Case report

**Typhoid fever as a cause of opportunistic infection: case report**
Claudia Colomba*1, Laura Saporito1, Laura Infurnari1, Salvatore Tumminia2 and Lucina Titone1

Address: 1Istituto di Patologia Infettiva e Virologia, Università di Palermo, Piazza Montalto 8, 90134 Palermo, Italy and 2Unità Operativa di Malattie Infettive, Azienda Ospedaliera Universitaria Policlinico, Palermo, Italy

Email: Claudia Colomba* - claudia.colomba@libero.it; Laura Saporito - laura.sapo@tin.it; Laura Infurnari - infurnari.laura@libero.it; Salvatore Tumminia - claudia.colomba@libero.it; Lucina Titone - titonel@unipa.it

* Corresponding author

**Abstract**

**Background:** Typhoid fever is a systemic infection caused by the bacterium *Salmonella enterica* subspecies *enterica* serotype *typhi*, which is acquired by ingestion of contaminated food and water. Each year the disease affects at least 16 million persons world-wide, most of whom reside in the developing countries of Southeast Asia and Africa. In Italy the disease is uncommon with a greater number of cases in Southern regions than in Northern ones.

**Case presentation:** We report on a 57-year-old Sri-Lankan male affected by typhoid fever, the onset of which was accompanied by oropharyngeal candidiasis. This clinical sign was due to a transient cell-mediated immunity depression (CD4+ cell count was 130 cells/mm³) probably caused by *Salmonella typhi* infection. Human immunodeficiency virus infection was ruled out. Diagnosis of typhoid fever was made by the isolation of *Salmonella typhi* from two consecutive blood cultures. The patient recovered after a ten days therapy with ciprofloxacin and his CD4+ cell count improved gradually until normalization within 3 weeks.

**Conclusion:** Our patient is the first reported case of typhoid fever associated with oropharyngeal candidiasis. This finding suggests a close correlation between *Salmonella typhi* infection and transitory immunodepression.

**Background**

Typhoid fever is a systemic infection caused by the bacterium *Salmonella enterica* subspecies *enterica* serotype *Typhi*, which is acquired by ingestion of contaminated food and water. Each year the disease affects at least 16 million persons world-wide, most of whom reside in the developing countries of Southeast Asia and Africa [1]. Typhoid fever is uncommon in industrialised regions such as the USA, Canada, Europe, Australia and Japan and new cases of the disease in these countries are related to travel to developing countries [2,3]. Based on such data, the public health authorities in most industrialised countries recommend vaccination against typhoid fever for travellers to the developing world, where sanitary conditions are poor [4]. Italy is a low endemicity country for typhoid fever and a greater number of cases occur in Southern regions than in Northern ones. Sicily is the second region of our country for incidence, with a mean of 100 annual cases in the last five years.

Although typhoid fever is classically described as an acute illness with fever and abdominal tenderness, the symp-
toms are non specific and may be insidious in onset [5]. The diagnosis of enteric fever should be seriously considered in the evaluation of travellers who return from tropical and subtropical areas with fever. Mortality rates associated with typhoid fever vary from region to region, with the highest reported from Indonesia, Nigeria, and India [6].

We report on an imported case of typhoid fever, the onset of which was accompanied by oropharyngeal candidiasis.

Case presentation
In November 2004, a 57-year-old Sri-Lankan male turned up at the emergency department of our hospital. The patient had been living in Italy for 14 years, when he went back home to Sri-Lanka. He was there for 2 months, before returning to Italy where, few days later, he began suffering from fever, malaise, headache and non productive cough. He turned up at the emergency department of our hospital after 10 days from the beginning of symptoms.

On the basis of anamnestic data no history of drinking, smoking and illicit drug abuse was reported. Moreover, in his medical history there was no evidence of serious illness, such as diabetes mellitus or human immunodeficiency virus (HIV) infection. The patient had not been using proton pump inhibitors of stomach acid tablets, neither oral corticosteroids or inhalation corticosteroids. Moreover, he did not need to take any antibiotics during his stay in Sri-Lanka.

