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CASE REPORT

Non-typhoidal *Salmonella* aortitis

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Abstract
Non-typhoidal *Salmonella* (NTS) spp. causes about 40% of all infective aortitis and it is characterized by high morbidity and mortality. Human infection occurs by fecal–oral transmission through ingestion of contaminated food, milk, or water (inter-human or zoonotic transmission). Approximately 5% of patients with NTS gastroenteritis develop bacteremia and the incidence of extra-intestinal focal infection in NTS bacteremia is about 40%. The organism can reach an extra-intestinal focus through blood dissemination, direct extension from the surrounding organs and direct bacterial inoculation (e.g. invasive medical procedures). Medical and surgical interventions are both needed to successfully control the infection. Here, we report a case of abdominal sub-renal aortitis caused by *Salmonella enterica* serovar Enteritidis in an 80-year-old man.

Keywords *Salmonella* · Aortitis · Extra-intestinal localization by *Salmonella*

Case report

In October 2018, a 80-year-old man came to the Emergency Department of ASST Spedali Civili Hospital in Brescia complaining of a 4 day history of fever (maximum temperature 39 °C) and a single day of diarrhea (2–3 episodes). At home, he had taken amoxicillin–clavulanate (1 gr bid) for 3 days without clinical benefit. His medical history was characterized by hypertension on medical treatment, diabetes mellitus managed by diet, chronic ischemic heart disease, dyslipidemia on medical treatment, valved prosthesis of the ascending aorta, widespread atherosclerosis and sigma diverticulosis.

Clinically, he was feverish, hemodynamically stable and with no evident focus of infection (no skin lesions, soft, non-tender, painless abdomen with normal bowel sounds, no Murphy sign, negative costovertebral angle (CVA) tenderness test, normal pulmonary and cardiac sounds). Laboratory tests showed mild leukocytosis with prevalence of neutrophils, mild normocytic anemia, increased C reactive protein (CRP 129 mg/mL, normal value < 5 mg/mL) and erythrocyte sedimentation rate (ESR 62 mm/h, normal value 3–46 mm/h), slight increase of transaminases, ALP (alkaline phosphatase), and GGT (gamma-glutamyl transpeptidase). Chemical–physical examination of urine, chest X-ray and abdominal ultrasound were normal.

He was admitted to the Department of Infectious and Tropical Diseases, where empirical therapy with piperacillin–tazobactam plus amikacin was started, after collecting blood samples for culture. A pansensitive strain of *Salmonella enterica* serovar Enteritidis grew rapidly from blood culture and the ongoing antibiotic therapy remained unchanged. Stool culture, performed under antibiotic therapy because of constipation, was negative. Blood cultures performed on hospital days 4 and 8 resulted negative.

The patient was asked about potential risk factors for *Salmonella* spp. infection. He lived alone in a rural area and he reported recent consumption of farmer's eggs (3–4 days before the onset of symptoms). He denied recent contacts with animals or persons with fever or gastrointestinal symptoms, and no history of recent travel was reported.

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He complained of constipation from the beginning of the hospital admission. After a few days, he complained of severe widespread abdominal pain with slight positive Blumberg sign (rebound tenderness) in the right hypogastric area and reduced peristalsis. Abdomen X-ray was performed showing mild coprostasis, so that he was treated with laxatives with rapid clinical benefit. The day after he was again feverish (maximum temperature 39 °C) and with severe persistent abdominal and lumbar pain. An urgent angio-CT scan was performed and sub-renal aortitis was diagnosed (see Fig. 1). Vascular surgeons urgently evaluated the patient and decided to postpone an intervention until a better control of the infection was reached, setting up a radiological weekly control. From hospital days 4 to 11, some other radiological investigations were performed to exclude the involvement of the heart and other parts of the aorta: thorax CT scan with contrast and trans-esophageal echocardiography were normal and fluorine-18-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography showed a pathological FDG uptake only in the sub-renal aortic wall and in the surrounding fatty tissue (see Fig. 2).

