Intravenous methylprednisolone induced acute pancreatitis: a case report

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ABSTRACT

Background: Acute pancreatitis (AP) is a common cause of hospitalization in gastroenterology. Drug-induced AP is a rare event, and only a few cases of corticosteroids induced AP are described in the literature.

Case Presentation: A 39-year-old woman with ankylosing spondylitis was hospitalized for an acute epigastric pain with vomiting 3 days after receiving a methylprednisolone bolus for an outbreak of her chronic disease. Her serum lipase concentration was found to be particularly elevated. She was then diagnosed of AP. An abdominal non-contrast CT demonstrated an exudative pancreatitis with a peripancreatic collection. The liver enzymes, her corrected calcium, and lipid profile were normal. An autoimmunity IgG4 screening was also found negative. The magnetic resonance imaging of the biliary tract found a normal pancreatic gland with a non-dilated common bile duct.

Conclusion: Due to the events chronology, the diagnosis of a methylprednisolone induced AP was retained after the exclusion of other causes of pancreatitis. It is important to think about this etiology when the most common causes have been ruled out.

Keywords: Acute pancreatitis, methylprednisolone.

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Background

Acute pancreatitis (AP) is a common gastrointestinal cause of hospitalization. The most common etiologies of AP are gallstone migration and alcohol. 15% of AP remain idiopathic, whereas 10% have a rare cause [1]. Drug-induced pancreatitis is a rare event, more and more described in the literature, with an estimated incidence that seems to be increasing of 0.1%-2% [2]. Corticosteroids are one of those drugs. We report a case of AP following high-dose intravenous (IV) methylprednisolone treatment for ankylosing spondylitis (AS).

Case Presentation

A 39-year-old woman with past medical history of AS presented to the emergency room of the Military Teaching Hospital Mohamed V of Rabat for an outbreak of her chronic disease. Four days of IV corticosteroids (methylprednisolone IV 240 mg/j) were administered, and she was then discharged on oral prednisone after a clinical and biological improvement. Three days after discharge, she presented to the Gastroenterology I unit for an acute epigastric pain with radiation to the back associated with nausea and vomiting. Her past medical history was ordinary other than her AS treated by nonsteroidal anti-inflammatory drug taken orally since 2011. She never had any biliary colic, didn't get a cholecystectomy. She denied alcohol use and did not take any other medication, including over-the-counter medications. She had no known medication allergies, and no medical history among her family. Her examination found a conscious, afebrile, anicteric patient, with normal vital signs. She had a normal body mass index. Her abdominal examination showed a soft, non-distended abdomen with no organomegaly but with an epigastric sensitivity. Her cardiovascular examination was otherwise normal. We performed an electrocardiogram and a troponin dosage that came back normal, while her serum lipase concentration was found to be particularly elevated (14 times the normal). The patient was then diagnosed of AP. The systemic inflammatory response syndrome (SIRS) criteria upon her admission were negative. An abdominal non-contrast computerized tomography (CT) was performed 72 hours later and demonstrated an exudative pancreatitis (Balthazar D) with a peripancreatic collection. The gallbladder, liver, spleen, and biliary tree were reported as normal. Laboratory tests performed upon her admission to the hospital were with normal limits except for an elevated blood lipase and an

elevated white cell count of 16,000/mm^3 with a negative C-Reactive Protein. Other than that, the liver enzymes including alkaline phosphatase, γ-glutamyl transferase, alanine transaminase, aspartate aminotransferase, and total bilirubin were within normal ranges as her renal function tests. Her corrected calcium, random glucose, triglycerides, and total cholesterol were normal too.

During her hospitalization, an magnetic resonance imaging of the biliary tract was conducted. It found a normal pancreatic gland and a non-dilated common bile duct, with the disappearance of the peri-pancreatic necrosis. An autoimmunity G4 Immunoglobulin (IgG4) screening was also found negative.

The diagnosis of a methylprednisolone induced AP was retained.

Indeed, the symptoms occurred 72 hours after the IV administration of high dose of methylprednisolone indicated in her AS with a negative investigation of all other common aetiologias. After a treatment based on bowel rest, IV fluids, thromboprophylaxis and analgesia for pain, the patient was discharged with a 1-month fat-free diet to be followed.

