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Mycotic aneurysm as a hidden cause of treatment failure of pyelonephritis caused by *Salmonella enterica,* serovar Enteritidis

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ABSTRACT

Invasive non-typhoidal Salmonella (NTS) infections are rare in developed countries but their incidence is increasing. One of the most severe complications of extraintestinal NTS infection is mycotic aneurysm. Its natural course is usually fatal and its treatment demands complex interdisciplinary management. We present a case of severe NTS sepsis complicated by mycotic aneurysm of the abdominal aorta and left internal iliac artery and obstructive pyelonephritis. Obstruction of the left ureter was caused by pressure from the left internal iliac artery aneurysm and surrounding edema. The patient presented with clinical symptoms of sepsis and pyelonephritis. Despite abdominal ultrasound and native computed tomography, the mycotic aneurysm eluded initial examination. It remained undiagnosed until the patient presented with recurrent symptoms after stopping 17 days of antimicrobial treatment and was finally revealed by magnetic resonance imaging and contrast computed tomography. The patient was successfully treated by ligation of the left internal iliac artery, partial extirpation of the aneurysm and prolonged parenteral antimicrobial treatment. This case raises concerns that mycotic aneurysm might be present in cases of obstructive pyelonephritis caused by NTS and its early recognition is vital for appropriate management.

Introduction

Non-typhoid Salmonella (NTS) infections predominantly cause food-borne diarrhea illnesses that are typically benign and self-limiting. On the other hand, extraintestinal or so-called invasive NTS infections are potentially life threatening and significantly contribute to the mortality and morbidity of NTS [1]. Invasive NTS infections are quite rare in developed countries but in the last two decades there has been a substantial increase in incidence [1,2]. Mycotic aneurysm is one of the most severe forms of invasive NTS disease. *Salmonella enterica,* serovar Enteritidis is the second most common cause of mycotic aneurysm worldwide [3]. Urinary tract infection and pyelonephritis are rare but possible forms of invasive NTS infection [4,5], occurring as a solitary disease or together with mycotic aneurysm of the abdominal aorta and iliac artery [5–9]. The close anatomic relationship between iliac arteries and ureters is believed to be important in the transmission of infection to the urinary tract. Mycotic aneurysm is a life-threatening condition with a relatively high rate of rupture and often requires surgical and prolonged antimicrobial treatment [3]. Other extra-enteric forms of invasive NTS infection, such as pyelonephritis, might obscure its presence [7,8], therefore a high level of vigilance is recommended for possible mycotic aneurysm in invasive NTS infections. We present a case of invasive NTS presented as pyelonephritis and sepsis, with recurrence of symptoms after discontinuation of antimicrobial treatment due to a large mycotic aneurysm of the abdominal aorta and internal iliac artery (Figs. 1, 2).

Case report

A 60-year-old male with a history of arterial hypertension visited the emergency department of the University Hospital Bratislava complaining of fever, chills, malaise, fatigue, anorexia and left flank pain. His illness started 16 days ago with abrupt onset of chills, nausea, vomiting and diarrhea. The vomiting and diarrhoea subsided after 5 days but the chills and malaise remained. Therefore, his general practitioner treated him with

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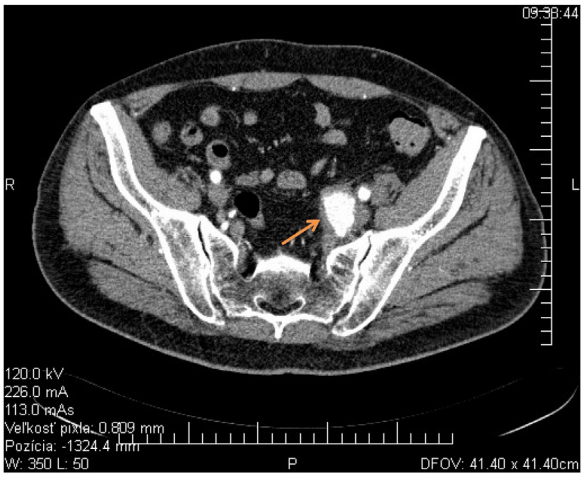

Fig. 1. Tomogram – transverse plane.
Tomogram with intravenous contrast in an arterial phase in transverse plane. It reveals a large aneurism of internal iliac artery on the left side.