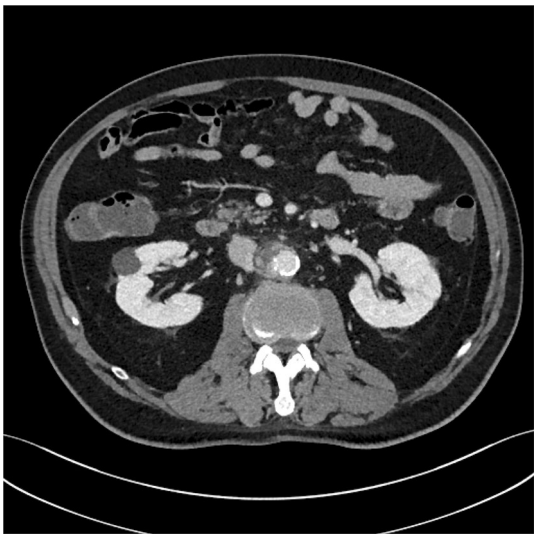

Fig. 1 Abdominal angio-CT scan performed on admission showed a sub-renal pseudoaneurysm with irregular and enhancing thrombus, consistent with aortitis

To exclude other major causes of aortitis, he was screened for syphilis (negative TPHA) and autoimmune diseases (normal C3, C4, anti-nuclear antibodies, anti-neutrophylic cytoplasmic antibodies and rheumatoid factor).

We also checked conditions that predispose to NTS bacteremia. He had no HIV infection, intestinal strongyloidiasis, hemoglobinopathies, abnormal immunoglobulin dosage (except from a mild increased of IgA) nor abnormal lymphocytic typing.

During the second week of hospitalization, he showed an improvement of the temperature curve, a mild abdominal pain under control of analgesic therapy, hemodynamic stability, symmetric and valid arterial pulses, improvement of inflammation indices; angio-CT showed a slight increase of the aortic diameter (pseudoaneurysm) and the disappearance of the thrombus on the right side of the aortic wall. A week after, the patient became tachycardic, feverish (maximum temperature 38.5 °C), with abdominal and lumbar pain that was no longer well controlled with medical therapy. Laboratory tests showed worsening anemia. A new angio-CT scan was urgently performed, showing a further increase (more than 3 cm) of the pseudoaneurysm (see Fig. 3). He was urgently transferred to the Department of Vascular