Discussion

Gallstone migration and alcohol are two of the most common etiologies of AP. Whereas nowadays, drugs represent 2% of AP etiologies in the general population [1].

In the literature, we only find case reports or small series about drug-induced acute pancreatitis (DIP). The first case of DIP was reported by Zion et al. [3] with the use of corticosteroids. Since then, more than 250 drugs were associated with AP. After reviewing all of the reported cases of DIP in PubMed since 1966 to 2004, Trivedi et al. [4] classified drugs into Class I, II, or III. Among all of the 100 most frequently prescribed medications, 44 have been implicated in AP and 14 fall under either Class 1 or 2 medications associated with pancreatitis. Methylprednisolone retained in our case stands 92 among those medications. More recently, Wolfe et al. [5] the most complete systematic review of DIP, that updated the previous one of Badalov et al. [6]. They identified 713 cases of potential drug-induced pancreatitis, implicating 213 unique drugs; and separated them in 6 drug classes. Methylprednisolone stands in Class Ia defined with at least one case report in humans with positive re-challenge and all other causes of AP and other drugs ruled out. With this rigorous classification, only six case reports were selected [7]. Our case report, following these criteria, does not stand in Class Ia but might be part of Class Ic. Indeed, our patient had only one episode of AP, did not have a case of re-challenge yet with all the most common aetiologias and all other drugs ruled out.

The diagnosis of DIP is retained by three elements [8]. First, you have to exclude the other aetiologias of AP. Second, the drug-induced AP must have been documented at least once. The list of all the drugs with pancreatic side effects can be found in a French website "Pancreatox" [9]. Finally, the events chronology is important. The shorter the time between the diagnosis of AP and the start of treatment, the more suspect the drug is. A clinical improvement right after drug stop, and a recurrence after re-administration of the drug represent a major imputability argument. The mechanism of action implicated in AP induced by corticosteroid in general has not been elucidated. There are two hypotheses: toxicity or immuno-allergy. The toxicity hypothesis is evocated after the study of Kimura et al. [10]. The *in vitro* study on isolated canine pancreas shows that the highest dose of corticosteroids induces a mild decrease of pancreas secretion with hyperviscosity. But other case reports in the literature described acute necrotizing pancreatitis with low dose of methylprednisolone which goes in the direction of the immuno-allergy hypothesis. On top of that, we know that IV form of methylprednisolone differs from oral form by the presence of hemi succinate which is suspected to cause the allergic immune response [11].

In general, the prognosis of DIP is excellent. Lankisch et al. [12] in their case series of 22 patients, described 19 edematous pancreatitis. None of them had an important necrosis nor death.

Conclusion

Drug-induced acute pancreatitis is a well-known entity and represents approximately 1% of AP. It is important to think about this etiology when the most common causes have been ruled out. Corticosteroids were incriminated in the occurrence of AP. The most evoked mechanism is about a viscous and high protein concentration in the pancreatic secretions. It might be a rare side effect, dose-dependent that occurs when high doses are used. The clinical picture is not specific but the symptoms chronology, the start of the incriminated drug, the clinical and the biological evolution might help to the diagnosis. Their prognosis is excellent.

What is new?

DIP is a rare event. In the literature, corticosteroids are one of those drugs. We add a new case report of an IV methylprednisolone induced AP.

List of Abbreviations

AP	Acute pancreatitis
AS	Ankylosing spondylitis
DIP	Drug induced pancreatitis
IV	Intravenous
MRI	Magnetic resonance imaging

Conflict of interest

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Consent for publication
Written and informed consent was taken from patient to publish this case report.

Ethical approval
Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of the case

1	**Patient (gender, age)**	Woman; 39 years old
2	**Final diagnosis**	Methylprednisolone induced acute pancreatitis
3	**Symptoms**	Abdominal pain radiated to the back; vomiting
4	**Medications**	Intravenous fluids; thromboprophylaxis; analgesia
5	**Clinical procedure**	Strict bowel rest + IV rehydration + low molecular weight heparin + nefopam for analgesia
6	**Specialty**	Gastroenterology