential medical causes, such as pancreatic malformation, diabetes,

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Correspondence Bouraoui Elouni
Centre de Pharmacovigilance, Hôpital Saint-Antoine, 75571 Paris cedex 12, France
Phone: +33-1.4347.5469; Fax: +33-1.430.7071
E-mail: elounibouraoui@yahoo.fr
URL http://www.serena.unina.it/index.php/jop/article/view/3829/4271

dyslipidemia, alcoholism, infectious agents, the resolution of clinical and biological signs when the bortezomib was withdrawn and evidence of a positive rechallenge. Recently, the beneficial effects of bortezomib in acute experimental pancreatitis have been reported. These effects of the drug seem to be mediated by the inhibition of nuclear factor kappa B activation and induction of heat shock protein synthesis [6]. Despite this possible anti-inflammatory effect in acute experimental pancreatitis, one should not exclude bortezomib as a possible cause of acute pancreatitis. Until now, no case of pancreatitis related to bortezomib has been published in the international literature and a search of OVIDSP (http://ovidsp.tx.ovid.com/), PubMed/MEDLINE (http://www.ncbi.nlm.nih.gov/sites/entrez) and EMBASE (http://www.embase.com) have also not revealed any previous case reports of pancreatitis associated with bortezomib. In conclusion, clinicians should be aware that acute pancreatitis may occur in patients taking bortezomib.

Conflict of interest None

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