Section A-Research paper
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CASE REPORT:Tacrolimus induced acute pancreatitis in the immediate post operative period in a kidney transplant recipient: A case report.

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Abstract:

Acute pancreatitis (AP) is an unusual complication in the immediate post operative period following kidney transplantation surgery and has significant morbidity and mortality. Considering post-operative pain status, it is difficult to diagnose acute pancreatitis only on clinical background, warranting early suspicion and diagnosis. Tacrolimus, a calcineurin inhibitor, is a commonly used drug in kidney transplantation immunosuppression protocols. Although various adverse effects, including hepatotoxicity, nephrotoxicity, neurotoxicity, infection have been reported, there has been limited data with tacrolimus associated pancreatitis in kidney transplantation. Herein, we report the case of Tacrolimus induced AP in a living related kidney transplant recipient in the immediate post operative period.

Introduction:

Acute pancreatitis (AP) is an uncommonly encountered complication in the immediate post kidney transplantation period. The incidence of acute pancreatitis in kidney transplant recipient ranges from 1% to 14% [1,2,3,4,5]. Development of acute pancreatitis in kidney transplant recipients has been attributed to various factors including cholelithiasis, viral infections, Hyperparathyroidism, and immunosuppression drugs. Drug-induced pancreatitis (DIAP) accounts for ~2–5% of all AP cases and is a rare cause for acute pancreatitis. [6,7]. Although tacrolimus use is frequent in immunosuppressive protocol of kidney transplantation, there have been very few case reports regarding development of AP with tacrolimus use [8,9].

Case report:

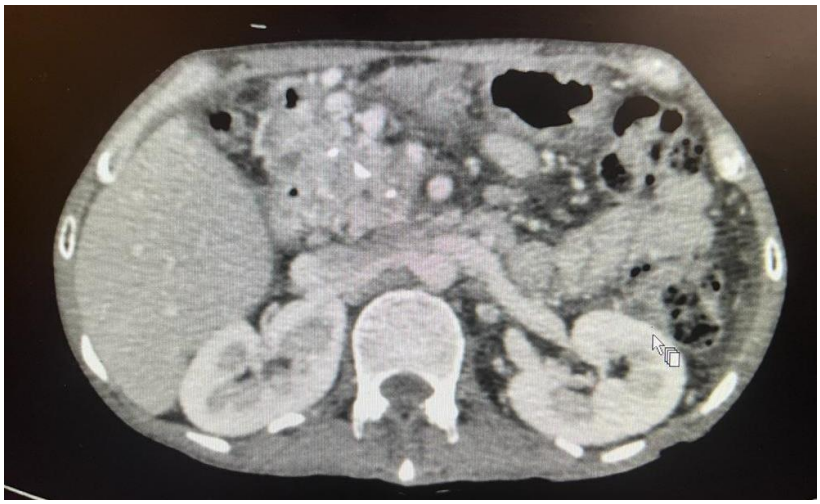
A 42-year-old male with end stage kidney disease underwent a live related kidney transplant with spouse as the donor. The patient was on twice weekly haemodialysis for a year previously. There was no history of jaundice, gallstones, alcohol intake, diabetes mellitus or hypertriglyceridemia. His body mass index was 26.53 kg/m2 (height, 179 cm; weight, 85 kg).

He received anti thymocyte globulin therapy (125 mg) as induction agent and immunosuppressive regimen consisted of tacrolimus (8.5 mg/day), enteric-coated mycophenolate sodium (1440 mg/day), and corticosteroids. the surgery was successful without any intra-operative complications. Also, the patient received methylprednisolone 1 g intra-operatively and post-operatively intravenous hydrocortisone in tapering doses (400 mg/day to 100mg tapering/day by post-operative day-4) and was then shifted to oral prednisolone 40 mg/day. Cefaperazone sulbactam (1.5 g 12 hourly) was used post-operatively for 7 days. Intravenous paracetamol 1 g (2-4 times a day) was used for pain control and nifedipine 10mg thrice a day was continued for hypertension.

Immediately next day after the operative procedure, he complained of intense abdominal pain in the epigastric and umbilical areas accompanied by nausea, and vomiting. Physical examination revealed moderate abdominal tenderness in umbilical area.

