Endotipsitis in a liver transplant patient: the role of positron emission tomography in a challenging diagnosis

M. Lepour[1], G. Dahlqvist[1]

(1) Department of Gastro-enterology, Cliniques Universitaires Saint-Luc, Brussels.

Abstract

Endotipsitis is a rare but serious infection of TIPSS, with no established diagnostic criteria or treatment guidelines. It presents significant diagnostic challenges, particularly in immunocompromised patients such as liver transplant recipients.

We report the case of a patient who underwent liver transplantation followed shortly thereafter by TIPSS placement due to refractory ascites (PSVD of the liver graft). He presented 10 years after with decompensation of cirrhosis and fever. Despite negative blood cultures, FDG PET-CT revealed intense hypermetabolism along the TIPSS suggesting endotipsitis. He was treated initially with antibiotics and required ultimately a liver retransplantation.

This case is notable for its occurrence in a transplant recipient, the absence of bacteremia, and the extremely delayed onset after TIPSS placement, the longest interval reported to date. Diagnosis was made through PET-CT, highlighting its critical role when conventional investigations are inconclusive. (Acta gastroenterol belg., **2025,** 88**, 367-370).**

Keywords: Endotipsitis, Liver Transplantation, Cirrhosis, PET-CT.

Introduction

Endotipsitis is a rare but potentially severe infectious complication of the Transjugular Intrahepatic Porto-Systemic Shunt (TIPSS) and remains both a diagnostic and therapeutic challenge. The reported prevalence is approximately 1% of TIPSS placements, but this figure is likely underestimated due to frequent underdiagnosis and the lack of standardized criteria (1,2).

Over the past 15 years, a few case-report-based literature reviews have been published, but no prospective studies or clinical guidelines are currently available on the topic (2-4).

We report here the case of a transplanted patient who presented with decompensation of cirrhosis due to an endotipsitis for which the diagnosis proved particularly challenging.

Case presentation

We report the case of a 61-year-old man who underwent liver transplantation (LT) in 2013 for alcohol-related cirrhosis, and TIPSS placement in 2014 for refractory ascites due to portal hypertension (hepatic venous-portal gradient of 15 mmHg) with refractory ascites, attributed to a porto-sinusoidal vascular disorder of the graft, as suggested by sinusoidal dilatation and stage F2 fibrosis (METAVIR) on liver biopsy. The TIPSS has been thrombosed since 2018 with no precipitant factor identified at that time. Ascites did not recur afterwards. The liver biopsy in 2018 showed extensive fibrosis (F3 METAVIR) with sinusoidal dilatation and congestion. He had a persisting mild inflammatory syndrome since 2018.

Five months before admission on a routine blood test, CRP was higher than usual at 20.9 mg/L (N<5 mg/L) with a mild elevation of total bilirubin at 1.21 mg/dL (N<0.6 mg/dL), with a stable chronic cholestasis (GGT to 5x upper the limit of normal (ULN) and alkaline phosphatase to 2x ULN). Two months before admission, CRP rose to 31.9 mg/L and total bilirubin to 2.09 mg/dL (direct: 1.14 mg/dL). A Doppler-ultrasound was performed in that time revealing a known splenomegaly at 20 cm, mild ascites in pelvis and the thrombosis of the TIPSS.

The patient was seen in our clinic a few weeks later for a 10-year post-LT protocolar liver biopsy. The subsequent histology showed F4 fibrosis (METAVIR), a mild lymphocytic inflammatory infiltrate in the portal spaces and no sign of graft rejection. A triphasic computed tomography (CT) of abdomen was performed in the course and showed a subcapsular collection of 5.5x1.5 cm in the left liver and mild ascites.

Two weeks later, he presented to the emergency department with a history of asthenia, fever up to 38.5°C, and acute increased of abdominal perimeter. An abdominal CT was performed and showed the subcapsular collection increasing in size (6.1x2.3 cm), repermeabilization of extra-hepatic venous shunts and important pluricompartimental ascites (Figure 1). Physical examination was marked by tense ascites and jaundice. Laboratory investigations showed moderate inflammation (CRP 63 mg/L), elevated bilirubin (4 mg/dL) and an INR of 1.60. Ascites was sterile with a macrophagic formula.

