CASE REPORT

Acute necrotising pancreatitis derived from low-dose corticosteroid use: an important reminder of clinical management

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SUMMARY

Although the exact mechanism is unknown, incidence of drug-induced pancreatitis from corticosteroids is well established in the medical literature. Commonly reported in chronic steroid-dependent individuals who require large doses for a wide array of pathologies, the incidence of damage to the pancreas from low-doses have not been well described. We report a case of a 68-year-old woman who presented with severe abdominal pain, nausea and vomiting, 3 days after the initiation of low-dose methylprednisolone for osteoarthritis. Inpatient laboratory analysis revealed an elevated lipase of 1770 U/L and CT scan showing extensive necrotising pancreatitis involving the head, body and tail. Cessation of the causative medication and conservative treatment successfully led to resolution of symptoms. We present this case to inform clinicians of the precipitance of pancreatitis from modest strength corticosteroid management, so that more accurate and improved performance in pharmacological decisions can be made for patient care.

CASE PRESENTATION

A 68-year-old Caucasian woman presented to the emergency department with vomiting, generalised left upper quadrant abdominal pain radiating to her back and lower substernal/epigastric chest pain of 3-day duration; which the patient had never experienced before. Her medical history included osteoarthritis, hypothyroidism, diverticulitis, hyperlipidaemia, hypertension, generalised anxiety disorder and major depressive disorder. Current home medications included estradiol, lisinopril, cymbalta, simvastatin, lorazepam, clonazepam and levothyroxine, of greater than 6 months duration, with the recent addition of methylprednisolone. Surgical history was significant for left parathyroidectomy for benign adenoma removal, right inguinal hernia repair, hysterectomy, bilateral salpingo-oophrectomy and right knee replacement. Social history revealed the patient to be divorced. She did not drink alcohol and denied abusing drugs or smoking tobacco. The patient had allergies to sulfa-derived medications.

BACKGROUND

The current literature suggests the third most common cause of acute pancreatitis is drug-induced, which accounts for roughly 3–5% of all causes.¹ Widely used in the management of different conditions, epidemiological studies have shown oral glucocorticoid use in approximately 1% of the US population.² The cause of a wide range of adverse systemic sequelae ranging from glucose intolerance to osteoporosis, corticosteroid use has also been associated with the incidence of pancreatitis. Extensive case reports have described pancreatic anomalies in systemic diseases that require high dosage of oral chronic steroid regimens for treatment or remission. Such conditions, which require the aforementioned glucocorticoid therapy and have documented pancreatitis, include, but are not limited to, systemic lupus erythematosus, inflammatory bowel disease, IgA nephropathy and Wegener's granulomatosis.³ Although the exact dosage of corticosteroid medication to elicit pancreatic damage has not been established, review of reported incidents of drug-induced pancreatitis reveal that these are after significantly high doses of medication. We report an incidence of steroid use that was not prescribed in chronic fashion and was not at drug levels that would normally alter the hypothalamic–pituitary–adrenal axis.

INVESTIGATIONS

On further investigation, the patient stated that she had started a methylprednisolone 4 mg dose pack 3 days prior for osteoarthritis of the knee. Shortly after taking this medication, she started to have severe nausea and vomiting. Despite the symptoms, the patient said she continued her home medications including the methylprednisolone for the past 3 days prior to admission. On admission, her vitals were: blood pressure of 119/87 mm Hg, heart rate (HR) of 118/min, respiratory rate of 14/min, O₂ saturation of 90% on 3 L of oxygen, temperature of 36.72°C and pain scale of 9/10. Physical examination revealed a well-developed, well-nourished woman in acute distress with severe epigastric and left upper quadrant abdominal tenderness, no bowel sounds and a mildly distended abdomen. Relevant laboratory values revealed a white cell count (WCC) count of $17.3 \times 10^3/\mu\text{L}$, glucose of 177 mg/dL and lipase of 1770 U/L. Liver function tests including fasting lipid panel were normal. Serum electrolytes were within normal range.

A CT scan of the abdomen and pelvis revealed moderate to severe pancreatitis with evidence of parenchymal necrosis involving a 2.801 cm segment of the pancreatic tail, body and neck (figure 1). The patient was made NPO, given intravenous fluids, intravenous narcotics for pain control and started empirically on vancomycin for

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Figure 1 CT image showing parenchymal necrosis involving a 2.801 cm (black) segment of the pancreatic tail, body and neck.

treatment or prevention of infection. Gastroenterology (GI) was consulted for evaluation of the patient. GI performed an abdominal ultrasound, which revealed no stones in the gallbladder. GI also ordered a hepatobiliary (HIDA) scan, which revealed a normal ejection fraction and showed no evidence of common bile duct obstruction.