The patient had a blood pressure of 180/100 mm Hg, a heart rate of 120 beats/min, a respiratory rate of 16 breaths/min, and a temperature of 38.9°C. On chest examination bilaterally scattered rhonchi and mild rales were audible at the base of both the man's lungs. A chest radiograph revealed accentuation of the pulmonary reticulum, more marked on the right, but no clear signs of consolidation. The rest of the examination was notable for a minimally distended abdomen which was diffusely tender. Laboratory examination revealed a white blood cells (WBC) count of 6,400 cells/mm³ (normal range 4,000–10,000 cells/mm³), a haemoglobin level of 15 g/dl (12–17 g/dl), a platelet count of 189,000 cells/mm³ (150,000–450,000 cells/mm³), an aspartate amino-transferase level of 71 U/L, an alanine aminotransferase level of 98 U/L; blood glucose level, serum electrolyte concentrations and renal function tests were within normal limits. A presumptive diagnosis of bronchitis was made, and the patient was transferred to our infectious disease department.

At the time of admission, the patient was persistently febrile (39°C). On physical examination we noted dry skin and oral candidiasis characterized by creamy white, curdlike patches on the tongue; this clinical picture was so typical that it did not need a culture to confirm the diagnosis of oral candidiasis. His abdomen was diffusely tender to palpation and without recognizable hepatosplenoymegaly. Cultures of blood and respiratory specimens were performed. Thick and thin blood smears for malaria were obtained.

Treatment with topical nystatin and empirical therapy with ciprofloxacin (500 mg iv every 12 hours) were started. Because of the oro pharyngeal candidiasis, lymphocyte count was taken, the absolute number of lymphocytes was 562 cells/mm³. The CD4+ cell count was 130 cells/mm³while the CD8+ was 240; as a second step an HIV test (ELISA) was performed and was negative. To rule out a very recent infection a qualitative HIV PCR was performed and HIV RNA was undetectable. On the 3rd day of hospitalisation, a Salmonella species identified as S. typhi was isolated from the two consecutive blood cultures obtained on the day of admission. Isolates were susceptible to ampicillin, cotrimoxazole, chloramphenicol, cefotaxime, ceftriaxone, and ciprofloxacin with the standard disk diffusion susceptibility testing method. The patient continued ciprofloxacin for a total of 10 days; he became afebrile after 3 days of therapy and his oral candidiasis improved slowly with nistatin. The patient recovered and was discharged from the hospital on the 10th day. At that time, his CD4+ cell count was 622 cells/mm³.

On the 20th day after discharge and in the 3rd month of follow-up, the patient was symptom free and his CD4+ cell count was raised to 1,080 and 1,200 cells/mm³ respectively.

Conclusion
In Italy, typhoid fever has become an uncommon disease occurring mainly as a sporadic disease in patients of any age and gender, and at any time of the year. The prevalence rate of typhoid fever has markedly decreased, from nearly 10,000 documented cases annually in the 1970s to a few hundred cases annually in the 2000s [7,8]. This data suggest that Italy is still a low endemicity country for typhoid fever, because of the presence of a moderate number of autochthonous cases mainly reported in the Southern regions of our country [9]. Nevertheless, S. typhi infection is one of the major causes of fever in patients admitted in hospital after returning from the tropics. Together with hepatitis A it represents the cause of a significant number of hospitalizations that pretravel vaccination strategies could have prevented [10].

Recently many strains of multidrug resistant (MDR) S. typhi have been identified worldwide [11-14]; in Italy an epidemiologic study conducted between 1980 and 1996.
showed that their spread was until now quite low [15]. However an accurate and continuous surveillance is necessary in order to quickly identify MDR S. typhi strains and prevent their spread.

We report on an imported case of typhoid fever as previously described in other developed countries [16].

Patients with typhoid fever usually have a history of prolonged fever, headache and abdominal discomfort. There are no distinctive clinical features, and definitive diagnosis requires isolation of S. typhi from blood, bone marrow, stool, or urine cultures [5]. Our patient had fever with upper airway symptoms and showed typical lesions observed in oral candidiasis.

To date, oropharyngeal candidiasis is an opportunistic infection that generally develops in patients who have been using inhaled steroids over a long period of time, and those with cancer and AIDS [17,18]. Because our patient did not belong to any of the three categories of patients reported above, we performed an HIV test to rule out any recent HIV infection; the result was negative [19]. We noticed that the CD4+ cell count was low in the acute phase of disease and improved gradually until normalization within 3 weeks. These findings support the hypothesis that S. typhi could lead to a progressive reduction of CD4+ T helper cell population as already demonstrated as a complication of inhaled corticosteroids.

In conclusion, to our knowledge our patient is the first reported case of typhoid fever the onset of which was accompanied by oropharyngeal candidiasis, suggesting a close correlation between S. typhi infection and transitory immunodepression.

