Serological Evidence of Human Coinfection by Brazilian Spotted Fever and Bartonellosis

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Abstract

Brazilian spotted fever and bartonellosis are zoonotic, emerging and under diagnosed diseases. Pets may be co-infected by multiple pathogens and become transmissions sources to humans. The study reports the first case of active co-infection by Brazilian spotted fever and bartonellosis based on serological evidence. The authors aim to demonstrate the importance of performing systematic syndromic investigations on nonspecific febrile syndromes, guided by the epidemiological history and considering the possibility of co-infection by zoonosis sharing the same ecological niche.

Keywords

Rickettsia rickettsii, Bartonella henselae, Brazilian Spotted Fever, Bartonellosis, Co-Infection

1. Introduction

Brazilian Spotted Fever (BSF) and bartonellosis are zoonotic diseases respectively considered reemerging and emerging. They are transmitted to humans by accident and are generally under diagnosed.

BSF, described in Brazil since the 1920s, is caused by Rickettsia rickettsii, and ticks are its vectors and reservoirs, especially those from Amblyomma sculptum species (from the Amblyomma cajennense complex), although other infected species may participate in its transmission [1]. It has wide geographical distribution with limited outbreaks in the Brazilian southeastern and southern regions, and in some locations in the midwest, northeast and north regions [2]. Its distribution is seasonal, between May and
October. On average, 55 cases are annually recorded in Brazil [3] and lethality ranges from 20% to 30% [2] [3]. The initial clinical presentation is nonspecific and may progress to sepsis and death mainly due to late diagnosis and consequent delay in the introduction of the specific treatment [1] [2] [3] [4].

Bartonellosis is caused by species from the Bartonella genus. The B. henselae species is the main pathogen for humans and it is often transmitted by scratching, biting, licking, or simple contact with cat’s fleas and other ectoparasites. In addition to cats, several other mammals may be reservoir and vector. The species has worldwide distribution and seasonality period between January and July [5] [6]. Its incidence is of 3.7/100.000 in inhabitants. Most cases are benign and self-limiting, but the disease may progress to prolonged bacteremia, get worse and lead to cutaneous, hepatic or splenic vasoproliferative effects, especially in immunocompromised patients [5].

Veterinary studies demonstrate that animals, especially dogs, may be co-infected by multiple Proteobacterium pathogens, and become transmission sources to humans who manipulate them. Co-infection by R. rickettsii and by some Bartonella species, except for B. henselae, had been reported [7] [8]. However, B. henselae had been identified in domestic dog fleas [9] [10]. Additionally, there are records of human co-infection by R. rickettsii and Ehrlichia chaffeensis [11]. Kordich performed a serological survey and found antibodies to B. henselae and R. rickettsii on healthy dog breeder [7]. Despite the finding could not be correlated with the presence of simultaneous infectious syndrome, the co-infection possibility could be taken under consideration. Nevertheless, literature has no report on human active co-infection by BSF and bartonellosis.

The current study aims to report the first human case with serological evidence of active co-infection by R. rickettsii and B. henselae, recorded in Rio de Janeiro, Brazil. It is an alert to health professionals about the possibility of co-infection, the impact of this event on the research algorithm, the following up of complications and the empirical choice for specific therapies.

2. Case Report

MAJD, female, 47 years old, lived in São João de Meriti (metropolitan region of Rio de Janeiro/Brazil). She was previously healthy with no comorbidities. In April 2014, she started presenting fever, chills, occipital headache, myalgia, hyporexia and hypogeusia. The patient sought the primary care unit several times between the 2nd and 13th day of the disease, time when the diagnostic hypothesis of dengue was considered and its supportive treatment was introduced. Between the 6th and 10th day of the disease, she presented aqueous diarrhea and vomiting. Since fever persisted, the patient was referred to the National Institute of Infectious Diseases in the 14th day of the disease. She reported the habit of collecting dogs and cats often parasitized by ectoparasites, which were abandoned. She also reported that one dog and one cat were being treated for “tick disease” and “infectious disease without etiology”, respectively. She took care of her pets without using personal protective equipment. At the 14th day she was febrile (38°C) and hemodynamically stable, without cutaneous rash or lymphadenopathy. La-
Laboratory tests performed on the 14th day showed increased C-reactive protein with no others hematological, renal and hepatic changes. Previous laboratory tests showed leukocytosis without deviation in the 2nd day of the disease and thrombocytopenia between the 3rd and 13th day of the disease. The diagnostic hypothesis of zoonosis: BSF, leptospirosis or bartonellosis was considered and specific tests were performed. In addition, dengue, viral hepatitis and other nonspecific bacterial infections investigated were complemented. Empirical treatment with doxycycline was immediately introduced at the dose of 200 mg/day. The patient evolved with defervescence and clinical improvement within 48 hours after starting the antibiotic, and was discharged within 60 days (Figure 1). All test results—except for the BSF and bartonellosis serological tests—were negative, including the molecular analysis (PCR) for both Proteobacteria. Indirect immunofluorescence presented IgG antibody title of 1/512 for R. rickettsii and 1/128 for B. henselae on the 15th day of the disease, and on the 50th day the IgG antibody title was 1/1024 for R. rickettsii and 1/256 for B. henselae (Table 1).

