

A case of Infective Endocarditis due to *Salmonella enterica* phagetype 35. First report

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Abstract

Infective Endocarditis (IE) has high morbidity and mortality. To date, in addition to classic Gram-positive pathogens were isolated exigent Gram negative bacteria responsible of endocarditis as *A. baumannii*, *A. lwoffii*, *C. burnetii*, *Bartonella*, *Chlamydia* and *Legionella*.

We report our experience about the isolation of *Salmonella enterica* phagetype 35 (PT35) from blood heart cavity of a 74-year-old woman after having consumed a portion of baked pasta bought in a rotisserie. Cardiovascular infections due to *Salmonella enterica* are infrequently reported, so their clinical features, prognosis, and optimal treatment are not completely known. To the best of our knowledge, after careful evaluation of existing literature, this is the first report of endocarditis due *S. enterica* PT 35. *Clin Ter* 2017; 168(6):e397-400. doi: 10.7417/CT.2017.2041

Key words: bacteremia; Infective Endocarditis; *Salmonella enterica* PT35

Introduction

Salmonella species are important pathogens which cause foodborne diseases both in developed and developing countries. In 2013, a total of 82,694 confirmed salmonellosis cases were reported by 27 EU Member States (MS), resulting in an EU notification rate of 20.4 cases per 100,000 population. *Salmonella* remained the most frequently detected agent causing food-borne outbreaks (22.5 % of total outbreaks), nevertheless the annual total number of *Salmonella* outbreaks within the EU has decreased markedly during recent years. From 2008 to 2013, *Salmonella* outbreaks within the EU decreased of 38.1 % (from 1,888 to 1,168 outbreaks). Fifty-nine fatal cases were reported by 9 EU MS among the 14 MS that provided data on the outcome of their cases (1).

Salmonellosis occurs with a symptomatology ranging from mild gastroenteritis (with the only involvement of the gastrointestinal tract) to a severe invasive infection, especially in vulnerable subjects (children, elders, immunosuppressed hosts, etc.) (2). All anatomic districts can

potentially be reached by bacteria, by the way of blood flow. Involvement of the cardiovascular system is rare but not impossible, causing serious impairment of the patient's clinical status and, sometimes even death (3). The pathogenesis of IE caused by *Salmonella* depend to the bacterial charge present in the ingested food, ability of the germ to adhere to the injured endothelium and to the conditions of the immune system of the host. The consequence of *Salmonella* endocarditis including valve perforation, valve ring abscess, atrioventricular wall perforation, and cusp rupture, can lead to an estimated mortality rate of up to 75% (4, 5).

The aim of manuscript is to bring to the attention of the scientific community to a new case of Infective Endocarditis due to *Salmonella enterica*, and to point out that the phagetype isolated was never involved in this type of infection.

Case presentation

A 74-year-old woman complained for dramatic onset of emesis and diarrhea after consumption of a meal without apparent organoleptic alterations, about 6-7 hours after its ingestion (long before the classic 24-36 hours of incubation). All the other exposed family members (younger and healthier than the deceased woman) showed similar symptomatology, but with milder symptoms: they only had the involvement of the gastrointestinal tract (abdominal pain, retching, diarrhea, low fever). They were hospitalized and discharged a few days later without any kind of sequelae, after antibiotic therapy.

About 24 hours after ingestion of contaminated food the woman was admitted at the Emergency Department. The patient's medical history revealed systemic arterial hypertension, psoriasis for about ten years and episodes of atrial fibrillation in treatment with new oral anticoagulant therapy (6,7). While performing the initial echocardiographic screening, ventricular fibrillation with cardiac arrest occurred, followed by death despite prompt cardiopulmonary resuscitation maneuvers (about 40 minutes after admission). The autopsy showed moderate myocardial hypertrophy with