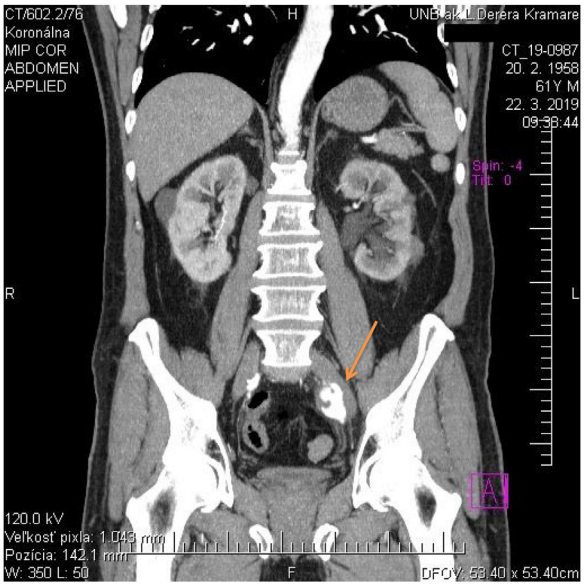

Fig. 2. Tomogram – frontal plane.
Tomogram with intravenous contrast in an arterial phase in frontal plane. It reveals a large aneurism of internal iliac artery on the left side.

amoxicillin-clavulanic acid (825/125 mg bid) for 7 days. Despite antimicrobial treatment, the malaise and fatigue worsened and a fever up to 40 °C developed. He also developed left flank pain and hematuria, and the diarrhea reappeared. At the emergency department, the patient presented with signs and symptoms of sepsis. He was febrile (38.5 °Celsius), hypotensive (arterial pressure of 90/50 mmHg), tachypneic (26 breaths per minute) and tachycardic (135 beats per minute). Abdominal ultrasound revealed an enlarged left kidney. In laboratory screening, there was significant leukocytosis (17 280 cells/mL) with neutrophilia (15 260 cells/ml), elevated C-reactive protein (CRP: 388.38 mg/L), procalcitonin (10.61 ng/mL), creatinine (2.68 mg/dL) and urea (45.93 mg/dL).

The patient was diagnosed with pyelonephritis and sepsis and admitted to the intensive care unit of the Department of Infectology and Geographical Medicine of the University Hospital Bratislava. He was treated with parenteral fluids and antimicrobial therapy (cefotaxime, 2 g tid). Blood and urine culture revealed *Salmonella enterica,* serovar Enteritidis resistant to cefuroxime, ciprofloxacin, gentamicin and amikacin and susceptible to ampicillin (MIC 1 μg/mL), cefotaxime (MIC 0.25 μg/mL), meropenem (MIC 0.12 μg/mL) and trimethoprim/sulfamethoxazol (MIC 0.12). Screening for *Clostridioides difficile* also revealed positive antigen and toxin in stool. Trimethoprim/sulfamethoxazole 960 mg every 24 hours and oral vancomycin 125 mg every 6 hours was added to therapy. In order to screen for other possible extraintestinal sites of infection, transthoracic echocardiography and native computed tomography (CT) of the abdomen were performed. Echocardiography was unremarkable and CT revealed just discrete inflammatory changes of fat around the left kidney. However, intravenous contrast was not used because of the high risk of contrast-induced nephropathy. The patient was treated with a combination of parenteral cefotaxime and trimethoprim/sulfamethoxazole for 10 days and discharged on his own request. He continued on oral trimethoprim/sulfamethoxazole and was recommended to continue therapy until the next outpatient visit. Five days after discharge he arbitrarily stopped the antimicrobial therapy.

