

First case of aorto-bi-iliac endograft thrombotic infection by *Listeria monocytogenes*: A case report

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Abstract. *Listeria monocytogenes* may cause serious vascular and graft infections. In the present case report, a 71-year-old man underwent partial prosthetic endograft replacement due to high-flow endoleak and limb occlusion. Following surgery, a multiple empiric antibiotic regime was initiated due to fever, malaise, abdominal tenderness and signs of an acute abdomen; however, in spite of this, the clinical condition of the patient worsened. An aorto-enteric fistula was discovered, and duodenal resection with duodeno-jejunal anastomosis packaging was performed. Gastrointestinal bleeding originating from this anastomosis both complicated and prolonged the clinical course, necessitating appropriate parenteral support and endoscopic hemostasis. The growth of *Candida lusitanae* in the drained abdominal and pleural effusion, and the isolation of *L. monocytogenes* from the thrombus inside the removed abdominal aorto-bi-iliac endograft allowed for establishment of a specific antibiotic treatment. After a suitable period of clinical improvement, the patient was transferred to a clinical rehabilitation center. At the present time, the patient maintains a good condition. To the best of our knowledge, the present study represents the first described case of thrombotic infection of an aorto-bi-iliac endograft by *L. monocytogenes*. In the event of graft thrombotic occlusion, *L. monocytogenes* infection should be considered as a potential cause. In case of complications requiring open conversion, even if not suspected from the medical history of the patient, the possibility of an underlying and occult infection should always be excluded with an in-depth preoperative work-up.

Introduction

Listeria spp whose genus currently includes 28 species and six subspecies are Gram-positive, facultative anaerobic

bacteria (1). *Listeria* species are separated into two phenotypically and genotypically distinct groups: *Listeria sensu lato* and *Listeria sensu stricto*; this latter category includes *Listeria monocytogenes*, a small Gram-positive intracellular bacillus, which is widespread in the environment.

Farm animals can lead to the spread of *L. monocytogenes* in the agricultural environment and consequently of its entry in the food chain if hygienic requirements are not respected (1). Indeed, *L. monocytogenes* is responsible for both foodborne diseases with mild gastroenteritis (non-invasive listeriosis) and life-threatening systemic infections (invasive listeriosis; e.g., sepsis and meningitis) (2).

L. monocytogenes has also been associated with primary aortitis (only a few cases reported in the literature) and serious vascular and graft infections in immunocompromised hosts, patients with malignancy or previously treated aneurysms (3-6). Infections of *L. monocytogenes* may be resistant to several antibiotics such as cephalosporins, first generation quinolones, sulfamethoxazole, fosfomycin, oxacillin, and lincosamides but seem to respond well to others such as penicillins, trimethoprim, aminoglycosides, macrolides, and vancomycin (1).

In the present case report, to the best of our knowledge, the first case of *L. monocytogenes* thrombotic infection of an abdominal aorto-bi-iliac endograft in a patient who had recently undergone a vascular intervention for repair of an aortic abdominal aneurysm is described. As detailed below, serious complications both affected and prolonged the clinical course of the infection.

Case report

A 71-year-old man with arterial hypertension, type II diabetes, dyslipidemia, previous splenectomy and abdominal aortic aneurysm (anteroposterior diameter of 69 mm) was hospitalized in a different hospital where he underwent an aorto-bi-iliac endograft (Medtronic Endurant™) with suprarenal attachment. The main body aortic endograft was implanted using a percutaneous right femoral approach with no intraoperative issues or abnormalities. However, the postoperative course was characterized by the appearance of left calf claudication 2 months after having performed the index endovascular aneurysm repair (EVAR) procedure. For

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this reason, catheter-directed thrombolysis was performed in another hospital without restoring the left limb perfusion.

Subsequently, after a further 8 months, due to the presence of abdominal pain and persistent left calf claudication, the patient was admitted to our hospital 'Campus Bio-Medico' University of Rome (Rome, Italy) on February 2019, where color Doppler sonography and computed tomography angiography (CTA) revealed an abdominal aortic type Ia endoleak, with graft thrombotic occlusion and a maximum diameter of the aneurysm of 91 mm (Fig. 1A-F). Neither gas bubbles nor any obvious indications of graft infection were present. Similarly, laboratory investigations failed to reveal any abnormalities, with the exception of the white blood cell count (13,800 cells/ μ l), a C reactive protein concentration of 2.1 mg/dl (normal value <0.5 mg/dl), and a creatinine reading of 1.3 mg/dl, albeit without clinical signs of systemic infection.