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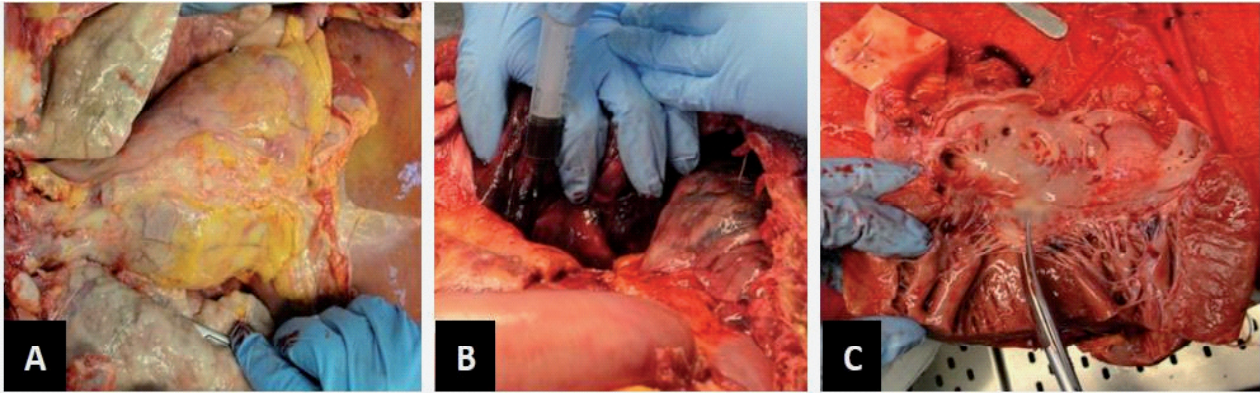


Fig. 1. Photos taken during the autopsy. A: cardiac cavity; B: blood sampling from the heart chambers; C: macroscopic examination of the heart section. (Photos E. Ventura Spagnolo).

interstitial edema, irregular swelling and focal vacuolar degeneration.

During autopsy, some samples including a blood sample from heart chambers were collected (Fig. 1). Microbiological analyses of samples showed the presence of *Salmonella enterica* in pure culture; in particular the bacterial charge found in cardiac blood sample was 120,000 CFUs/ml (Fig. 2). Biochemical-enzymatic identification of the bacterial strain was performed by API 20 E profiles (bioMérieux, Marcy l'Etoile, France), and its serological typing by an agglutination test (Biogenetics, Denka Seiken co., Tokio, Japan). An antibiogram was obtained by the Kirby-Bauer method; the bacterial strain did not show any particular resistance (Tab. 1). Finally, the strain was shipped to the National Institute of Health (Istituto Superiore di Sanità - ISS - Rome) for phage and molecular typing (PFGE). Analyses confirmed the presence of *Salmonella enterica* PT35, electrophoretic profile 001. Data from the necroscopic investigation documented that “death occurred in acute heart failure with terminal pulmonary edema, septic shock and multiorgan dysfunction, in subject with widespread necrotizing enteritis”.

Discussion

Infective Endocarditis (IE) has high morbidity and mortality. To date, in addition to classic pathogens (*S. aureus*, *Streptococcus* sp, *Enterococcus* sp) were isolated exigent Gram negative bacteria, for example those belonging to the group HACEK (*Haemophilus* sp, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae*). Moreover, there are studies reporting cases of endocarditis caused by *A. baumannii*, *A. lwoffii*, *C. burnetii*, *Bartonella*, *Chlamydia* and *Legionella* spp as the responsible of associated forms with negative blood culture (8-11). Often these bacteria can be spread and, especially in hospital environment, to be transmitted by the most disparate vehicles such as water, aerosols, surfaces, hands, foods, etc. (12-17).

Salmonellosis in particular is a possible cause of subacute myocarditis. In fact autopsy documented findings such as hemorrhagic necrosis, leukocyte infiltration, biventricular dilatation, coronary artery thrombosis with acute myocardial infarction, myocardial and aortic aneurysms, pulmonary