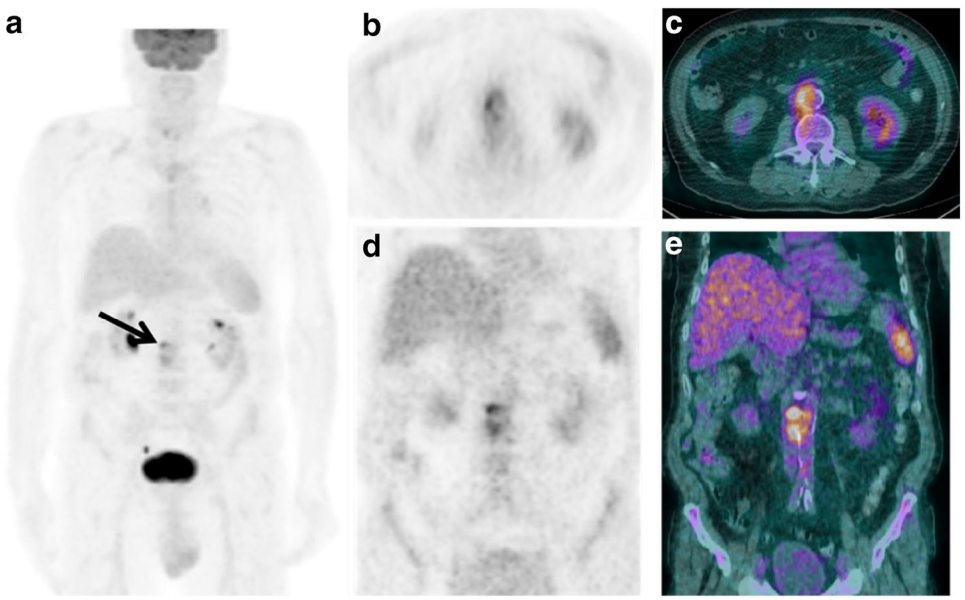

Fig. 2 **a** Maximum intensity projection showing the presence of increased FDG uptake in the abdomen near the aorta. **b** Axial PET images. **c** Axial PET/CT fused images. **d** Coronal PET images. **e** Coronal PET/CT fused images confirming the hypermetabolic lesion in the right para-aortic tissue

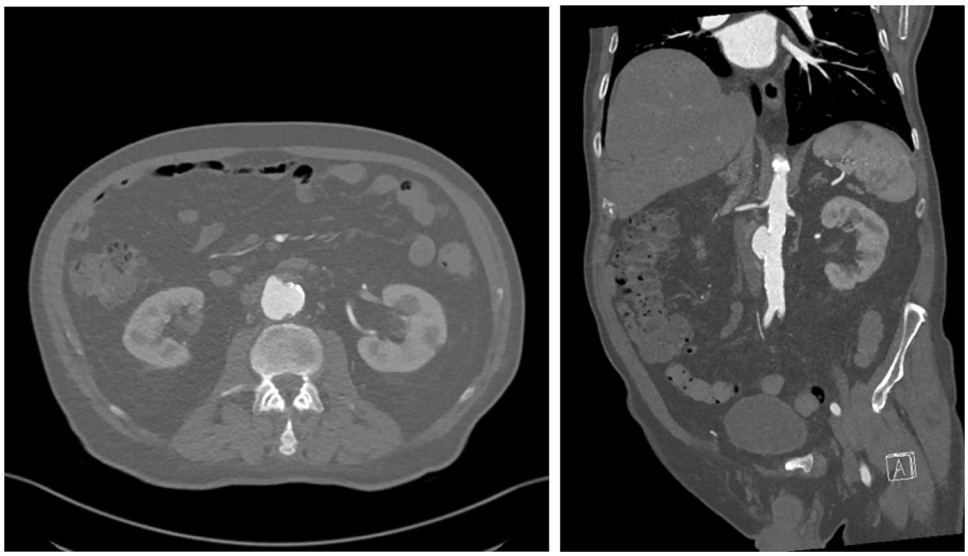

Fig. 3 Abdominal angio-CT scan performed 2 weeks after admission revealed an increasing sub-renal pseudoaneurysm without significant thrombosis

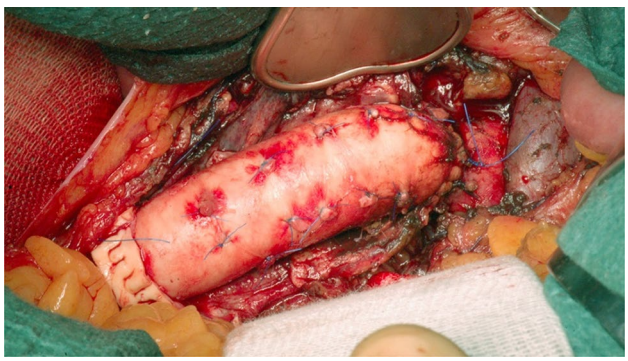

Fig. 4 Segment of the aorta from renal arteries to the carrefour replaced by a cryopreserved allograft

Surgery and an open surgery was performed. After performing a median laparotomy and opening retroperitoneum, a diffuse lymphatic involvement of the periaortic tissue with greater lymphadenopathies surrounding the pseudoaneurysm and an aortic dissection from the supra-renal plane to the aortic bifurcation were revealed. The segment of the aorta from renal arteries (juxta-renal anastomosis) to the carrefour was replaced by a cryopreserved allograft (see Fig. 4). A homograft patch was then positioned around the distal anastomosis as reinforcement. The homograft was finally covered with a pedunculated omental flap fixed by multiple stitches to the retroperitoneum.