Laboratory analysis done one day post-transplant showed haemoglobin 8.3 g/dL white blood cells 13,100 /uL, neutrophils 7,320/uL, , platelets 2,00,000/uL, blood creatinine 2.18 mg/dL, blood urea nitrogen 45 mg/dL, serum sodium 135 mmol/dL potassium 3.5 mmol/L , serum calcium 7.4 mmol/L (corrected calcium-8.12 mmol/L), serum phosphorus 4.8 ,serum albumin 3.1g/L serum total cholesterol 126mg/dl serum triglycerides 114mg/dl , serum amylase 142 IU/L (normal 25–115 U/L), lipase 2604 U/L (normal 73–393 U/L), and trough concentration of tacrolimus 28.9 ng/ml (dosage was 8.5 mg/day). Ultrasonography showed no obvious pathology in the hepatobiliary tract. Pancreas could not be visualized due to overlying bowel gas.

On day 2, his abdominal pain worsened, and physical examination revealed moderate abdominal tenderness and rebound tenderness. Subsequently the patient underwent an abdominal CT can with contrast suggestive of a slightly enlarged pancreas with inhomogeneous head consistent with mild interstitial pancreatitis.



Based on these factors, the patient was diagnosed with acute pancreatitis. No evidence of CMV (cytomegalovirus), zoster, adenovirus or other virus infections was found. On day 2, tacrolimus was stopped, with mycophenolate sodium and corticosteroids continued. supportive care included fluid replacement, analgesics, and nil by mouth for initial 2 days. Four days after transplantation the patient's condition improved significantly, his abdominal symptoms were relieved, her blood amylase and lipase levels normalized. Tacrolimus levels done on 7th day were 9.9 ng/ml . The patient was discharged on day 10 post-transplant with a creatinine of 1.56 mg/dl. On follow-up after 1 month patient presented with uncontrolled sugars and was diagnosed with NODAT. There was no recurrence of pancreatitis at the 4 months follow-up.

Discussion –

Acute pancreatitis is an infrequently encountered complication in the immediate post-transplant period but has been associated with immunosuppressive (IS) treatment previously. AP in KTRs was first reported by Starzl in 1964. [(10)]. The aetiology of AP in KTRs can be multifactorial and not always obvious. [(11)] The traditional causes, i.e., gall stones and alcoholism are rarely seen in KTRs; and IS drugs and viral infections are the predominant causes. Based on the published weight of evidence for each agent and the pattern of clinical presentation, the various drugs causing AP are classified (Class I-IV; Class I and II drugs have the greatest potential.[(12,13)]. Azathioprine is strongly associated with AP and a causal relationship with AP has been established with rechallenge (Class I drug). The relative risk of AP with each one of the immunosuppressive drugs can be graded as: Azathioprine and dexamethasone (Class I drugs) >>prednisolone and cyclosporine (Class III) > Tacrolimus, mycophenolate mofetil and Everolimus (Class IV). [(14)]

In our case, at the time onset of pancreatitis, the patient was receiving varies of drugs including tacrolimus, mycophenolate mofetil, corticosteroids, antibiotics, paracetamol. Besides tacrolimus, only corticosteroids were strongly associated with pancreatitis. However,

presence of significantly raised tacrolimus levels in association with pancreatitis and resolution of pancreatitis with withdrawal of tacrolimus favoured tacrolimus induced pancreatitis strongly. Also, pancreatitis was relieved and did not persist with continuation of corticosteroids and other drugs. Hence, in this case ruling out traditional causes of pancreatitis (alcohol,infection,gall stones,hypercalcemia) and corticosteroid use , pancreatitis could be reasonably attributed to Drug induced (Tacrolimus) as etiology of pancreatitis.

Conclusion – AP should be considered as a possibility in all KTRs with unexplained abdominal pain in the immediate post-operative period. Tacrolimus use can rarely cause acute pancreatitis. Timely diagnosis and de-escalation or withdrawal of suspected offending drugs is pivotal in management of post kidney transplantation acute pancreatitis.

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Conflicts of interest: Nil