These findings were consistent with a subacute decompensation of graft cirrhosis characterized by recurrent ascites and jaundice. Portal hypertension worsened, with increased ascites and extra-hepatic shunts. An infectious cause was initially suspected.

Correspondence to: Maxence Lepour, MD, Department of Gastroenterology, Cliniques Universitaires Saint-Luc, Avenue Hippocrate 10, 1200 Brussels, Belgium.

Email: max.lepour@gmail.com
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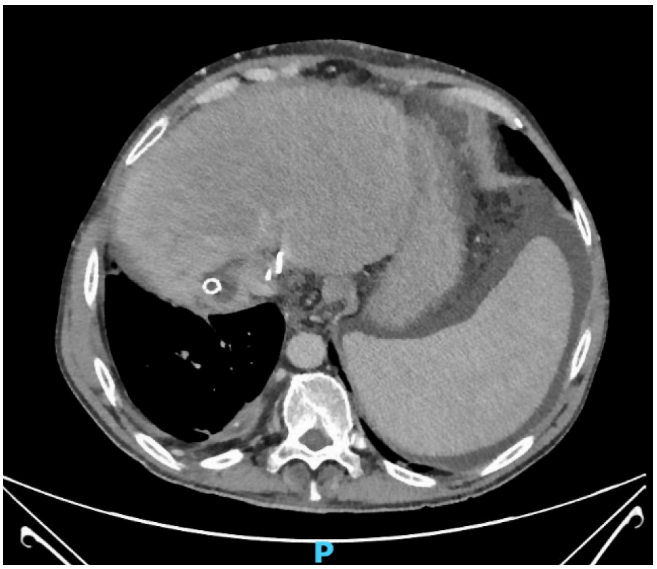

Figure 1.

However, blood and ascites culture remained sterile, even after prolonged incubation. The subcapsular liver collection was first interpreted by radiologists as a potential infected hematoma, but this hypothesis was ruled out since the recent liver biopsy had been performed in the right lobe, whereas the collection was in the left. To further investigate the source of infection, a fluorodeoxyglucose positron emission tomography (FDG PET-CT) was performed. It revealed intense hypermetabolism along the TIPSS and at both ends of the shunt (Figure 2), suggesting endotipsitis.

An initial puncture attempt failed due to poor ultrasound visualization. A second ultrasound-guided attempt finally yielded purulent fluid from the proximal collection with Escherichia coli within the cultures. Endotipsitis was then confirmed. The patient initially received a six-week course of targeted antibiotic therapy, starting with intravenous ceftriaxone for 2 weeks, followed by oral amoxicillin. He was subsequently relisted for liver transplantation with exception points granted for endotipsitis. During oral antibiotic treatment (amoxicillin), he experienced a recurrence of sustained fever. A repeated drainage of the proximal TIPSS collection was performed, and

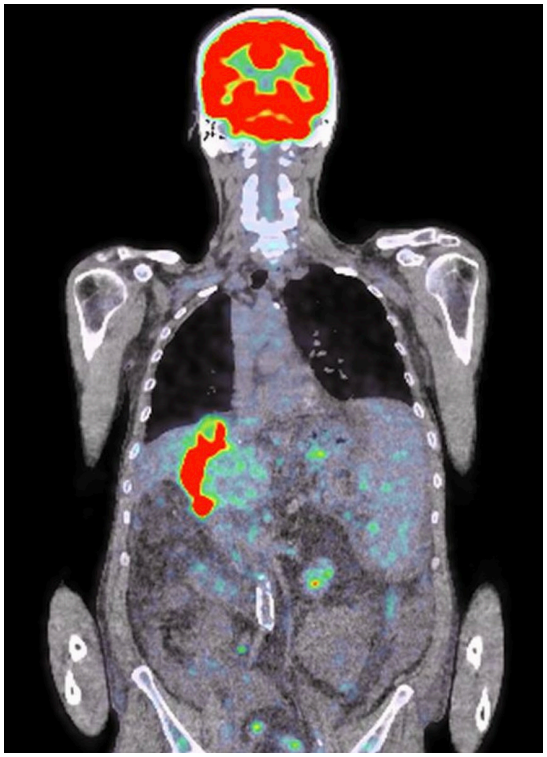

Figure 2.

cultures once again identified Escherichia coli, now amoxicillin-resistant. He then received 12 weeks of IV antibiotics, followed by suppressive prophylactic antibiotherapy (trimethoprim-sulfamethoxazole) while awaiting transplantation. He was transplanted 5 months after the diagnosis of endotipsitis with evacuation of purulent liquid around the TIPSS during the transplant surgery, with Escherichia coli identified on the culture. No recurrence of infection was observed in the postoperative course.