Considering the stent graft limb occlusion (with a previously failed revascularization attempt) and the type Ia endoleak without graft migration (i.e., the proximal stent graft was in a good position relative to the lowest renal artery), a proximal aortic positioning was excluded. A fenestrated endograft and chimney procedures were also excluded, given the good clinical condition (preoperative work-up revealed a 60% ejection fraction and normal pulmonary function tests) and the relatively young age of the patient (7); therefore, an open surgical approach was preferred, and a partial stent-graft explant was planned.

Using a left lombotomic extraperitoneal access, the aorta was exposed from the left iliac bifurcation up to the suprarenal portion without dissection of the native right iliac axis; after systemic heparinization (70 IU/kg), the aortic cross-clamp was placed below the lowest renal artery (including the first covered stent of the endograft), and the left external and hypogastric arteries were clamped in the proximal region. Subsequently, the aneurysm was opened through a longitudinal arteriotomy extended cranially below the first covered stent, and distally at the level of the iliac branches of the stent-graft. At this point, the main body of the stent-graft was carefully transected below the first covered stent, and the right iliac limb was resected at its proximal portion; back-bleeding from the right iliac branch was rapidly achieved using a catheter used for intraluminal control (Bard Medical Division). The left stent-graft limb was resected at the proximal portion and, together with the thrombus, sent for culture, whereas the distal part was left in place as it was chronically occluded. Once the stent-graft had been partially explanted, the proximal anastomosis was performed using a 3/0-polypropylene suture in an end-to-end fashion with a Silver Dacron bifurcated graft (18x9 mm), which included all the first covered stent of the endograft; to obtain a tight reinforced anastomosis, a Teflon stripe (10-cm x 6-mm regular polytetrafluoroethylene) was used (Fig. 2A and B). However, the postoperative clinical condition of the patient quickly worsened with the onset of a 39°C fever, malaise, nausea, vomiting, abdominal swelling and tenderness and development of an acute abdomen. A course of adequate parenteral hydration with 1,000 ml glucose and saline solution (1,000 ml a day) was promptly started. Laboratory investigations showed a C reactive protein concentration of 27.3 mg/dl (normal value, <0.5 mg/dl), a procalcitonin level of

1.43 ng/dl (normal value, <0.5 ng/dl), an adrenomedullin level of 4.17 nmol/l (normal value, <0.5 nmol/l), a white blood cell count of 23,690 cells/ μ l, a neutrophil count of 19,460 cells/ μ l (82.2%), a red blood cell count of 3,410,000 cells/ μ l, a hemoglobin level of 9.2 g/dl, a platelet count of 277,000/ μ l, and a creatinine level of 1.43 mg/dl.

On the 4th day after surgery, CTA was performed, which led to the detection of the presence of aorto-enteric fistula (AEF), abdominal effusion and left pneumothorax. Emergency surgery, consisting of duodenal resection with duodenojejunal anastomosis packaging and omentum transposition to cover the aneurismatic sac, was performed a few hours after obtaining the CTA findings (Fig. 2C-E). Before knowing the culture results, a multiple empiric intravenous antibiotic treatment (4.5 g piperacillin/tazobactam administered every 8 h, 50 mg tigecycline once a day and 250 mg ciprofloxacin administered every 12 h) was started and continued for several days, albeit without the patient receiving any clear benefit. Laboratory investigations showed a C reactive protein level of 10.18 mg/dl, a procalcitonin level of 0.21 ng/dl, a white blood cell count of 25,390 cells/ μ l, a neutrophil count of 20,600 cells/ μ l (81.1%), a red blood cell count of 2,790,000 cells/ μ l, a hemoglobin level of 8.4 g/dl, a platelet count of 451,000/ μ l, a creatinine level of 0.67 mg/dl, as well as measurements of 128 mmol/l sodium, 3.6 mmol/l potassium and 1.9 g/dl albumin.

When tested, the culture of material from the abdominal and left thorax drainages, placed near the abdominal aorta and in the posterior basal region of the left lung, was found to be positive for *Candida lusitanae*. The culture examination of the removed graft and the thrombotic material found inside the graft revealed the growth of *L. monocytogenes*. The previous antibiotic regime was discontinued and, according to antibiogram sensitivity, specific antimycotic and antibiotic treatments (intravenous fluconazole at 200 mg once a day and intravenous meropenem at 1 g every 8 h) were started. In order to broaden the antibacterial spectrum, vancomycin (500 mg) and clindamycin (600 mg), both intravenously administered every 8 h, were also added for a period of 21 days according to the C reactive protein dosage and clinical status.

