IDCases 9 (2017) 17–20

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcases

Case report

Severe interstitial pneumonia due to murine typhus in a patient returning from Bali

Luís Malheiro[a,b,*], Filipa Ceia[a], João Alves[e], Ana Cláudia Carvalho[a], Joana Sobrinho-Simões[c], Rita Sousa[d], António Sarmento[a,b], Lurdes Santos[a,b]

[a] Serviço de Doenças Infecciosas (Infectious Diseases Department), Centro Hospitalar de S. João, Porto, Portugal
[b] Unidade de Cuidados Intensivos de Doenças Infeciosas (Intensive Care Unit of Infectious Diseases), Centro Hospitalar de S. João, Porto, Portugal
[c] Clinical Microbiology Department, Centro Hospitalar de S. João, Porto, Portugal
[d] Instituto Nacional de Saúde Doutor Ricardo Jorge (National Institute of Health Doutor Ricardo Jorge), Centro de Estudos de Vectores e Doenças Infecciosas Dr. Francisco Cambournac (CEVDI) (Center for Vectors and Infectious Disease Research (CEVDI) and Gastrointestinal Infections Laboratory), Aguas de Moura, Portugal
[e] Serviço de Doenças Infecciosas e Medicina Tropical, Hospital de Egas Moniz, Centro Hospitalar de Lisboa Ocidental, E.P.E., Lisboa, Portugal

A B S T R A C T

Murine typhus has been increasingly reported as a cause of fever in returning travelers from Southeast Asia. We report a case of a previously healthy traveler returning from Bali with an non-specific febrile illness which quickly progressed to a severe form of interstitial pneumonia. After a careful epidemiological evaluation and laboratory analysis, murine typhus was diagnosed.

Due to their non-specific presentations, most febrile illnesses in returning travelers are hard to diagnose clinically. While many of them are self-limited, others like malaria, dengue and typhoid fever require specific treatment due to their complications and must be quickly excluded. Some diseases like murine typhus, require a high level of suspicion and careful epidemiologic evaluation to be diagnosed, as sometimes they may present in severe forms. Awareness is important, especially in countries where the disease is not endemic and may be not included in the differential diagnosis. We draw attention to murine typhus as an important differential diagnosis in travelers returning from Southeast Asia and to its uncommon, but important, pulmonary complications.

Introduction

Murine typhus is a systemic disease caused by *Rickettsia typhi*, a Typhus group bacteria from the *Rickettsiaceae* family, transmitted to the human by the rat flea *Xenopsilla cheopsis* [1]. The reservoirs are two murine rodents known as the brown (*Rattus norvegicus*) and black (*Rattus rattus*) rat [2]. As the reservoirs and vector are common in most countries, the disease is spread worldwide, especially in temperate climates and coastal/harbor areas, depending on rodent control programs and hygiene standards. Murine typhus is mainly characterized by a mild self-limited syndrome with fever, myalgia and headache, although some severe manifestations as pneumonitis, hepatitis and meningoencephalitis may also occur.

In Portugal, murine typhus incidence is unknown [3]. It may be a relevant differential diagnosis due to potential complications, especially in the traveler presenting with fever coming from an endemic country such as those in Southeast Asia. We present a case of a traveler returning from Bali, an Indonesian island in the Pacific Ocean, with a non-specific febrile illness complicated by severe interstitial pneumonia.

Clinical report

A 38 year-old previously healthy woman returned from a 2 week-long trip to Bali. She had no pre travel consultation and did not take any malaria prophylaxis. During her stay, she travelled around rural areas of the island where she had close contact with people living in poor water and sanitation conditions. She mentioned seeing rats around the accommodation and recalled several mosquito bites, apart from sporadic contact with dogs and cats, with no scratching or biting episodes. She returned to Portugal asymptomatic, but a week after arrival she presented to the emergency department complaining of fever, chills, malaise, myalgia and conjunctival congestion. Her initial blood tests