Discussion

The pathophysiology of endotipsitis involves bacterial colonization of the stent material, resulting in a persistent, often low-grade infection. Most reported cases involve early (< 120 days), monomicrobial infections, most often occurring after initial TIPSS placement (2). Nevertheless, delayed have also been documented, though much less frequently and typically following TIPSS revision. In transplant recipients, long-term immunosuppression may promote subclinical or atypical presentations, further complicating early detection.

The definition of endotipsitis remains debated. Historically, Sanyal et al. proposed classifying endotipsitis as "definite" or "probable," based primarily on persistent bacteremia and radiological signs of stent infection (appearance of thrombus or vegetation) (5). However, these criteria may be insufficient, particularly in transplant patients, who receive immunosuppressive therapy, and often antibiotherapy, potentially masking classic signs. Other authors have suggested revised definitions, but they still rely heavily on repeatedly positive blood cultures, which were absent in our patient (1,6).

In this case, FDG PET-CT was decisive, demonstrating marked hypermetabolism along the TIPSS, in the absence of any contribution of repeated blood cultures. Strict reliance on bacteremia-based criteria may underrecognize atypical cases.

FDG PET-CT is highly sensitive and specific for vascular graft infections, with a strong negative predictive value (7,8). While a very few case reports have described PET-CT supported diagnosis of endotipsitis, they all involved positive blood cultures fulfilling classical diagnostic criteria, unlike the present case (9,10,11). This highlights the added value of PET-CT in the diagnostic algorithm, especially when standard investigations remain inconclusive.

There are no official guidelines for managing endotipsitis. Important to note that the infected TIPSS is irremovable without liver transplantation. Therefore, first treatment is an antibiotic therapy, typically prolonged (at least 6 weeks), based on experience from the management of other endovascular graft infections (4). In some cases, infection may recur, requiring escalation to second-line antibiotics and an extended treatment course, or, when feasible, liver transplantation which is a particularly challenging option in the setting of active infection and depending on the anatomical position of the TIPSS.

It is also worth noting that no clear recommendations exist regarding prophylactic antibiotic use prior to TIPSS placement or revision. Current European guidelines do not advocate for routine prophylaxis, citing the lack of robust evidence linking it to improved infectious outcomes (12). However, they acknowledge the paucity of high-quality data in this area. As a result, the decision to use prophylactic antibiotics is often individualized, depending on institutional practices and operator experience. Liver transplanted patients are at increased risk of infection which should be taken in consideration.

Our case stands out for several reasons. First, it occurred in a liver transplant recipient, an exceptionally rare setting. To date, we found only two cases reporting endotipsitis occurring after liver transplantation (13,14). In both cases, the patients presented with bacteremia and thrombus formation within the stent, fulfilling classical diagnostic criteria. In the first report, the infection occurred following TIPSS revision, and the patient ultimately underwent liver retransplantation. In the second, the infection developed spontaneously without recent TIPSS manipulation; however, the patient was not eligible for retransplantation due to significant comorbidities and the technical complexity of the TIPSS configuration.

Moreover, our case is particular in four other key aspects:

1. The infection appeared very late, more than 10 years after TIPSS placement, which, to our knowledge, represents the longest interval reported in the literature.
2. There was no associated bacteremia, which historically has been considered a major diagnostic criterion.
3. Diagnosis relied on FDG PET-CT findings, which is uncommon.
4. Despite prolonged antibiotic therapy, infection control was not achieved, and liver transplantation was ultimately required, which remains the only definitive option in selected cases.

Conclusion

This case highlights the diagnostic and therapeutic challenges of endotipsitis, particularly in immunocompromised patients. TIPSS infections may occur very late, over a decade, and present with atypical features, including absence of bacteremia. Given these complexities, FDG PET-CT should be considered in any TIPSS patient with unexplained fever or persistent inflammatory syndrome, especially when conventional cultures and imaging are inconclusive. Liver transplantation is the only curative treatment, though rarely feasible. Greater awareness and improved diagnostic criteria are needed to better recognize and manage this rare but serious condition.

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