On the 10th day following surgical intervention, the patient had an episode of hematemesis due to serious bleeding originating from the duodenojejunal anastomosis; this caused severe anemia (red blood cell count, 2,280,000 cells/ μ l; hemoglobin, 6.9 g/dl) requiring a red blood cell transfusion, endoscopic hemostasis and positioning of metallic clips (Fig. 2F), and subsequent placement of both naso-gastric and naso-jejunal tubes. The patient was maintained in a fasting state with infusion of total parenteral nutrition and albumin to allow the healing of the intestinal mucosa, to ensure sufficient caloric intake and to restore electrolyte and protein balance.

After 1 week, the abdominal and pleural drainages were removed and, 1 week later, the patient could resume feeding on a soft diet, without any signs of bleeding. A control CTA revealed both a significant reduction in pleural and abdominal effusions and patency of the bifurcated Silver Dacron graft (Fig. 3A-C); therefore, the intravenous antibiotic therapy was discontinued, and treatment with oral clarithromycin (500 mg every 12 h) was started. After a further week, the patient was transferred to a Rehabilitation Centre, where he followed a plan of re-education with a continuance of oral antibiotic

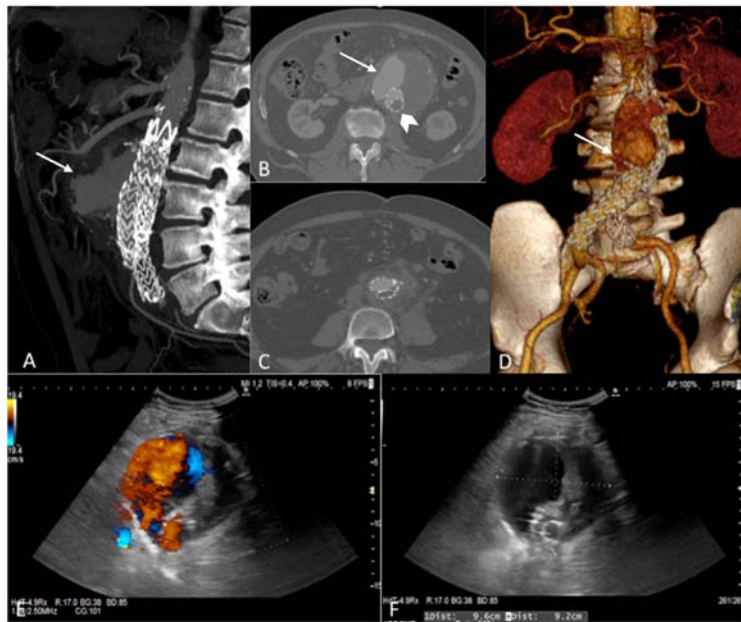


Figure 1. Preoperative computed tomography angiography (CTA) showing (A-D) perfusion of the sac due to type Ia endoleak (white arrows) and left limb occlusion (arrowhead). (E and F) Preoperative duplex ultrasound also showing the huge aneurysm with high-flow endoleak.



Figure 2. Intraoperative details showing the suprarenal aortic exposure. (A) Left thoracophreno-laparotomy and retronephric extraperitoneal approach and the inflammatory reaction in the abdominal aorta (white arrow). (B) Final result with an interposition bifurcated Silver Dacron graft after partial stent-graft removal. (C) Aorto-enteric decubitus in the second duodenal part. (D) Duodenectomy. (E) Latero-lateral duodeno-jejunal anastomosis between the first part of the duodenum and the first jejunal loop. (F) Endoscopic clipping for treatment of gastrointestinal bleeding proximal to the enteral anastomosis.