On inpatient day 2, an MRI was ordered, revealing a large amount of retroperitoneal and peripancreatic inflammation, and severe inflammatory changes to the pancreas consistent with pancreatitis, including multifocal areas of hypo-enhancement consistent with pancreatic necrosis in the mid-body with a length of 3.5 cm and in the pancreatic tail, 2 cm in size (figure 2).

DIFFERENTIAL DIAGNOSIS

Based on the information derived from the labs and imaging, along with the history obtained from the patient, differential diagnosis for acute necrotising pancreatitis at this time was switched from mechanical pathology involving gallstones or alcohol use, to other common causes such as of a possible pharmacological aetiology. Investigation revealed a medication that had been linked with pancreatitis. This involved the new addition of methylprednisolone to the patient's medication regimen.

Figure 2 MRI showing large amount of retroperitoneal and peripancreatic inflammation, severe inflammatory changes to the pancreas and pancreatic necrosis in the mid-body with a length of 3.5 cm (red) and in the pancreatic tail, 2 cm in size (blue).

TREATMENT

The patient continued on conservative management consisting of remaining *nil per os*, and was kept on antibiotic course and further supportive care with fluid resuscitation and analgesics. In addition, the methylprednisolone was removed from her medication regimen.

OUTCOME AND FOLLOW-UP

Close monitoring of this patient showed slowly decreasing lipase levels towards baseline over the next 8 days (figure 3). During this time the patient's clinical presentation improved, her abdominal pain resolved and WCC returned to a normal baseline value of $7.1 \times 10^3/\mu\text{L}$. On inpatient day 8, the patient's diet was advanced as tolerated and she was stable for discharge on day 9.

DISCUSSION

Inflammatory changes to the tissues of the pancreas can be caused by many commonly prescribed medications for a myriad of pathological conditions. Although the pathophysiological mechanism behind corticosteroid-induced pancreatitis remains unclear, recent data suggest it may be related to the systemic effects of these medications, and specific alterations of lipid and calcium metabolism in pancreatic cells.⁴ The current literature on epidemiological incidence of oral corticosteroid use suggests that the risk of acute pancreatitis was increased among current users compared with non-users, and the risk for development of this condition was highest 4–14 days after the medication was taken.³ This well-described period when acute onset of pancreatitis likely manifests is important for physicians to be aware of when a patient presents with the clinical symptoms of this disease and with recent history of corticosteroid use.

Based on pharmacological principles, formulations of corticosteroid medications that allow for wide-spread distribution in the body are more likely to cause systemic adverse effects. As such, there is no literature that indicates an association between the use of inhaled steroid use and acute pancreatitis arising out of negligible systemic uptake. Disease manifestations other than through the oral route have been elucidated. Ungprasert *et al*⁵ reported that an intra-articular injection of high-dose corticosteroids may lead to acute pancreatitis and, with subsequent readministration of the corticosteroid at the same strength, will create a recurrence of symptoms.

Anagnostou *et al*⁶ described the same medication that was used by the patient in our case, methylprednisolone and its link to the incidence of acute pancreatitis, but the patient they managed had been on a regimen of 58 mg/daily for a month before onset of clinical symptoms. As such, our report is the first incidence of low-dose ethylprednisolone use with only a combined 12 mg over 3 days that elicited the onset of acute necrotising pancreatitis. Although the patient was taking other medications that are linked to pancreatitis, those medications were used by the patient chronically for over 6 months; we believe the current presentation was because of the addition of the methylprednisolone to the patient's regimen. Resulting cessation of the medication along with supportive care showed appropriate patient response and recovery. We hope, from this report, that healthcare providers have gained a firmer understanding of the powerful systemic nature oral corticosteroids have on the human body and that significant side effects from these medications may be elicited even from limited doses. From this knowledge, we hope to

Figure 3 The levels of lipase in U/L graphed over inpatient stay. The following table has the corresponding information of the lipase taken each inpatient day, which is visualised in the chart.

	DAY #1	DAY #2	DAY #3	DAY #4	DAY #5	DAY #6	DAY #7	DAY #8
LIPASE LEVELS (U/L)	1770 H	1050 H	125 H	50	21 L	17 L	13 L	13 L

better prepare the healthcare professional in making smarter, more informed decisions in the pharmacological management of their patients who require these medications.

Learning points

- ▶ Drug-induced acute pancreatitis is the third most common cause of pancreatitis, accounting for roughly 3–5% of all causes.
- ▶ Corticosteroids are an important pharmacological medication, widely used in clinical practice, with 1% of the population of the USA on oral corticosteroids.
- ▶ The risk of developing acute pancreatitis is highest within days 4–14 of the management of a wide array of medical conditions.
- ▶ From our case, it is evident that even modest doses of corticosteroids can elucidate complications such as acute necrotising pancreatitis.

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