

New Case of Endotipsitis: Urgent Need for Clinical Practice Guidelines

Yeni Bir Endotipsitis Vakası: Acil Klinik Uygulama Kılavuzu İhtiyacı

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ABSTRACT

Transjugular intrahepatic portosystemic shunt (TIPS) is a minimally invasive procedure used for the decompression of portal pressure since the early 1990s. Bacteremia with an infection of the TIPS or endotipsitis is a serious complication with 32% mortality. To date and including the present case, only 56 cases have been reported in the literature. There are concerns regarding underdiagnosis. We report a case of a patient with endotipsitis and recurrent bacteremia treated successfully in our institution. In addition, previous reported cases were reviewed regarding microbiological data and mortality. Clinical practice guidelines including uniform disease definition, prophylaxis, and treatment of this nosocomial prosthetic-related infection are urgently needed.

Keywords: Prosthesis-related infections, portosystemic shunt, transjugular intrahepatic, sepsis

Öz

Transjuguler intrahepatik porto-sistemik şant (TIPS) 1990'ların ilk yıllarından bu yana portal basıncın azaltılması için kullanılan minimal invaziv bir yöntemdir. TIPS enfeksiyonu ile bakteremi ya da endotipsitis %32 mortalite oranı ile ciddi bir komplikasyondur. Literatürde günümüze kadar, bizimki de dahil, sadece 56 vaka bildirilmiştir. Yetersiz tanı ile ilgili kaygılar mevcuttur. Bu çalışmada, kurumumuzda başarılı bir şekilde tedavi edilen endotipsitisi ve tekrarlayan bakteremisi olan bir hasta sunulmaktadır. Ayrıca, rapor edilen diğer vakalar mikrobiyoloji ve mortalite açısından incelenmiştir. Tek bir hastalık tanımını, profilaksi ve bu nozokomiyal proteze bağlı enfeksiyonun tedavisini içeren klinik uygulama kılavuzlarına acilen ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Proteze bağlı enfeksiyonlar, portosistemik şant, transjuguler intrahepatik, sepsis

Introduction

Transjugular intrahepatic portosystemic shunt (TIPS) is a minimally invasive procedure used for the decompression of portal pressure. Moreover, it has mainly replaced the surgical side-to-side porta-caval shunt when other procedures fail to control variceal bleeding and ascites since the early 1990s, although the list of indications for TIPS has progressively broadened [1,2]. Infection of the TIPS or endotipsitis is a serious complication but it has been seldom reported, and there are concerns regarding underdiagnosis. A recent extensive review included 53 cases and subsequently only two additional cases were reported in the literature [3-5]. We report a case of a patient with endotipsitis and recurrent bacteremia successfully treated in our institution. We also review previous reported cases regarding microbiological data and mortality. Clinical practice guidelines for this emerging nosocomial prosthetic-related infectious disease are urgently needed.

Case Report

A 60-year-old woman was admitted to our hospital with a one-day history of fever and chills in June 2015. Due to radiotherapy for breast cancer with liver metastasis diagnosed in 2003, she had developed liver fibrosis with portal hypertension and refractory ascites. In 2008, a TIPS had been implanted with excellent evolution. In December 2014, occlusion of the TIPS due to thrombosis was confirmed and a stent angioplasty with re-stenting was performed. Three days later, the patient developed fever and chills, and *Escherichia coli* was isolated in multiple blood cultures. She was treated with ceftriaxone 2 g daily for 2 weeks. In February 2015, fever and chills relapsed and *E coli* was again isolated in multiple blood cultures; a 5-week course of ceftriaxone was administered and the patient was discharged asymptomatic. In September 2015,



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Table 1. Distribution of all reported cases of endotipsitis to date and their mortality by microbiological agent. (Adapted from Navaratman AMD et al. World J Hepatol 2015; 7 (4): 710-716; from Jessani LG et al; Trop Gastroenterol 2015; 36 (4): 280-282; and McCarty TR et al. J Dig Dis 2017 Jan doi: 10.1111/1751-2980).

*Including our case report

Etiological agent	Number of cases reported	Outcome death
<i>Enterococcus spp (faecalis, faecium)</i>	14	3
<i>Staphylococcus spp (aureus, epidermidis, MRSA)</i>	9	4
<i>Escherichia coli</i>	7*	3
<i>Candida spp (glabrata, albicans)</i>	7	4
<i>Lactobacillus spp (rhamnosus, acidophilus)</i>	3	2
<i>Streptococcus spp (sanguis, bovis)</i>	2	0
<i>Gemella morbillorum</i>	2	0
<i>Lactobacillus spp (rhamnosus, acidophilus)</i>	3	2
<i>Klebsiella spp (pneumonia, oxytoca)</i>	3	1
<i>Serratia marcescens</i>	1	0
<i>Enterobacter cloacae</i>	1	0
<i>Salmonella typhi</i>	1	0
"Polimicrobial infection"	6	1
Total	56	18 (32.1%)

MRSA: Methicillin Resistant *Staphylococcus Aureus*



Figure 1. Hepatic tenuous area of inflammation was observed in Indium-111-labeled leukocyte scintigraphy (arrow)

high-grade fever of 40°C and chills recurred, and the patient was admitted to our hospital.