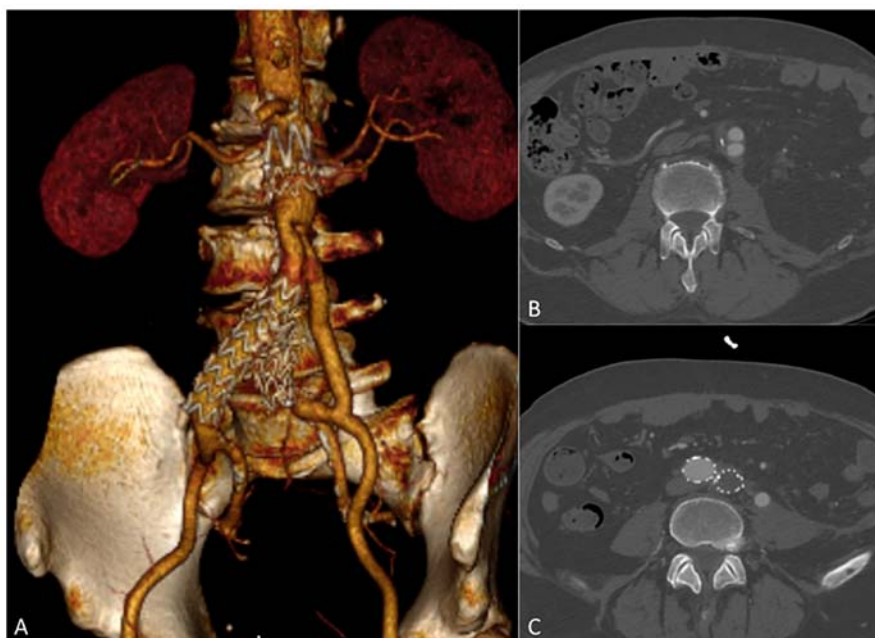


Figure 3. (A-C) Three-dimensional reconstruction of postoperative computed tomographic angiography underlying the aorto-bi-iliac reconstruction after the partial explantation of the stent-graft.

therapy for 3 months in accordance with his clinical conditions and the laboratory tests. After 3 months, the patient was discharged from the Rehabilitation Centre and after 9 months of follow-up, the patient was in good clinical condition without signs or symptoms of reinfection.

Discussion

Aortic endograft is an efficacious option of treatment for aortic aneurysm burdened with several ischemic and vascular complications (8). However, only partial and limited information is available on graft-associated infective complications, as that they occur infrequently (with an estimated incidence of 6.2/1,000 person-years), are difficult to manage and have high mortality rates (9-12).

Reports in the literature indicate that Staphylococci, *Escherichia coli* and *Pseudomonas aeruginosa* are the most common organisms isolated in endograft infections whereas very few cases are due to *L. monocytogenes* (13).

This case study, to the best of our knowledge, presents the first-ever described case of *L. monocytogenes* aorto-bi-iliac endograft and thrombotic infection. Prior to surgery, clinical signs of systemic infection were not reported. Preoperative blood investigations were found to be normal, with the exception of the white blood cell count and a small increase in the level of C reactive protein; however, over the course of the previous 10 years, the patient had shown persistent mild leukocytosis that was related to a previous splenectomy. A critical revision of the preoperative CTA revealed only a slight hyperdensity of periaortic adipose tissues, and consequently this was judged to be a case of purely dormant stent-graft infection incidentally detected on culture. It was possible to speculate that AEF already existed at the time of conversion, even though it had not been recognized, a likely consequence of *L. monocytogenes* infection acquired through ingesting food.

Since an infection was not suspected, given the good clinical condition and relatively young age of the patient, a partial stent-graft explant was performed, according to our standard approach in case of EVAR failure requiring conversion (14).

Certain cases of AEF following aortic repair have been reported in the literature (15-18), and although it is known that its onset may not occur until 15 years after (17), data regarding its incidence are lacking. It has been generally recognized that, when AEF following aortic repair does occur, it prolongs the stay in hospital extensively. The appearance of symptoms depends on the site of origin of the AEF; in our case study, AEF was severe, and therefore a duodenal resection and omental transposition were necessary.

Although only a few cases of endograft infections caused by *L. monocytogenes*, for example, two cases of infective endocarditis via *L. monocytogenes* (one of which was complicated by a distal popliteal embolization of a mycotic aneurysm) and one case of thrombotic infection of the vascular graft of the right leg, have been reported (2,4-5,19-24), to the best of our knowledge no case of aortic endograft associated with thrombotic infection has ever been reported, making sure that our case is novel. Certain risk factors, including immunosuppression, immunization against human papilloma virus in vaccinated subjects, infective endocarditis, HIV infection, intravenous drug use, giant cell aortic aneurysm and sepsis, as well as the presence

of aneurysm, may predispose a patient to *L. monocytogenes* endograft infection (11,25,26).