* Corresponding author at: Infectious Diseases Department of Centro Hospitalar de São João, Faculty of Medicine of the University of Porto, Alameda Prof. Hernâni Monteiro, 4200-319, Porto, Portugal.
E-mail addresses: lmalha@gmail.com (L. Malheiro), fsfceia@gmail.com (F. Ceia), joaovazalves@hotmail.com (J. Alves), anaclaudiacarvalho@gmail.com (A.C. Carvalho), Jssimoes@hsjoao.min-saude.pt (J. Sobrinho-Simões), rita.sousa@insa.min-saude.pt (R. Sousa), antoniosarmento55@sapo.pt (A. Sarmento), maria.lurdes.uci@gmail.com (L. Santos).

http://dx.doi.org/10.1016/j.idcr.2017.05.006
Received 7 May 2017; Received in revised form 10 May 2017; Accepted 10 May 2017

Table 1
Blood analysis results. Legend: ALT – alanine aminotransferase; AP – Alcaline Phosphatase; AST – aspartate aminotransferase; B – Bilirrubin; DB – direct bilirrubina; CK – creatinine kinase; CRP – C-reactive protein; Eos – Eosinophyles; gGT – Gamma glutamyl transpeptidase; Hb – Hemoglobin; Leuc. – Leucocytes; LDH – Lactate desidrogenase; Lym – Lymphocytes; Neu – Neutrophiles; PLT – Platelets; SCr – serum creatinine; U – urea.

	Range	Day 1	Day 3	Day 4	Day 5	Day 7	Day 9	Day 11	Day 23
Hb (g/dL)	12–16	12.9	13.1	12.2	13.0	11.5	9.8	11.9	11.2
Leuc (*10^9/uL)	4–11	4.850	4.970	6.540	5.59	15.10	13.12	12.29	9.03
Neu(%)	53-69	65.4	79.6	84.5	78.4	62.4	39.5	39.5	25.4
Lym(&)	22–36	24.1	7.7	12.2	14.1	29.2	41.5	41.4	62.4
Eos(%)	0.6 – 4.6	0.0	0.0	0.0	0.0	0.1	1.0	1.2	1.0
PLT(*10^9/uL)	150–400	265	135	69	51	60	193	403	636
ALT/AST (U/L)	(10–31)	36/53	116/128	191/237	328/403	169/118	111/89	139/105	67/36
AP/gGT (U/L)	(7–32/30 – 120)	109/25	167/73	175/80	187/91	204/69	349/122	445/212	155/69
B/DB (mg/dL)	(< 1.2/ < 0.4)	0.42/0.11	0.79/0.22	1.03/0.4	0.9/0.23	1.38/0.52	0.95/0.24	0.86/0.26	1.00/0.21
LDH (U/L)	135–255	297	351	507	677				
CK (U/L)	10–149	110	95	105	127				
SCr (mg/dL)	0.51 – 0.95	0.74	0.66	0.61	0.53	0.51	0.51	0.47	0.6
U (mg/dL)	10–50	32	30	19	17	31	29	19	25
CRP (mg/L)	< 3.0	20.9	56.7	102	193	256	87.1	23.1	

