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CASE REPORT
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Pancreatic tuberculosis in a liver transplant recipient: a case report

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ABSTRACT

The pancreatic form of tuberculosis (TB) is rare and its diagnosis is challenging, since it manifests itself with non-specific symptoms and non-pathognomonic radiological findings, mimicking a neoplasia of the pancreas. Here, we report the case of a patient who had previously undergone liver transplantation and sought care for abdominal pain, weight loss, anorexia, hematochezia and postprandial fullness. Following an exploratory laparotomy and nucleic acid amplification testing on a pancreatic sample that had been collected, the patient was diagnosed with pancreatic TB. The patient received anti-tubercular pharmacological therapy and required percutaneous biliary drainage. Awareness of the possibility of a pancreatic TB diagnosis is important for clinicians. This attention should be even greater in patients who have undergone transplants, who are immunodeficient or who are from endemic areas.

KEYWORDS: Tuberculosis. Pancreas. Abdominal pain. Liver transplantation. Schistosomiasis.

INTRODUCTION

Tuberculosis (TB) is a disease caused by *Mycobacterium tuberculosis*. With an estimated 10.6 million cases in 2021, accounting for 1.6 million deaths in HIV-negative patients and 187,000 deaths in HIV-positive patients, TB constitutes, in 2021, the second leading cause of death from a single infectious agent, losing only to COVID-19[1].

While TB most frequently affects the lungs, it can also infect other parts of the body. These extra-pulmonary cases of TB correspond to approximately 12.5% of the total and have been shown to affect a multitude of organs, including in the abdominal cavity[2]. One rare but possible occurrence is the infection of the pancreas, which can affect both immunosuppressed and immunocompetent individuals[3].

Among the immunosuppressed are recipients of solid organ transplants. In these patients, a thorough review of the literature by Abad *et al.*[4] reported the median incidence of TB in cohort studies to be 2.37%, with extra-pulmonary presentations accounting for 29.48% of cases. Disease onset typically began after one year of transplantation and was frequently due to latent TB reactivation[4]. Although the study's data description combined all gastrointestinal occurrences without specifically mentioning the pancreas, two case reports of pancreatic TB were found among the study references[4].

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Due to its rarity and relevance to clinical practice, this report aims to describe the case of a patient who had previously undergone liver transplantation and was diagnosed with pancreatic TB a few years later. This case report was approved by the Research and Ethics Committee of the institution (CAAE 66678923.2.0000.5192).

CASE REPORT

A 54-year-old female patient sought medical assistance due to abdominal pain, anorexia, hematochezia, postprandial fullness and an unexplained weight loss of 20 kg in the past three months. Four years previously, she had undergone orthotopic liver transplantation, but was not screened for latent tuberculosis infection prior to the procedure. Likewise, the patient did not undergo prophylaxis with isoniazid and had since been on immunosuppressive therapy with tacrolimus and mycophenolate, without experiencing acute graft rejection. Although the patient came from an endemic area for TB, she had no recollection of any prior exposure.

By reason of her persistent condition, she was admitted to the hospital's general surgery department. Upon admission, the patient underwent a computed tomography (CT) scan of the abdomen that identified a dilated pancreatic duct. This finding was later reiterated by a magnetic resonance cholangiopancreatography (MRCP) (Figure 1) which also detected an expansive pancreatic process (Figure 2).

Afterward, an esophagogastroduodenoscopy (EGD) was performed, detecting a vegetating lesion in the major duodenal papilla. Thus, a possible neoplasia in the pancreas with duodenal invasion was put forth. Subsequently, the patient underwent an exploratory laparotomy during which a tumor measuring approximately 6 cm was found in the head of the pancreas. The examination also revealed an infiltration in the hepatic hilum and duodenum, as well as ascites and secondary lesions in the jejunal loops. Biopsies from the liver, jejunum, and pancreas lesions were collected, and a Roux-en-Y gastrojejunoanastomosis was performed.