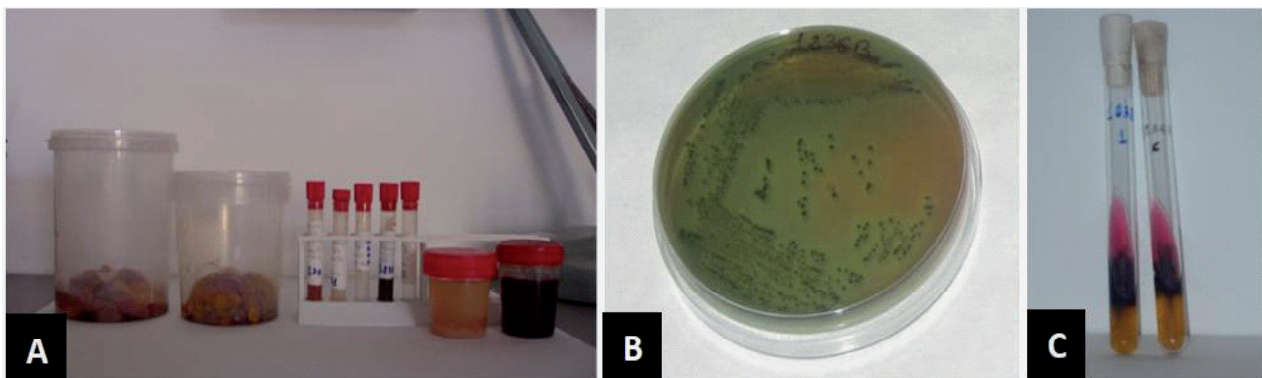


Fig. 2. Photos taken in the Laboratory of Bacteriology. A: containers with different biological samples (gastric and duodenum content, bile, stomach mucus, etc.). The last container on the right contains cardiac blood; B and C: media used for isolation and presumptive germ identification (Hektoen Enteric Agar in plate and Triple Sugar Iron in tubes (Oxoid, Milan, Italy)). (Photos S. Delia, P. Laganà).

Tab. 1. Results of antimicrobial susceptibility testing for *Salmonella enteritidis* PT35 (Kirby Bauer Method) isolated from cardiac blood sample.

Sensitive (S)		Intermediately resistant (I)	Resistant (R)
nalidixic acid (30 µg)	ossolinic acid (2 µg)	cefalotin (30 µg)	amoxicillin + clavulanic acid (20 µg+10 µg)
pipemidic acid (20 µg)	ampicillin (10 µg)	gentamycin (10 µg)	carbenicillin (100 µg)
aztreonam (30 µg)	cefotaxime (30 µg)	nitrofurantoin (300 µg)	cefazolin (30 µg)
cefoxitin (30 µg)	ceftazidime (30 µg)	rifampicin (30 µg)	imipenem (10 µg)
ceftriaxone (30 µg)	cinoxacin (100 µg)	tobramycin (10 µg)	tetracycline (30 µg)
ciprofloxacin (5 µg)	chloramphenicol (30 µg)		
colistin sulphate (10 µg)	fosfomicin (50 µg)		
levofloxacin (5 µg)	mezlocillin (75 µg)		
netilmycin (30 µg)	norfloxacin (10 µg)		
ofloxacin (5 µg)	piperacillin (100 µg)		

The diameter of the zone of inhibition around each disk was measured with a precision caliper (Mitutoyo, Andover, UK). The strain tested was classified as Resistant (R), Intermediately resistant (I) or Sensitive (S) according to the breakpoints established by Clinical Laboratory Standards Institute (CLSI, 2006).

and systemic embolism. Arrhythmias and conduction disorders are rare, but abscess localized in proximity of the atrioventricular conduction system can result in a complete atrioventricular block. Cardiovascular infections due to *Salmonella enterica* are infrequent so their clinical features, prognosis, and optimal treatment are not completely known. Mortality associated with aortitis and endocarditis caused by not typhoid *Salmonella* remains exceedingly high (18-20). Availability of rapid echocardiographic analysis with the objective of ruling out chronic structural cardiac abnormalities and acute onset diseases, are to date crucial elements in order to manage even rare pathologic conditions and guide the clinician towards the best therapy (21). It is important to emphasize that, to the best of our knowledge after careful evaluation of existing literature, this is the first report of salmonellosis due to PT35. This particular phage-type of *Salmonella* have been isolated from chickens and his pathogenicity has been analyzed only in experimental studies (22).