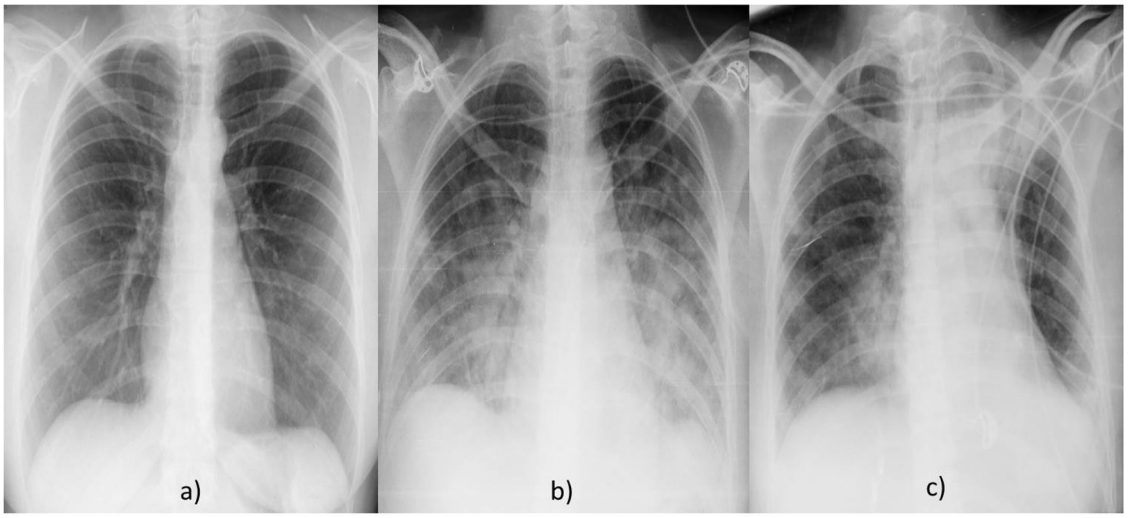

Fig. 1. a) Chest X-ray on the 1st day of fever; b) Chest X-ray on the 4th day of fever and on admission to the ICU; c) Chest X ray on the 7th day of antimicrobial.

(Table 1-Day 1) showed unremarkable changes. Chest X-Ray (Fig. 1a) was normal. Initial investigations for malaria and dengue were negative and she was discharged home with symptomatic treatment with acetaminophen. Forty-eight hours later the patient was re-evaluated in ambulatory and fever persisted, along with malaise and myalgia. Her general condition was good and physical examination was normal.

At this point, her blood tests presented relative neutrophilia, elevated hepatic aminotransferases and elevated LDH, with mildly increased C-reactive protein (Table 1-Day 3). Chest X-ray and abdominal ultrasonography had no abnormalities. Two blood samples were collected for culture in aerobic conditions and a first serologic screen was requested (Table 2). The patient was admitted to the Infectious Diseases Ward for observation.

On the 1st day after admission (day 4 of symptoms) her clinical and analytical condition deteriorated with shortness of breath (respiratory rate of 32/minute, SatO2 90–92% on room air), hypotension (70–80/30–40 mmHg), headache, nausea and a faint, transient, macular rash in the abdomen, trunk and arms. She looked acutely ill. Arterial blood gas examination revealed a respiratory alkalosis with a pO2/FiO2 ratio of 327 and hyperlactacidemia (2.88 mg/dL). Her chest X-ray (Fig. 1b) revealed a bilateral interstitial infiltrate in the lung parenchyma suggestive of interstitial pneumonia.

The patient was admitted to the Intensive Care Unit (ICU) with volume expansion with Intravenous (IV) fluids, IV ceftriaxone (2 g per day), IV doxycycline (100 mg twice daily) and oseltamivir (75 mg twice daily). Oxygen support was delivered by high flux nasal prongs. At this point, new microbiological exams were requested (Table 2).

While in the ICU, the patient condition improved progressively, with no need of invasive ventilation or vasopressive support. Oliguria was reverted. There was a transient decrease in hemoglobin and worsening thrombocytopenia and coagulopathy, which recovered spontaneously. The patient became afebrile by the 4th day of antimicrobial, was discharged from ICU on day 5 and fully recovered by the 7th day of antimicrobials (10th day of disease). Ceftriaxone was given for 8 days, while doxycycline was given for a total of 14 days (7 days by IV route and 7 days by oral route).

At discharge from the hospital (day 13), the patient was asymptomatic. Chest X-ray (Fig. 1c) confirmed resolution of the pulmonary infiltrates. A molecular diagnostic test using polymerase chain reaction (PCR) for *Rickettsia spp*. subgroup Typhus was later found to be positive. All other microbiological exams were negative.

To confirm the diagnosis of *R. typhi* infection, serum samples from acute (day 4 of disease) and convalescent (2 weeks after discharge) phases were sent to the Center for Vectors and Infectious Disease Research (*Centro de Estudos de Vectores e Doenças Infecciosas* – CEVDI) of the National Institute of Health in Águas de Moura, Setúbal, Portugal, were they were tested by immunofluorescence assay using a commercial Rickettsia IFA Substrate Slide kit® (Focus Diagnostics, USA). Seroconversion in two consecutive samples of the patient was demonstrated by the appearance of antibodies levels in second sample with