Histopathological analysis of the biopsied material revealed mild chronic liver disease with a biliary pattern in the liver injury, chronic atrophic pancreatitis without signs of malignancy in the pancreas lesions, and chronic inflammatory schistosomal fibrosing reaction, with the presence of numerous viable eggs of the parasite in the peritoneum jejunal lesions. Due to the finding of the schistosoma, the hospital's infectious disease department was consulted. A joint follow-up was started, and peritoneal schistosomiasis was treated with two doses of praziquantel 20 mg/kg.

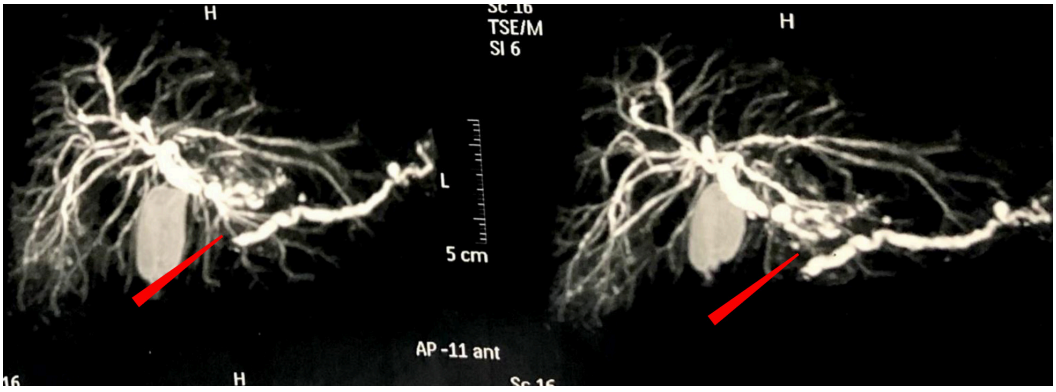

Figure 1 - MRCP showing dilation of the pancreatic duct and a failure in continuity present in the bile duct, suggesting obstruction by a periampullary tumor.

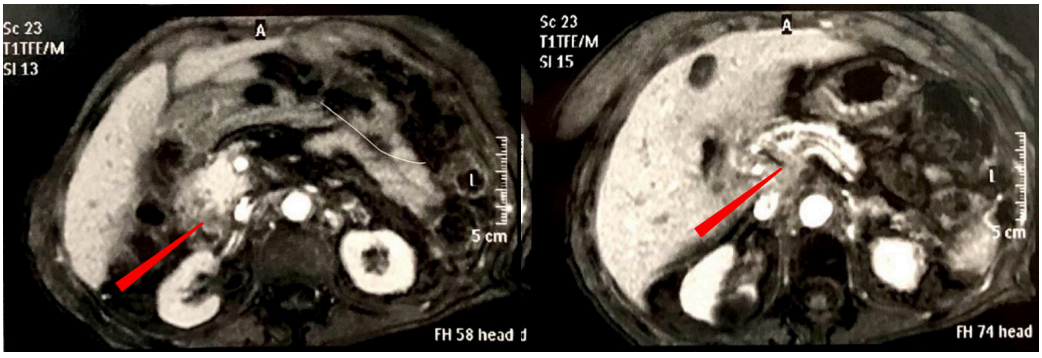

Figure 2 - MRCP showing a pancreatic expansive process, causing upstream dilation of the main pancreatic duct.

As the pathology report ruled out any malignancy, a differential diagnosis of TB was proposed to justify the tumor in the pancreas. Hence, the patient was re-submitted to an EGD and a new biopsy of the pancreatic mass was collected. This sample was sent to GeneXpert testing for *Mycobacterium tuberculosis*. The exam yielded a positive result and characterized the bacteria as being sensitive to rifampicin. With this confirmation, treatment for TB was instituted, consisting of rifampicin, isoniazid, pyrazinamide and ethambutol. However, after seven days of treatment, the patient presented with dizziness, asthenia, jaundice and an elevation of transaminases. Therefore, pharmacological treatment was suspended and the patient was transferred to the infectious disease ward.