Three days after discontinuing antimicrobial treatment, the patient visited the emergency department again. He was suffering from progressive weakness, night sweating and dull pain in the lumbar and sacral region. Laboratory screening revealed only elevated CRP (66.33 mg/L). Physical examination and abdominal ultrasound were unremarkable. The patient was admitted and therapy was started with 2 g of parenteral ceftriaxone every 24 hours and 125 mg of oral vancomycin once daily as a prophylaxis for *Clostridioides difficile* infection recurrence. Follow up blood culture revealed *Salmonella enterica,* serovar Enteritidis with the same antibiotic susceptibility profile. Because of suspicion of vertebral osteomyelitis magnetic resonance imaging of the lumbar spine was performed, which showed no vertebral affection but revealed dilatation of the infrarenal part of the abdominal aorta. Therefore, a contrast CT of the abdomen was performed, which revealed a fusiform aneurysm of the abdominal aorta ranging from offset of renal arteries to bifurcation. The aneurysm was 36 mm at its largest diameter and was partially obliterated with dense thrombus. CT also revealed aneurysm of the left internal iliac artery, saccular in shape and 25 mm at its largest diameter, compressing the left ureter, which was dilated, and the left kidney showed signs of grade 2 hydronephrosis. Vascular surgeons were consulted but they recommended conservative therapy due to the relatively small diameter of the aneurysm. The patient was treated with ceftriaxone for 30 days. CT follow-up showed progression of the aneurysm diameter to 36 mm. The infrarenal aorta was recanalized without any signs of progression in the aneurysm diameter. Therefore, the patient underwent surgery with ligation of the left internal iliac artery and partial extirpation of the aneurysm. Total extirpation was not possible because of tight adhesions between the aneurysm and the left ureter. Aneurysm of the abdominal aorta was left intact. A histologic examination of an extirpated material revealed nonspecific inflammation of arterial wall and all cultures were sterile. Then the patient was treated for another 14 days with parenteral antimicrobial therapy. CT follow-up showed complete obliteration of the residual aneurysm of the left internal iliac artery. The patient was discharged and continued oral therapy with trimethoprim/sulfamethoxazole (960 mg bid) for the next 7 days until normalization of the CRP level. At a 3-month follow-up, the patient was completely asymptomatic and the CRP level remained in the reference range.

Discussion

Mycotic aneurysm is one of the most serious complications of invasive NTS infection [1] and NTS strains are the second most

common etiology found in cases of mycotic aneurysm in developed countries [3]. Due to the extreme rarity of mycotic aneurysm in high-income countries, its incidence has never been accurately established and most of our knowledge comes from occasional case reports and their summaries. In the last two decades there has been a substantial increase in the incidence of invasive NTS infections [1,2], therefore we can assume that the incidence of mycotic aneurysm may also rise. Atherosclerosis and advancing age are considered to be the most important risk factors for the development of mycotic aneurysm [10–13], therefore the aging of populations in developed countries may lead to an increased incidence of this disease.

On the basis of the available knowledge on mycotic aneurysm caused by NTS, we can conclude that it presents as a serious condition associated with high lethality. The natural course of untreated mycotic aneurysm often ends with rupture or sepsis [10,11]. Management of mycotic aneurysm is very demanding and often requires vascular surgery [3,10]. Antimicrobial therapy alone for the mycotic aneurysm without any kind of surgical intervention is associated with a poor outcome: 50% of patients die during hospitalization and 1-year event-free survival is less than 33% [14]. Most authors therefore recommend surgical intervention along with prolonged parenteral antimicrobial therapy for at least 6 weeks [10,11]. In 2012, Guo et al. presented one of the most extensive reviews of cases of NTS mycotic aneurysm in which 48 of 53 reviewed cases were treated by a combination of surgery and antimicrobial therapy. Of the 53 patients, eight died and six suffered from recurrence of infection. For the four patients treated only by antimicrobial therapy, three died and one suffered a recurrence [3].