3. Discussion

The patient presented initially a nonspecific febrile syndrome. There was a delay in diagnosis and treatment due to the relative unawareness about the occurrence of the zoonosis among humans. Additionally, the overlap of hyperendemic diseases, such as Dengue, has also been a frequent confounding factor. Epidemiological history suggests that the infection has been acquired through the unprotected handling of her own pets, some of them known to be sick. The delay in the first sampling and effective treatment can in part explain our inability to demonstrate the perfect seroconversion and the
Table 1. Representation of the relevant laboratory tests.

<table>
<thead>
<tr>
<th>Disease time in days</th>
<th>Complete Blood Count</th>
<th>CRP (mg/dL)</th>
<th>Rr (IgG)</th>
<th>Bh (IgG)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hb (g/dL)</td>
<td>Ht (%)</td>
<td>Leuk (mm³)</td>
<td>Plat (mm³)</td>
</tr>
<tr>
<td>HUPC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd</td>
<td>13.8</td>
<td>42.0</td>
<td>15,400</td>
<td>180,000</td>
</tr>
<tr>
<td>3rd</td>
<td>12.6</td>
<td>37.8</td>
<td>8,200</td>
<td></td>
</tr>
<tr>
<td>4th</td>
<td>11.7</td>
<td>34.7</td>
<td>7,200</td>
<td>53,000</td>
</tr>
<tr>
<td>6th</td>
<td>11.9</td>
<td>35.6</td>
<td>7,000</td>
<td>57,000</td>
</tr>
<tr>
<td>7th</td>
<td>12.2</td>
<td>36.1</td>
<td>7,900</td>
<td>101,000</td>
</tr>
<tr>
<td>13th</td>
<td>12.2</td>
<td>35.1</td>
<td>8,100</td>
<td>65,000</td>
</tr>
<tr>
<td>14th</td>
<td>11.6</td>
<td>36.3</td>
<td>9,140</td>
<td>209,000</td>
</tr>
<tr>
<td>INI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15th</td>
<td>11.8</td>
<td>36.4</td>
<td>6,500</td>
<td>113,000</td>
</tr>
<tr>
<td>50th</td>
<td>-</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>

Nomenclature and benchmarks: HUPC = Health Unit Primary Care; INI = National Institute of Infectious Diseases; Hb = Hemoglobin (11 - 16 g/dL); Ht = Hematocrit (34 - 45 g/dL); Leuk = leukocytes (4000 - 10,000 mm³); Plat = Platelets (150,000 - 450,000 mm³); CRP = C-reactive protein (0 - 0.3 mg/dL); Rr = Rickettsia rickettsii; Bh = Bartonella henselae; IgG = Immunoglobulin G.

The possibility of *R. rickettsii* and *B. henselae* molecular detection is higher in the early stages of the disease, with greater sensitivity in severe and fatal cases. Furthermore, the excellent therapeutic response, as well as the epidemiological history, reinforces the BSF and bartonellosis diagnostic. Usually serology is an essential and largely available method to laboratory confirmation for both zoonosis, however, it depends on the opportunity of the investigation [1] [4] [12].

The authors of the current study intend, by means of this report, to emphasize the importance of performing a syndromic investigation strongly guided by the epidemiological history, especially in an undifferentiated febrile syndrome. In addition, the possibility of co-infection by *Proteobacteria* zoonosis which shares the same ecological niche must be considered, and this possibility needs to be included in diagnostic algorithm for the choice of the most appropriate antimicrobial medication in order to decrease morbidity and mortality caused by the zoonosis.

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Conflict of Interest

The authors declare that there is no conflict of interest.
Consent

Written consent was obtained from the patient under a research project approved by the Ethic Committees of IPEC/FIOCRUZ: “Detecção de formas não usuais de dengue a partir da vigilância de síndromes febris agudas”, CAAE 0026.0.009.000-07.

References


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