International Journal of Infectious Diseases 33 (2015) e5–e6

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

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

Case Report

A case of visceral leishmaniasis and pulmonary tuberculosis in a post-partum woman

Claudia Colomba [a,*], Lucia Adamoli [a], Marcello Trizzino [a], Lucia Siracusa [a], Silvia Bonura [a], Manlio Tolomeo [a], Massimo Cajozzo [b], Giovanni Maurizio Giammanco [a]

[a] Dipartimento di Scienze per la promozione della salute e materno-infantile, Università di Palermo, Italy
[b] Dipartimento di Discipline chirurgiche, oncologiche e stomatologiche, Università di Palermo, Italy

ARTICLE INFO

Article history:
Received 18 November 2014
Received in revised form 9 December 2014
Accepted 10 December 2014

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Visceral leishmaniasis
Pulmonary Tuberculosis
Pregnancy

ABSTRACT

Visceral leishmaniasis due to *Leishmania infantum* is a vector-borne zoonotic disease transmitted by sand fly bites endemic in rural or periurban areas of the Mediterranean basin. Pregnancy is accompanied by changes in immune response, mainly a decrease in cellular immunity and a proportional increase in humoral immunity. These physiological events result in increased risk of infection by pathogens whose immunity is based on a T-helper 1 predominant response. We describe a case of visceral leishmaniasis and pulmonary tuberculosis diagnosed in a post-partum woman four days after delivery. The diagnosis of leishmaniasis should be considered in pregnant women with fever and haematologic abnormalities in endemic regions or if a history of exposure in endemic areas is reported.

1. Background

Visceral leishmaniasis (VL) due to *Leishmania infantum* is a vector-borne zoonotic disease transmitted by sand fly bites endemic in rural or periurban areas of the Mediterranean basin. An estimated 47% of the population in Sicily, the largest island in the Mediterranean Sea, lives in areas at risk for Leishmania infection. In the Mediterranean the incidence of leishmaniosis is estimated to be at least 1000 cases per year, and dogs provide the reservoir for *Leishmania infantum*. The disease disproportionately affects children and immunodepressed patients, more frequently involved because of a relative inability to contain the infection.[1] Few case reports of VL in pregnancy have been reported in the literature.[2] Co-infection of visceral leishmaniasis and tuberculosis is an important public problem; both diseases appear to be risk factors for each other. We describe a case of VL and pulmonary tuberculosis diagnosed in a post-partum woman.

2. Case presentation

In January 2014, a previously healthy Romanian female aged 22 years, recently immigrated from Eastern Europe, was admitted to the Infectious Diseases Unit of the University Hospital of Palermo, Italy, due to fever, headache and sweats. The symptoms had begun six days before, a few hours after delivery.

On admission, the patient was febrile (body temperature 37.7 °C); blood pressure 110/70 mm Hg, oxygen saturation of 97%. The complete blood count demonstrated a white blood cell count of 2850 cells/mm3, haemoglobin 11.8 g/dL, platelets 84000-111000 cells/mm3; erythrocyte sedimentation rate 48 mm/h, C-reactive protein 9.12 mg/dL and a very slight increase of gamma globulins (19.3% at the serum protein electrophoresis, range value 10,5- 18,8). Physical examination demonstrated hepatosplenomegaly, confirmed by ultrasound (spleen size approximately 20 cm). A chest X-ray demonstrated radiopaque rounded areolas in the right superior-middle and left middle lung fields.

Blood cultures were performed and resulted negative; empiric anti-microbial therapy with meropenem, amikacin and clindamycin was initiated without improvement. Persistent fever, progressive anemia, splenomegaly and a history of a first daughter

Abbreviations: VL, Visceral leishmaniasis; BCG, Bacillus Calmette–Guérin; PCR, Polymerase chain reaction; IGRA, Interferon Gamma Release Assays; TB, tuberculosis.

* Corresponding author. Tel.: +390916554054; fax: +390916554050.
E-mail addresses: claudia.colomba@libero.it (C. Colomba), lucia.adamoli5@gmail.com (L. Adamoli), marcellotrizzino@hotmail.it (M. Trizzino), luciasira@gmail.com (L. Siracusa), bonurasilvia@libero.it (S. Bonura), mtolomeo@hotmail.com (M. Tolomeo), massimo.cajozzo@unipa.it (M. Cajozzo), giovanni.giammanco@unipa.it (G.M. Giammanco).

http://dx.doi.org/10.1016/j.ijid.2014.12.020

recently treated for leishmaniasis led us to perform specific testing for antileishmanial antibodies. Immunofluorescent antibody-test (IFAT) test was positive 1:3200; ELISA IgG positive. Quantitative polymerase chain reaction (PCR) assay on blood and on bone marrow aspirate for detection of leishmania-DNA were both positive (1200 n.leish/ml on blood; 5500 n.leish/ml on bone marrow aspirate). Light-microscopic examination of the stained bone marrow specimen was positive for Leishmania amastigotes.