On examination, the patient was febrile, blood pressure was 140/60 mmHg, and heart rate was 90 beats per minute. Mild proximal jaundice was evident, along with a 5-cm splenomegaly.

Laboratory tests revealed a white cell count of $10.2 \times 10^9/L$, hemoglobin of 98 g/L, platelet count of $74 \times 10^9/L$, aspartate transaminase of 108 U/L, alanine aminotransferase of 62 U/L, alkaline phosphatase was 300 U/L, and gamma-glutamyltranspeptidase was 201 U/L; total bilirubin was 3.2 mg/dL (1.3 mg/dL indirect),

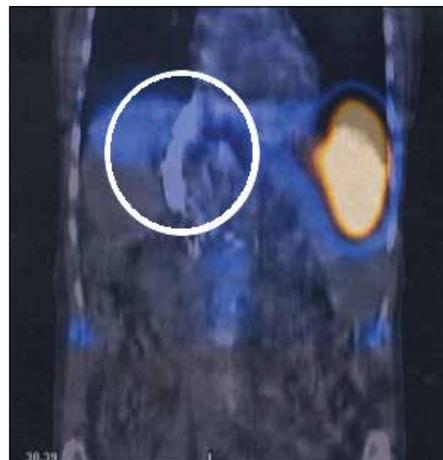


Figure 2. As expected, no focal lesion was objectivized in the scan (TIPS is surrounded by a circle)

procalcitonin was 2.6 ng/mL, and C-reactive protein (CRP) was 9.6 mg/L. Urine culture was negative and cephalosporin-sensitive *E. coli* was isolated from all four blood cultures.

Diagnostic workup included doppler ultrasound of the liver showing patency of the TIPS; trans-thoracic echocardiogram did not show any abnormality, and thoracic and abdominal computer scan showed changes related to chronic liver disease and an apparently patent portosystemic shunt. Indium-111 labeled leukocyte scintigraphy showed a hepatic tenuous area of inflammation (Figure 1), although, as expected, no focal lesion was objectivized in the scan (Figure 2).

Endotipsitis was diagnosed based on the presence of initial thrombus and recurrent bacteremia immediately after re-stenting with no other obvious source of infection. Following recommendations by Mizrahi M. et al. [6], we administered ceftriaxone (2 g/day) intravenously for 6 weeks and due to the recurrence of bacteremia after the 2- and 5-week antibiotic course and the absence of toxic effects, we decided to maintain oral treatment with cefuroxime (500 mg twice daily) through 12 months until September 2016. At 6-month follow-up, the patient remained asymptomatic. Written Informed consent for publication of this clinical experience was provided by the patient.

Discussion

Implantation of TIPS involves creation of an intrahepatic tract between the hepatic and portal veins. Its widespread use since the 1990s has led to the recognition of both systemic (encephalopathy, hepatic failure, sepsis, and death) and local complications (hemorrhage, pneumothorax, migration, and misplacement) [7].

Bacteremia associated with endovascular infection of TIPS stent is a serious but rare complication. We conducted a search of English-language literature in PubMed database for all cases of endotipsitis reported using the following index words: "trans-jugular intrahepatic portosystemic," "TIPS," "endotipsitis," and "infection." We also reviewed references from initially selected reports observing for other potential cases. A total of 55 cases have been reported in the literature. The pathogenesis implies a damaged pseudoendothelium in the luminal surface of the stent graft, or less frequently the development of a bilio-venous fistula [8]. Early infection (<120 days) has been hypothesized to be the result of bacterial seeding during the initial procedure, and late infection may occur months to years after TIPS insertion, mostly following TIPS revision including balloon dilatation of stent stenosis, as it was in our case [2, 6]. Enteric bacteria were most frequently encountered as the etiological cause of TIPS infection; however, probably due to the invasive nature of the procedure, bacteria of the skin flora, fungi, and even multidrug resistant pathogens are importantly changing current epidemiology [3, 4]. This phenomenon is also observed in any bloodstream infection in patients diagnosed with liver cirrhosis [9]. Including the present case, 18 out of the 56 patients diagnosed with endotipsitis died (to date mortality of 32.1% was noted). Although the number of cases is still limited, mortality appears to be higher in those produced by *Staphylococcus aureus* or *Candida* (Table 1). The gold standard on