After surgery, no post-operative complications were observed and the patient remained without fever with descending inflammatory indices. Intravenous antibiotic therapy with piperacillin–tazobactam was never interrupted, and about 4 weeks after admission, the patient was discharged with amoxicillin–clavulanate (1 gr qds). About 4 weeks after discharge, he denied any pathological symptoms, presented normal inflammatory indices, and the abdominal angio-CT was negative and showed no surgical complications (see Fig. 5). Therefore, antibiotic therapy was stopped after a total of 8 weeks (4 weeks of intravenous therapy and 4 weeks of oral therapy). Six months after the onset of his original symptoms, the patient was asymptomatic; he had no signs of relapse and his angio-CT scan remained negative.

Discussion

Non-typhoidal *Salmonella* is a typical cause of aortitis characterized by high morbidity and mortality. Human infection occurs by fecal–oral transmission through ingestion of contaminated food, milk, or water (inter-human or zoonotic transmission).

It is mandatory to search for extra-intestinal foci of infection in patients with *Salmonella* spp. bacteremia, especially if the clinical and/or laboratory picture exhibits slow improvement during appropriate antibiotic therapy or rapid worsening after interruption of antibiotics. In fact, the incidence of extra-intestinal focal infection in NTS bacteremia is high (about 40%) [1], and with regard to cardiovascular infection, it increases when there are predisposing conditions such as male gender, age over 50 years, hypertension, diabetes, pathological alterations of the aortic wall (e.g. atherosclerosis), invasive catheterization or post-traumatic lesions, immunodeficiency (e.g. HIV infection), solid-organ cancer, atrial fibrillation, hemoglobinopathies, abnormal gastrointestinal barrier and intestinal strongyloidiasis [1–10].

Our patient did not report any risk factors for *Salmonella* spp. infection, except for farmer's eggs consumption some days before. *S.* Enteritidis probably reached the

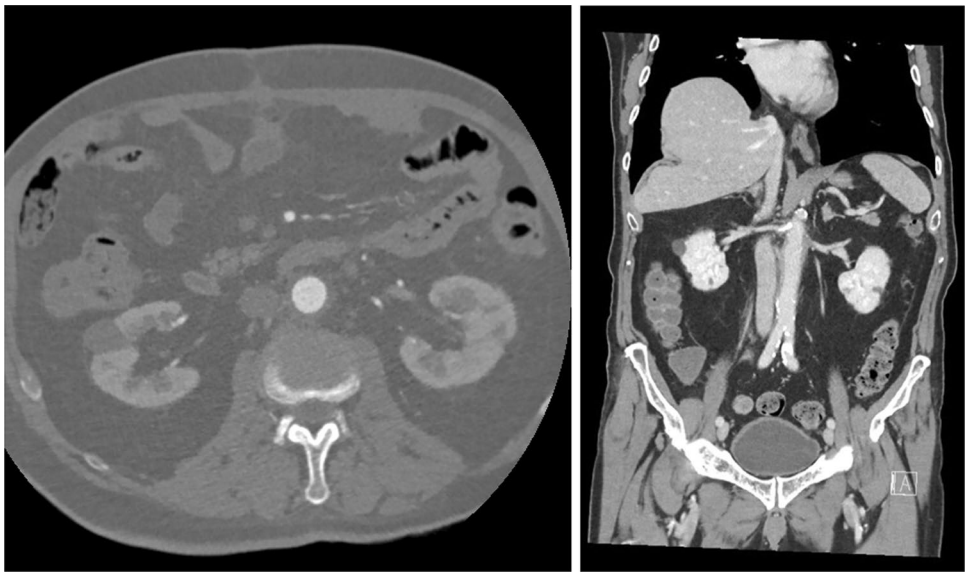

Fig. 5 Abdominal angio-CT scan performed after surgery showed no signs of infection or complications

patient's aorta through haematogenous spread after a primary gastrointestinal infection.

