CASE REPORT

Case Report: Acute pancreatitis as a complication for the use of furosemide during transurethral resection of the prostate [version 1; peer review: 2 not approved]

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Abstract

Background: Pancreatitis caused after transurethral resection of the prostate (TURP) is an uncommon complication, with few reports found in the literature. Here we present the case of a middle-aged patient without comorbidities with this pathology.

Clinical case: A 66-year-old male patient with no prior medical history underwent TURP surgery due to benign prostatic hyperplasia. The evolution was unfavourable, leading to post TURP syndrome. On the fifth day after surgery, the patient was admitted for emergency dialysis. During his emergency stay, the patient was unstable; he was diagnosed with pancreatitis, moving to an intensive care unit for management. The patient progressed favourably from renal failure and pancreatitis, and on the 5th day the patient was discharged, tolerating oral feeding and stabilized renal failure.

Conclusions: Pancreatitis caused by TURP is very rare. This complication has been reported in the literature infrequently and should be suspected when there is pain in the epigastrium. If this complication is suspected, imaging tests and pancreatic enzyme levels should be immediately requested, as it can have an unfavourable evolution until death.

Keywords

Furosemide, pancreatitis, Transurethral Resection of Prostate, Drug-Related Side Effects and Adverse Reactions

Open Peer Review

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Any reports and responses or comments on the article can be found at the end of the article.

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Introduction

Acute pancreatitis caused after transurethral resection of the prostate (TURP) is an uncommon complication, with few reports found in the literature. It usually occurs in those who develop TURP syndrome¹.

The prognosis depends on suspicion of this complication in a timely manner because it lead to multi-organ failure and even death¹.

The case presented herein describes the case of a middle-aged patient who develops pancreatitis after TURP. The report describes how this was managed, the treatment used, and a review of the literature to identify similar cases.

Clinical case

A timeline of the patient's case can be seen in [Figure 1](#).

Patient information

A 66-year-old male with a prior history of high blood pressure (treatment, Valsartan 80 mg bid), without any prior history of alcoholism, previous pancreatitis episodes, or gallbladder disease underwent TURP surgery after diagnosis with obstructive benign prostatic hyperplasia (BPH). This was detected with an approximate weight of 45 gr by ultrasound and a verum-neck distance of 3 cm in cystoscopy. The patient had no family history of hypertriglyceridemia or gallbladder stones.

Monopolar TURP surgery was performed using 13 liters of distilled water for continuous bladder irrigation. During surgery, 80mg of furosemide EV was used to reduce the risk of dilutional hyponatremia. The operative time was 55 minutes, removing 17gr of prostate tissue; with no intraoperative complications. No lesion of the capsule or any significant bleeding was reported.

Figure 1. Timeline of the important points in the patient's medical history, interventions and follow-up.

Clinical findings

After surgery, a physical abdominal and genitourinary exploration was carried out. There was evidence of oral intolerance, abdominal distention and increased abdominal resistance, with pain at the epigastrium that radiated to the lumbar region. Permeable Foley catheter with clear urine was reported.

Diagnostic assessment

At 24 hours post-surgery, the patient presented elevation of azoles (Cr = 3.7mg/dl; Urea = 92 mg/dl) and oliguria, therefore furosemide 20mg was administered twice a day. After 72 hours of follow-up, the condition persisted, and it was decided to increase treatment with furosemide to 20 mg EV three times a day; despite this, it evolves in an unfavourable manner. On the fifth day after surgery, elevation azoles continued (Cr = 12.43 mg/dl; Urea = 235mg/dl), and there was also an increase in pancreatic enzymes (Amylase = 329U/L(Normal value <105); Lipase = 304U/L(Normal value: <50) ; leukocytes = 20880ml/mm³ (Normal value = 4500 ml/mm³ to 10500 ml/mm³). The aggregate infectious process was improved. An abdominal-pelvic CT scan was performed, finding a slight increase in the density of peripancreatic mesenteric fat with the presence of low laminar free fluid (Figure 2). The patient was transferred to the Intensive Care Unit (ICU) for emergency dialysis and stabilization.