Competing interests
The author(s) declare that they have no competing interests.

Authors’ contributions
All authors contributed equally to this work

Acknowledgements
Written consent was obtained from the patient for publication of this case report.

References
1. Centers for Disease Control and Prevention: Traveler’s health. Preventing typhoid fever: a guide for travellers. Atlanta 2003 [http://www.cdc.gov/travel/diseases/typhoid.htm].
2. Papadimitropoulos V, Vergidis PI, Bliziotis I, Falagas ME: Vaccination against typhoid fever in travellers: a cost-effectiveness approach. Clin Microbiol Infect 2004, 10:681-683.
3. Taylor DN, Pollard RA, Blake PA: Typhoid in the United States and the risk to the international traveler. J Infect Dis 1983, 148:599-602.
4. Centers for Disease Control and Prevention: Health information for international travel 1996–1997. Atlanta 1996.
5. Parry CM, Hen TT, Dougan G, White NJ, Farran JJ: Typhoid fever. N Engl J Med 2002, 347:1770-1780.
6. Miller SI, Hohmann EL, Pegues DA: Salmonella (including Salmonella Typhi). In Principles and practice of infectious diseases Volume 2. 4th edition. Edited by: Mandell GL, Bennet JR, Dolin R. New York: Livingstone; 1994:2013-2033.
7. Bollettino Epidemiologico Nazionale. Ministero della Salute [http://www.ministerosalute.it/promozione/malattie/bollettino.jsp]
8. Scuderi G: A review of the Salmonellosis surveillance systems in Italy: evolution during the course of time within the international framework. Eur J Epidemiol 2000, 16:861-8.
9. Rizzo G, De Vito D: Typhoid fever and environmental contamination in Apulia, Italy. Ann Ig 2003, 15:487-92.
10. Antinori S, Galimberti L, Gianelli E, Calattini S, Piazza M, Morelli P, Moroni M, Galli M, Corbellino M: Prospective observational study of fever in hospitalized returning travelers and migrants from tropical areas, 1997–2001. J Travel Med 2004, 11:35-42.
11. Nkemngu NJ, Asonganyi EDN, Njunda AL: Treatment failure in a typhoid patient infected with nalidixic acid resistant S. enterica serovar Typhi with reduced susceptibility to Ciprofloxacin: a case report from Cameroon. BMC Infect Dis 2005, 5:49.
12. Akinyemi KO, Smith SI, Oyefolu AO, Coker AO: Multidrug resistance in Salmonella enterica serovar typhi isolated from patients with typhoid fever complications in Lagos, Nigeria. Public Health 2005, 119:321-7.
13. Shakespeare WA, Davie D, Tonnerre C, Rubin MA, Strong M, PetticSA: Nalidixic acid-resistant Salmonella enterica serotype Typhi presenting as a primary psoas abscess: case report and review of the literature. J Clin Microbiol 2005, 43:996-8.
14. Huang DB, DuPont HL: Problem pathogens: extra-intestinal complications of Salmonella enterica serotype Typhi infection. Lancet Infect Dis 2005, 5:341-8.
15. Scuderi G, Fantasia M, Niglio T: The antibiotic resistance patterns of Salmonella Typhi isolates in Italy, 1980–96. The Italian SALM-NET Working Group. Salmonella Network. Epidemiol Infect 2000, 124:17-23.
16. Su CP, Chen YC, Chang SC: Changing characteristics of typhoid fever in Taiwan. J Microbiol Immunol Infect 2004, 37:109-114.
17. Simon MR, Houser WL, Smith KA, Long PM: Esophageal candidiasis as a complication of inhaled corticosteroids. Ann Allergy Asthma Immunol 1997, 79:333-338.
18. Menez Jr, Merz VG, Romagnoli MJ, Keruly JC, Moore RD, Gallant J: Infection due to fluconazole-resistant Candida in patients with AIDS: prevalence and microbiology. Clin Infect Dis 1997, 24:28-34.
19. Syrjanen S, Valle SL, Antonen J, Suni J, Saxinger C, Krohn K, Ranki A: Oral candidal infection as a sign of HIV infection in homosexual men. Oral surg 1988, 55:36-40.
20. Gupta S: Priming of T-cell responses in mice by porins of Salmonella typhimurium. Scandinavian J Immunol 1988, 48:136-143.

Pre-publication history
The pre-publication history for this paper can be accessed here:

http://www.biomedcentral.com/1471-2334/6/38/prepub