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References

1. EFSA and ECDC. The EU summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2013; EFSA Journal 2015; 13(1):3991
2. Cheng WL, Li CW, Li MC, et al. *Salmonella* infective endocarditis. J Microbiol Immunol Infect. 2016; 49(3):313-20. doi: 10.1016/j.jmii.2015.02.659
3. Chapple W, Martell J, Wilson JS, et al. A Case Report of *Salmonella muenchen* Enteritis causing rhabdomyolysis and myocarditis in a previously healthy 26-Year-Old Man. Hawaii J Med Public Health 2017; 76(4):106-9
4. Ortiz D, Siegal EM, Kramer C, et al. Nontyphoidal Cardiac Salmonellosis: Two Case Reports and a Review of the Literature. Tex Heart Inst J 2014; 41(4):401-6
5. Fernández Guerrero ML, Aguado JM, Arribas A, et al. The spectrum of cardiovascular infections due to *Salmonella enterica*: a review of clinical features and factors determining outcome. Medicine (Baltimore). 2004; 83(2):123-38
6. Imbalzano E, Casale M, D'Angelo M, et al. Cardiovascular risk and psoriasis: a role in clinical cardiology? Angiology. 2015 Feb;66(2):101-3. doi: 10.1177/0003319714527339.
7. Dattilo G, Imbalzano G, Casale M, et al. Psoriasis and Cardiovascular Risk: Correlation Between Psoriasis and Cardiovascular Functional Indices. Angiology. In Press. DOI: 10.1177/0003319717699329.
8. Laganà P, Melcarne L, Delia S. *Acinetobacter baumannii* and endocarditis, rare complication but important clinical relevance. Int J Cardiol. 2015;187:678-9. doi: 10.1016/j.ijcard.2015.04.019
9. Jia B, Zhang F, Pang P, et al. *Brucella* endocarditis: Clinical features and treatment outcomes of 10 cases from Xinjiang, China. J Infect. 2017;74(5):512-4. doi: 10.1016/j.jinf.2017.01.011
10. Samuel V, Bajwa AA, Cury JD. First case of *L. pneumophila* native valve endocarditis. Int J Infect Dis. 2011; 15(8): e576-7. doi: 10.1016/j.ijid.2011.04.007
11. García-Granja PE, López J, Vilacosta I, et al. Infective Endocarditis due to *Listeria monocytogenes*: A Report of 4 Patients. Rev Esp Cardiol (Engl Ed). 2016;69(7):700-2. doi: 10.1016/j.rec.2016.04.006
12. Montagna MT, Cristina ML, De Giglio O, et al. Serological and molecular identification of *Legionella* spp in water and surrounding air samples in Italian healthcare facilities. Environ Res. 2016;146:47-50. doi: 10.1016/j.envres.2015.12.015
13. Laganà P, Caruso G, Piccione D, et al. *Legionella* spp., amoebae and not-fermenting Gram negative bacteria in an Italian university hospital water system. Ann Agric Environ Med. 2014;21:489-93. doi: 10.5604/12321966.1120623
14. Montagna MT, De Giglio O, Napoli C, et al. *Legionella* spp. contamination in indoor air: preliminary results of an Italian multicenter study. Epidemiol Prev. 2014;38(6 Suppl 2): 62-5
15. Laganà P, Moscato U, Poscia A, et al. The Geostatistics, tool applied to the distribution of *Legionella pneumophila* in a hospital water system. Ann Agric Environ Med. 2015;22(4):655-60. doi: 10.5604/12321966.1185769
16. Mauro A, Laganà P, Bruno G, et al. Isolation of *Yersinia enterocolitica* biotype 1A from raw meat products. J Prev Med Hyg. 2008;49:76-9

17. Stilo A, Troiano G, Melcarne L, et al. Hand washing in operating room: a procedural comparison. *Epidemiology Biostatistics and Public Health*. 2016; 13, 3, e11734-1/e11734-7
18. Tsugawa Y, Futatsuyama M, Furukawa K, et al. Infective endocarditis caused by *Salmonella enteritidis* in a dialysis patient: a case report and literature review. *BMC Infect Dis*. 2009;9: 161. doi: 10.1186/1471-2334-9-161
19. Gönen C, Topeli A, Cetinkaya YS. Prosthetic valve endocarditis caused by *Salmonella enteritidis*. *Scand J Infect Dis*. 2004;36:72-5
20. Abdikarim M, Shahari S, Idris MA, et al. Misdiagnosed infected aneurysm presenting as pyrexia of unknown origin (PUO). *Clin Ter*. 2014;165(4):199-201. doi: 10.7417/CT.2014.1733
21. Dattilo G, Imbalzano E, Lamari A, et al. Ischemic heart disease and early diagnosis. Study on the predictive value of 2D strain. *Int J Cardiol*. 2016 Jul 15;215:150-156. doi: 10.1016/j.ijcard.2016.04.035
22. Akhtar A, Hair-Bejo M, Omar AR, et al. Pathogenicity of *Salmonella enteritidis* phagetypes 3a and 35 after experimental infection of white leg horn chicks. *The Journal of Animal & Plant Sciences*; 2011;21:4:770-7