Therapeutic interventions

Three sessions of haemodialysis and treatment of pancreatitis were required to stabilize the condition. On the fourth day of admission to the ICU, the patient progressed favourably from renal failure and pancreatitis by reduction in levels of pancreatic enzymes and creatinine, and on the 5th day the patient was discharged, tolerating oral feeding and stabilized renal failure.

Follow-up and outcomes

Amoxicillin/clavulanic acid 500mg three times a day was prescribed for five days. The Foley catheter was removed on

Figure 2. Abdominopelvic CT scan. Pancreas is not increased in size, no pancreatic necrosis, no peripancreatic collections. Slight increase in the density of mesenteric fat. Presence of low laminar free liquid.

the fifth day after surgery as it was not necessary to monitor urine volume. Renal impairment was progressively restored, and the level of creatinine three months after surgery was 0.98mg/dl. No urethral stricture or any other urinary complications were reported.

Discussion

Acute pancreatitis is an inflammatory disease of the pancreas that can also involve neighbouring tissues or organs, with a highly variable clinical presentation. In some cases, it has significant morbidity and mortality^{1,2}; 20% of patients adopt a severe evolutionary course, with persistent organ failure leading to mortality in 25%. The reported age range is between 50 and 75 years, as the incidence of acute pancreatitis increases with age^{1,2}.

Approximately 80–90% of cases are due to alcohol consumption and gallbladder lithiasis, while 10–20% have variable aetiology, including idiopathic, hyperlipaemias, viral infections, impaired pancreatic perfusion, ductal obstructions, drugs, and hypercalcemia^{3,4}.

Drug-associated pancreatitis is an underreported entity with an incidence of 0.1 to 2%⁵. Drugs that have been associated with causing pancreatitis that have been reported in the literature include antihypertensive agents, proton pump inhibitors, anticonvulsants, and chemotherapeutic agents⁵.

Lesions in the pancreatic tissue is caused by aggressor factors (drugs, infection, or metabolic disorder) and by the secondary activation of digestive zymogens within acinar cells, which trigger a subsequent inflammatory response³. The mechanisms by which these complications develop are not fully understood, but intestinal endotoxins and inflammatory mediators play an important role¹.

The diagnosis of drug-associated pancreatitis is by exclusion, so it is recommended to use the “Naranjo Scale of drug adverse reaction probability” in order to calculate the probability of adverse drug effect (Table 1). In 1981 Naranjo *et al.* validated this scale for cases of adverse drug reactions. In our case, the total score of our patient was 5 (answered affirmatively in questions 1, 2, 3 and 10), classified as probable in relation to furosemide⁶.

Drugs such as furosemide have been described that could damage pancreatic perfusion by decreasing intravascular volume, affecting blood flow, producing ischemia and the subsequent development of acute pancreatitis. It may also stimulate the exocrine pancreas producing a hypersensitivity reaction^{1,6,7}.

In our patient, Valsartan was suspected of having contributed to the presentation. However, due to the prolonged exposure time, it was dismissed as a possible aetiology.

In the literature, risk factors associated with drug pancreatitis have been described, of which our patient presented advanced age and vascular risk factors. As a result of these factors an

Table 1. Naranjo scale of drug adverse reaction probability.

Naranjo scale of drug adverse reaction probability	YES	NO	NK
Are there conclusive notifications about this reaction?	+1	0	0
Did adverse reaction occur after administering the suspect drug?	2	-1	0
Did AR improve after stopping drug administration or after administering a specific antagonist?	1	0	0
Did AR improve after stopping drug administration or after administering a specific antagonist?	2	-1	0
Are there alternative causes (other than the drug) that could have caused the reaction itself?	-1	2	0
Did AR reappear after administering placebo	-1	1	0
Was the drug detected in the blood (or other fluids) in toxic concentrations?	1	0	0
Was the reaction more severe when increasing the dose or less severe when decreasing it?	1	0	0
Did the patient have a similar reaction caused by the same or similar drug in any previous exposure?	1	0	0
Was the adverse event confirmed by any type of evidence of objective evidence?	1	0	0