According to an interesting survey published previously, the clinical course of vascular infection caused by *L. monocytogenes* was found to be milder than that caused by other bacteria, such as *Staphylococcus aureus*, *Enterobacteriaceae* and anaerobic flora (27). On the other hand, embolization following endocarditis by *L. monocytogenes* and the mortality rates associated with aneurysmal or vascular endograft infection had rates of frequency similar to those found with other bacteria (27). Although the mortality rate due to endocarditis caused by *L. monocytogenes* was similar to that of *S. aureus*, it was 10 times higher than that reported for *Streptococcus* (27).

Although, in the majority of cases, the source of *L. monocytogenes* infection is unknown, it is known that it may depend on eating habits, such as the consumption of raw meat and the intake of unpasteurized milk and other milk products, not forgetting the possible role of transmission from asymptomatic personnel handling such products. Moreover, the possibility of *L. monocytogenes* contamination occurring during the first surgical procedure or the secondary reintervention for limb occlusion cannot be eliminated. Even though a correlation between hostile anatomy and AEF has not been clearly established in the literature, it is well known that EVAR is associated with a high reintervention rate during follow-up (14-25%) (28,29). Although a great majority of such secondary procedures are endovascularly managed and are associated with low mortality rates (30), reinterventions are, however, accompanied by a high risk of EVAR infection (10). The high percentage of reinterventions is likely associated with the largescale use of EVAR, and also applies to patients with suboptimal or an hostile anatomy (31).

In the present case study, the patient showed limb occlusion and a Type Ia endoleak at short-term follow-up, suggesting the presence of suboptimal or hostile anatomy at the time of the EVAR procedure, although reliable data and details on aortic neck and iliac anatomy were missing (the EVAR procedure was not performed at our Centre, and performing CTA prior to EVAR was no longer an available option). Consequently, the initial decision to use EVAR as the first treatment was not ideal, particularly as the patient was relatively young and in good clinical condition at the time of EVAR. It may be speculated that the patient would have successfully tolerated an open repair as a first-line treatment, which, in hindsight, would probably have been the most appropriate action to have taken in the light of the subsequent complications.

The underlying mechanism of the pathogenesis of thrombotic *L. monocytogenes* infection remains unclear, although it is likely that, in the present case study, a persistent aortitis favored thrombotic infection. In this regard, an interesting *in vivo* animal study has provided some evidence for the pivotal role of a lethal listeriosis infection in inducing coagulopathy and thrombus formation through the upregulation of factor XI of the coagulation cascade (32).

It remains impossible at the present time to either confirm or deny that this is the mechanism through which *L. monocytogenes* induced graft thrombotic occlusion in our patient; instead, it is desirable that the role of *L. monocytogenes* infection in favoring a thrombophilic state be explored in greater detail in subsequent studies.

At present, there are no available therapeutic recommendations or guidelines for *L. monocytogenes* endograft infection (27); however, we do know that surgical treatment may be unsuccessful, and with or without lifelong antibiotic treatment, mycotic aneurysms are burdened by moderate rates of mortality (12%) and morbidity, although to a lesser extent than for endocarditis (27). In the present study, our patient benefited from a rapidly performed surgical aortic resection and new silver graft positioning, as well as a specific long-term antibiotic treatment strategy based on an antibiogram against both *L. monocytogenes* and *C. lusitanae*. This is likely to account for why our patient was again asymptomatic at the 9 months' follow-up stage.

In the event of a complication requiring open conversion, even if not suspected from the patient's medical history, an underlying infection should always be excluded with an in-depth preoperative work-up, including ¹⁸F-fluoro-D-deoxyglucose positron emission tomography with low dose CT (¹⁸F-FDG PET/CT) or white blood cell scintigraphy (33); in addition, an esophagogastroduodenoscopy may be useful both for appreciation of an occult AEF and to determine the subsequent course of treatment.

In conclusion, it may be said that *L. monocytogenes* infection, though not widespread, should be considered in patients with prosthetic devices, especially those with graft thrombotic occlusion.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

All authors confirmed the authenticity of all the raw data. EMZ was responsible for the conception and design of the report, and was the major contributor in writing the article. NM, VC, TG and DMZ analyzed and interpreted the patient data, and revised the article. MC was responsible for the duodenectomy and latero-lateral duodeno-jejunal anastomosis and interpretation of data. FSp, FSt and NM were responsible for the prosthetic endograft replacement and acquisition of data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

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