Following the suspension of treatment, transaminases and bilirubin levels decreased. Gradual reintroduction of the medication was attempted, but symptoms of hepatotoxicity resurfaced. Thus, treatment was changed to an alternative regimen consisting of ethambutol, moxifloxacin and amikacin. Unfortunately, the patient developed acute kidney injury secondary to amikacin use, and the medical staff opted for its suspension.

Even with the alternative regimen, the blood bilirubin levels remained elevated. Therefore, a new MRCP was requested to better evaluate the biliary and pancreatic duct, as well as the pancreatic mass. The exam displayed an increase in the pancreatic mass. After reviewing the results with the medical staff responsible for the care of the patient's liver transplant, it was decided upon performing a percutaneous biliary drainage. The procedure was carried out successfully.

Since the obstructive cause of the increased bilirubin and transaminase parameters was excluded following the mechanical drainage of the bile ducts, the initial pharmaceutical protocol was re-established. The patient responded well to treatment, with no further complications. For this reason, the patient was discharged and received a referral to follow-up the anti-tuberculosis treatment at a hospital in her hometown. In addition, she was asked to return a month later to the surgery department, as it would be necessary to reassess the inserted biliary catheter. Finally, the patient was recommended to undergo weekly exams for blood biochemistry assessment.

DISCUSSION

In transplant recipients, TB has been demonstrated to be more common[5,6]. In a group of patients undergoing organ transplantation, a higher incidence of TB (4.9/1,000 person-years) was shown compared to non-transplanted patients (0.8 person-years)[5]. Further research has shown that liver transplant recipients have an eighteen-fold increase in the prevalence of active TB infection compared to the general population, with 67% of those having extrapulmonary involvement[6]. As it relates specifically to pancreatic TB, Coelho et al. recounted a case which was diagnosed following orthotopic liver transplantation[7]. To the best of our knowledge, this was the only case of pancreatic TB following a hepatic transplant previously reported in the literature, which highlights its remarkable rarity.

It's also important to emphasize the significance of screening for latent tuberculosis infection before undergoing transplantation. Unfortunately, our patient did not receive this screening which should involve both the tuberculin skin test and the interferon-γ release assay[8]. In case of positivity, prophylactic pharmacological treatment should be administered[8].

Another particularity identified in our case was the co-infection with *Schistosoma mansoni* detected in a peritoneal biopsy. As far as we know, this is the first description of *Schistosoma mansoni* co-infection with TB located specifically in the pancreas. However, other co-infections have been previously reported in cohort and case-control studies conducted in the Sub-Saharan Africa, with rates ranging from 4.3% to 34%[9]. Co-infection is significant since *Schistosoma mansoni* can weaken the host's immune response to latent TB, potentially resulting in its reactivation[9]. This may have played a role in our patient's disease onset.

Because it's a rare condition, pancreatic TB presents challenges. Its non-specific symptoms complicate and delay the diagnosis. Symptoms of pancreatic TB include abdominal pain, the presence of an abdominal mass, malaise, anorexia, weight loss, night sweats, backache, jaundice and fever[3]. When the head of the pancreas is involved, jaundice and abdominal pain are the most common symptoms[3]. With regards to its clinical presentation, a pancreatic mass is predominant (79.5% of cases) with the head being its most common location (59% of cases)[2].

The radiological findings, in turn, are atypical and not pathognomonic[10]. Pombo *et al.*[11] analyzed six different patients with pancreatic TB, and described that "the most common CT finding was a focal pancreatic mass lesion, often associated with low-attenuation peripancreatic and periportal lymphadenopathy and/or bile duct dilatation". Nevertheless, there was a wide variability of symptoms, especially in HIV-positive patients. With regards to the use of MRCP, it has been previously described in the literature. In a previous case report, the main finding was recounted as the dilation of the pancreatic and bile ducts by a mass in the pancreas[12]. This finding is similar to the one exhibited in our case report.