Considering the risks and obstacles in the management of mycotic aneurysm, it is very important to recognize its presence in patients with invasive NTS infection. The elusive nature of the clinical picture of mycotic aneurysm often complicates early diagnosis. We present a rare case of invasive NTS infection in which mycotic aneurysm of the abdominal aorta and left iliac artery was obscured by the clinical picture of parallel pyelonephritis. Urinary tract infection and pyelonephritis are other possible forms of invasive NTS infection. They seem to be quite frequent but, to our knowledge, there are no reliable estimates [5–9]. Gorelik et al. described 17 cases of urinary tract infection out of 77 cases of invasive NTS infection [5]. NTS urinary tract infections might occur as a solitary disease or together with mycotic aneurysm of the iliac artery [7–9]. In 2002, Chen et al. described a case of invasive salmonellosis presented as pyelonephritis with hydronephrosis and unrecognized mycotic aneurysm of the aorta at the time of first presentation. In their case, the aneurysm ruptured on the second day of antimicrobial therapy and was diagnosed using an abdominal CT scan. The patient was successfully treated by prompt surgical intervention followed by prolonged antimicrobial therapy [8]. Five years later, Gagnon et al. described a case of obstructive pyelonephritis caused by *Salmonella* along with a huge mycotic aneurysm of the common iliac artery. In that case, mycotic aneurysm was not recognized at the time of first presentation. They diagnosed aneurysm 30 days later when the patient presented with left flank pain and fever. They also used contrast CT to visualize the aneurysm [9] and treated their patient with surgical intervention and antimicrobial therapy. These cases and our case have several common features. First, in all three cases pyelonephritis was associated with hydronephrosis as a hallmark of urinary tract obstruction caused by the aneurysm. Second, despite comprehensive diagnostic workup at the time of first presentation, mycotic aneurysm remained unrecognized.

In our case, neither abdominal ultrasound nor native CT was able to visualize the aneurysm. Magnetic resonance imaging revealed aneurysm of the abdominal aorta and CT angiography revealed aneurysm of the internal iliac artery and abdominal aorta. Multi-detector CT angiography is regarded as the gold standard in the diagnosis of mycotic aneurysm of the abdominal aorta, with a sensitivity greater than 95% [11]. Ultrasound has a relatively low sensitivity in finding aneurysm of the abdominal aorta. In one large clinical study of patients with abdominal aorta aneurysm of non-infectious aetiology, its sensitivity ranged from 57.1% to 70.4%. In the same study, native CT showed a better sensitivity of nearly 83% but this is still far below the sensitivity of CT angiography [15]. Another important trait of mycotic aneurysm is the lack of typical symptoms and signs of disease [1,2], therefore its diagnosis requires a high level of vigilance. Regarding the severity, lethality and also the demands on intensive interdisciplinary management of mycotic aneurysm, a high level of vigilance while managing extraintestinal NTS is advisable, bearing in mind that mycotic aneurysm might also be present. Particularly in cases of NTS obstructive pyelonephritis, CT angiography of the abdominal aorta and its branches should be considered.

Conclusions

Despite the fact that mycotic aneurysm caused by invasive NTS infection is rare in developed countries, awareness of this disease is important because of its life-threatening nature and demanding interdisciplinary management. The clinical picture is not specific and often elusive. CT angiography of the aorta and its major branches is the most reliable method for diagnosing mycotic aneurysm. In elderly or immunocompromised patients with a septic course of NTS infection, a high level of vigilance for extra-enteric forms is advised. In patients presenting with NTS pyelonephritis, imagining of the abdominal aorta and its major branches should also be considered.

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Consent

This case study has been conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee of the University Hospital Bratislava. Written informed consent was obtained from the patient for publication of this case report and the accompanying images. A copy of the written consent is available for review by the Editor-in Chief of this journal on request.

Final statement

All authors read the revised manuscript and accepted all the changes to the original manuscript.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

CRediT authorship contribution statement

Peter Sabaka: Writing - original draft, Conceptualization. **Mária Kachlíková:** Writing - original draft. **Matej Bendžala:** Writing - original draft, Visualization. **Igor Stankovič:** Conceptualization.

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