In this patient, predisposing factors for NTS bacteremia and aortic infection included male gender, age over 50 years, hypertension, diabetes mellitus, widespread atherosclerosis, and sigma diverticulosis. He had not HIV infection, hemoglobinopathies, intestinal strongyloidiasis, abnormal immunoglobulin dosage nor abnormal lymphocytic typing.

To exclude other major causes of aortitis, he was screened for syphilis and autoimmune diseases with negative results.

Antibiotics alone are unsuccessful resulting in a mortality of nearly 100% of cases, reduced to 40% with surgery [1–5, 9]. Therefore, surgical treatment must always be considered. There are two options: endovascular treatment and open surgery. The first one has a lower early mortality rate, but late aneurysm-related events including mortality and complications seem to be more common than conventional surgery, because the infected tissue cannot be removed. At present, endovascular technique has consequently restricted indications: absence of gross purulence, gross infection, aorto-digestive fistula, uncontrolled sepsis and the presence of a high operative risk [2, 5]. Therefore, as in this case, a conventional surgery should be preferred when operative risks are not prohibitive. Homograft should be the graft of choice, whenever it is available because of its highest resistance against reinfection [13].

Evidence from the literature suggests that surgery should be performed as soon as possible. On the other hand, the best timing depends on the clinical context. If the patient is hemodynamically stable with good fever and pain control, slow reduction of inflammation indices and no signs of aortic rupture, surgery can be delayed as long as a month from the clinical onset, never interrupting intravenous antibiotic therapy [1, 3, 7–9]. Otherwise, prompt surgical intervention is necessary.

Optimal antibiotic duration is unclear. Some authors suggest long-life suppressive therapy, whereas others suggest antibiotic therapy lasting for at least 6–8 weeks with at least 3–4 weeks of intravenous therapy [1, 3, 7–9]. Essential factors for choosing antibiotic duration are the possibility to associate a surgical intervention and the type of surgery used (open vs endovascular): we should consider long-life suppressive therapy in case of only medical management and of endovascular treatment.

Patients who have had aortic infection by *Salmonella* spp. have to be followed with clinical, blood, and radiological examinations for years to be able to act rapidly in case of complications or relapses after the completion of antibiotic therapy [11, 12]. In this case, the patient was treated with antibiotics for a total of 8 weeks, four of which intravenously, planning a clinical and radiological long-term follow-up.

Conclusion

Non-typhoidal *Salmonella* aortitis is a serious infection that carries a poor prognosis if unrecognized and not promptly treated. It is mandatory to perform tests to search for extra-intestinal infective localizations in patients with *Salmonella* spp. bacteremia, especially if the clinical and/or laboratory picture shows slow improvement during appropriate antibiotic therapy or rapid worsening after interruption of antibiotics.

In case of *Salmonella* spp. aortitis, predisposing conditions for bacteremia and vascular localization should be checked (see Table 1).

Table 1 Predisposing factors for cardiovascular localization by *Salmonella* spp. [1–5, 7–10]

Male gender
Age over 50 years
Hypertension
Diabetes
Pathological alterations of the aortic wall (e.g. atherosclerosis)
Invasive catheterization or post-traumatic lesions
Immunodeficiency (e.g. HIV infection)
Solid-organ cancer
Atrial fibrillation
Hemoglobinopathies
Abnormal gastrointestinal barrier
Intestinal strongyloidiasis

If possible, surgical treatment should always be performed together with antibiotic therapy, to reduce mortality. The best timing for surgical intervention depends on the patient's clinical status. Antibiotic therapy should be continued for at least 6–8 weeks, considering long-life therapy mostly in case of contraindications to conventional surgical intervention or in case of performed endovascular procedure.

Patients who have had aortic infection by *Salmonella* spp. have to be followed with clinical, blood, and radiological examinations (angio-CT or angio-MRI) for years to be able to act rapidly in case of complications or relapses after antibiotic suspension.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

Informed consent A consent for the use of the clinical data was provided.

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