Due to its non-specific symptoms, the usual radiological finding of a mass in the pancreas and its low prevalence in the population, pancreatic TB is commonly described as a mimicker of pancreatic neoplasia[2,3]. Thus, direct analysis of biopsied material becomes essential for its diagnosis. For this purpose, endoscopic ultrasound fine needle aspiration biopsy has been recognized as an effective and less invasive sampling method[2,13]. However, what is most often seen in practice is the diagnosis of pancreatic TB occurring only after an exploratory laparotomy with the collection of material for histopathological analysis in the suspicion of malignancy[2,10,13,14]. The recurrence was evident in our case report and the diagnosis was made after surgery.

After sampling, TB can be identified by microscopic analysis, culture technique and nucleic acid amplification test (NAAT)[15]. Among these, the culture for *Mycobacterium tuberculosis* remains the gold standard[15]. However, as a disadvantage, the culture may require up to 60 days for a definitive result to be achieved[15]. NAAT, in turn, provides a quick result[15]. GeneXpert assay, a form of NAAT testing, was applied in our case report. Its sensitivity and specificity have been previously studied in extra-pulmonary TB. Hence, a Cochrane Review published in 2018 evaluated GeneXpert sensitivity and specificity for TB diagnosis and found a sensitivity of 31-97% – depending on the specimen evaluated – and a specificity of ≥ 98%[16]. Nonetheless, the study didn't analyze pancreatic samples.

Finally, treatment for pancreatic TB involves the use of antitubercular pharmacological therapy[14]. The use of rifampicin, isoniazid, pyrazinamide and ethambutol for two months followed by the use of isoniazid and rifampicin for four months is the mainline treatment for most cases of extra-pulmonary TB[17]. Hepatoxicity can happen and lead to a change in pharmacological regimen[17]. In transplant recipients, rifampicin has been linked to reduced serum levels of calcineurin inhibitors[18,19]. This reduction leads to a higher incidence of acute rejection and graft loss[18]. As a consequence, in these patients, it has been recommended that either rifampicin use should be avoided or that immunosuppressant doses should be increased during the course of treatment[20]. When a biliary obstruction is present, patients require surgical intervention to offset the ductal narrowing, since it can persist despite pharmacological treatment[14]. This was observed in our patient's case.

CONCLUSION

Pancreatic TB is a rare disease that presents with nonspecific clinical symptoms and radiological findings. This makes it a mimicker of neoplasia and complicates its diagnosis. Thus, analysis of a pancreas biopsy is necessary for diagnostic confirmation. Since pancreatic TB is often assumed to be a malignancy, cases are usually diagnosed after an exploratory laparotomy. However, fine needle aspiration biopsy has been described in the literature as a less invasive possibility to the surgical procedure. For the immediate biopsy analysis, the use of GeneXpert is an accessible and fast option and has been previously demonstrated to have variable sensitivity and high specificity in extra-pulmonary samples.

The treatment for TB is already well-established, effective and usually curative. Early diagnosis is crucial for a better prognosis, underscoring the importance of timely detection. Yet, for a successful intervention, careful monitoring for hepatotoxicity and the optimization of immunosuppression is needed. Clinicians should be aware of the possibility of pancreatic TB in patients who have previously undergone transplantation, are immunodeficient or come from endemic areas.

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AUTHORS' CONTRIBUTIONS

DRV: conceptualization, methodology, data curation, writing: original draft, project administration; PHTMP: conceptualization, data curation, writing: original draft; PRAM: writing: review and editing, visualization; HCBN: writing: review and editing, visualization; AMORS: supervision, validation; MERV: writing: review and editing; TLLF: supervision.

CONFLICT OF INTERESTS

The named authors have no conflict of interests, financial or otherwise.

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