diagnosis would be to perform a biopsy from the pseudoepithelium of the TIPS, which could only be performed at autopsy or after liver transplantation, both of which are impractical from a clinical point of view [3, 6]; in this regard, although the exact definition of endotipsitis is still being debated [6], the currently accepted definition is as follows: (1) *Definite infection*: clinically significant continuous bacteremia (fever and multiple positive blood cultures for the same organism) with vegetation or thrombus inside the TIPS and (2) *Probable infection*: sustained bacteremia and unremitting fever in a patient with an apparently patent TIPS and no other obvious source of infection. A six-week course of intravenously administered antibiotic therapy has been recommended, but it is not yet well defined and courses longer than 1000 days and even intention to treat indefinitely with suppressive oral antibiotic treatment have been reported [2, 3, 6].

We hypothesized that the *E. coli* strain in our patient might be biofilm producer; thus, it evolved as persistent but not resistant after two antibiotic courses of ceftriaxone. In this sense, in light of the high risk of relapsing bacteremia, the inability to remove the infected TIPS and the relatively inexpensive and well-tolerated treatment with cephalosporins, we decided to maintain a more prolonged course of antibiotic treatment with oral cefuroxime to eliminate all persistent bacteria [10, 11].

There are concerns regarding underdiagnosis and an urgent need for recording all diagnosed and treated cases; optimally, a prospective mul-

ticenter trial should be performed to establish the overall number of TIPS procedures performed, along with providing a uniform disease definition and specific recommendations regarding prophylaxis and treatment [3].

In conclusions, endotipsitis is a serious complication with a 32% mortality to date. We report a new case due to *E. coli* that was successfully treated. Fifty-six cases have been reported to date and underdiagnosis is suspected. A uniform disease definition, specific recommendations regarding prophylaxis, and treatment are urgently needed.

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

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References

1. Sanyal AJ, Rajjender Reddy K. Vegetative infection of transjugular intrahepatic portosystemic shunts. *Gastroenterology* 1998; 115: 110-5. [\[CrossRef\]](#)
2. Armstrong PK, MacLeod C. Infection of transjugular intrahepatic portosystemic shunt de-

3. vices: three cases and review of the literature. *Clin Infect Dis* 2003; 36: 407-12. [\[CrossRef\]](#)
3. Navaratnam AMD, Grant M, Banach DB. Endotipsitis: a case report with a literature review on an emerging prosthetic related infection. *World J Hepatol* 2015; 7: 710-6. [\[CrossRef\]](#)
4. Jessani LG, Nayak S, Lingam P, et al. Endotipsitis caused by extremely drug-resistant *Klebsiella pneumoniae*. *Trop Gastroenterol* 2015; 36: 280-2. [\[CrossRef\]](#)
5. McCarty TR, Sack J, Syed B, Kim R. Fungal endotipsitis: a case report and review of the literature. *J Dig Dis* 2017; 18: 237-40. [\[CrossRef\]](#)
6. Mizrahi M, Adar T, Shouval D, Bloom AI, Shibolet O. Endotipsitis-persistent infection of transjugular intrahepatic portosystemic shunt: pathogenesis, clinical features and management. *Liver Int* 2010; 30: 175-83. [\[CrossRef\]](#)
7. Mizrahi M, Roemi L, Shouval D, et al. Bacteremia and "Endotipsitis" following transjugular intrahepatic portosystemic shunting. *World J Hepatol* 2011; 3: 130-6. [\[CrossRef\]](#)
8. Kochar N, Tripathi D, Arestis NJ, Ireland H, Redhead DN, Hayes PC. Tipsitis: incidence and outcome-a single centre experience. *Eur J Gastroenterol Hepatol* 2010; 22: 729-35. [\[CrossRef\]](#)
9. Bartoletti M, Giannella M, Lewis RE, Viale P. Bloodstream infections in patients with liver cirrhosis. *Virulence* 2016; 7: 309-19. [\[CrossRef\]](#)
10. Cergole-Novella MC, Pignatari AC, Guth BE. Adhesion, biofilm and genotypic characteristics of antimicrobial resistant *Escherichia Coli* isolates. *Braz J Microbiol*; 46: 167-71. [\[CrossRef\]](#)
11. Lebeaux D, Chigo JM, Beloin C. Biofilm-related infections: bridging the gap between clinical management and fundamental aspects of recalcitrance toward antibiotics. *Microbiol Mol Biol Rev* 2014; 78: 510-43. [\[CrossRef\]](#)