Therapy was initiated with liposomal amphotericin B (l-AmB) at the dosage of 3 mg/kg at days 1–5 and at day 10. The patient defervesced and clinically improved.

Because of a positive (20 mm) tuberculin skin test (TST), an Interferon-Gamma Release Assay (1,04 IU/ml) (QuantiFERON-TB Gold, Cellestis, Ltd., Carnegie, Australia) was performed and confirmed immune reactivity to *Mycobacterium tuberculosis (Mtb)*.

A computed tomography of the chest demonstrated the presence of numerous nodules in the right upper lobe, images of micronodulia as "tree-in-bud", and interstitial thickening in the right middle lobe and in the left apical-dorsal segments. These findings were suspicious for pulmonary TB, so bronchoscopy was performed. A bronchoalveolar lavage specimen was positive for Mtb PCR, and cultures grew Mtb which was susceptible to rifampin, isoniazid, pyrazinamide, and ethambutol. She was started on standard 4-drug TB therapy. The newborn was investigated for Leishmaniasis, the serological test was positive and consistent with the result obtained from the mother, but PCR for leishmania-DNA on peripheral blood resulted negative. The infant also was evaluated for tuberculosis with TST test and chest radiography, according to CDC guidelines, and resulted negative.

3. Discussion

Normal pregnancy is accompanied by changes in immune response, mainly a decrease in cellular immunity and a proportional increase in humoral immunity, which may in part account for the successful growth and delivery of the fetus hemi-allograft. These physiological events result in an increase in the risk for infections sustained by some infectious agents whose immunity is based on a T-helper 1 predominant response. Although on the basis of this immunological evidence the risk of VL during pregnancy may be higher, no specific epidemiological data support the hypothesis. These changes in immune response may potentially have some effects on *Mycobacterium tuberculosis* infection too, even if literature indicates that pregnancy does not affect the course of tuberculosis.

Clinical findings of VL in immunocompetent hosts varies from asymptomatic to severe forms, even fatal if not treated. Various factors have been associated with the development of symptomatic VL, including age less than five years, malnutrition, decreased lymphocyte proliferation, low production of interferon gamma, HIV infection and pregnancy.[3] Asymptomatic infection is the most common clinical form of Leishmania infection in endemic areas.[3,4] Family members and neighbors of patients with a history of classic VL are more susceptible to acquiring the disease due to similar exposures.[5]

In our report, the patient was young and she had no underlying diseases; her risk factors consisted of living in a rural area, and a daughter with a recent diagnosis of Leishmaniasis. She showed the typical clinical features of the disease, with fever, hepatosplenomegaly and pancytopenia. A careful evaluation of the diagnosis of leishmaniasis in pregnant women with fever and haematological abnormalities is necessary in an endemic area or if a history of exposure in endemic areas is reported. Therapy with l-AmB confirmed its efficacy.[6]

With respect to tuberculosis, Italy is considered a country with low prevalence, but the increasing immigration from countries with a high risk level (i.e. East Europe) suggests a need for increased awareness of the problem.

The diagnosis of tuberculosis in pregnancy or during puerperium may be more difficult, as certain symptoms (e.g., increased respiratory rate, malaise, fatigue) may initially be ascribed to the pregnancy.

In our report, the patient had no respiratory symptoms and presented with only fever and malaise. Only the positive result of TST and IGRA screening tests led to additional evaluation and treatment for TB.

Considering the very limited number of cases reported in the literature, VL in pregnancy should be considered to be a rare occurrence. However, the present report demonstrates that the risk of VL during pregnancy has to be considered in endemic areas. The patient we described lived in and possibly contracted the infection in a rural area of Sicily where she recently immigrated from Eastern Europe. Adults moving from non-endemic to endemic countries could be at higher risk of contracting VL due to lack of previous immunity. However, VL in pregnant women also should be considered among urban and peri-urban residents who are less likely to have been exposed to *Leishmania* during childhood. Therefore, a careful evaluation of the diagnosis of leishmaniasis in pregnant women with fever and haematological abnormalities would be necessary in an endemic area or if a history of recent exposure in endemic areas is reported. Early diagnosis of VL in pregnancy also would be needed to rule out the risk of congenital infection and establish appropriate treatment. TB is generally acknowledged to complicate VL since both clinical syndromes are influenced by the quality of the cell mediated immune response and the prognosis for progression to active disease of co-infected individuals is likely to be different from those with a single infection.

As demonstrated by the present report, LTBI screening would be advisable in VL patients in order to detect co-infection.

Acknowledgements

We have not received substantial contributions from non-authors.

Competing interests: The authors declare that they have no competing interests.

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