Total score is the sum of the subcategories. The relationship is categorized as Definitive if the score is > 8; likely if it is between 5 – 8; possible if it is between 1 – 4; and doubtful if the score is 0

increase in pancreatic toxicity may have occurred, due to atherosclerosis of mesenteric vessels, resulting in furosemide making the perfusion worse by diuresis and intravascular volume depletion⁸. However, the exact mechanism is not yet known. However, some hypotheses include that furosemide could stimulate exocrine secretion of the pancreas, or mechanisms of hypersensitivity or immune response against a drug-protein. As evidenced in multiple reports, there are many confounding factors, but they only increase pancreatic susceptibility. In our case, the precipitating event is the administration of furosemide.

The present patient did not present capsule perforation or post-surgery bleeding. Berber-Deseusaa *et al.* present the case of a patient who presents capsule perforation during the intraoperative period¹. In our case, pancreatitis was mild, presenting improvement on the eighth post-surgery day after dialysis. However, the case reported by Berber-Deseusaa *et al.* presented severe necrotizing pancreatitis, leading to the death of the patient¹.

Acute pancreatitis is an infrequent complication reported after TURP^{1,9–11}; it can delay diagnosis if it is not considered as a possibility¹. In our patient, the surgery was without complication, unlike previous cases presented in the literature

where capsule perforation was observed¹. The present surgical time was 55 minutes.

On the other hand, the evolution of our patient was favourable in contrast to what was presented by Berber *et al.*, where the two patients presented unfavourable evolution with acute renal failure, ventilatory-circulatory deterioration, and death¹.

Conclusions

The clinical features of pancreatitis following TURP surgery has been reported previously in the literature but infrequently. This condition should be suspected when dealing with pain in the epigastrium post TURP. If this complication is suspected, imaging tests and pancreatic enzyme levels should be immediately requested, as it can have an unfavourable evolution until death.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

Consent

Written informed consent for publication of their clinical details and clinical images was obtained from the patient.

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Hrishi Joshi

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The authors introduce a case of acute pancreatitis requiring intensive care support. The initial causation is argued to be the surgical procedure (transurethral resection of the prostate), however, it becomes conflicted with the arbitrary use of furosemide peri-procedure without presented rationale.

The clinical diagnosis of pancreatitis isn't wholly convincing with borderline enzyme levels which in other countries of the world is only just diagnostic.

There is no information regarding prior patient details regarding BPE and trials of medical management. Procedure details are also not consistent with normal global practice including the use of distilled water as the irrigation fluid and use of loop diuretic both peri-procedure and post-procedure.

The leap to conclude that the operation is the cause of the pancreatitis isn't explained with any substantial supporting evidence and there are a plethora of alternative diagnoses equally as likely. There is little relevance to the practicing urologist from this case.

Is the background of the case's history and progression described in sufficient detail?

No

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

No

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

No

Is the case presented with sufficient detail to be useful for other practitioners?

No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Urology

We confirm that we have read this submission and believe that we have an appropriate level of expertise to state that we do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 15 February 2021

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The authors present a case report of mild pancreatitis that was diagnosed 5 days after TURP. Valuable information about the indication for TURP, patients PSA level, the trial of medical management for BPH, associated medical conditions is missing.

There is no description of the possible cause of postoperative Acute kidney injury after TURP. What were serum electrolytes levels? What was the ABG report?

Why was frusemide given? A detailed account of postoperative labs including CBC, BMP, and culture if performed will be useful. Was there any hydronephrosis? Any element of resection close to ureteric orifice causing a transient bilateral ureteric obstruction? It will be beneficial to the reader to have a chart of pre and post-operative biochemical investigations. Was the patient on any nephrotoxic medications?

Acute pancreatitis can occur in post-operative cases and due to any metabolic disorders. (PONKA JL, LANDRUM SE, CHAIKOF L. Acute Pancreatitis in the Postoperative Patient. *Arch Surg*. 1961;83(3):475-490.)¹

How can authors be so sure that frusemide is the potential cause? It appears multifactorial in the present case.

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Is the background of the case's history and progression described in sufficient detail?

No

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: endourological management of kidney stone and enlarged prostate

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

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