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Visceral leishmaniasis as a cause of postpartum pyrexia - case report

Case Report

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Abstract: Introduction: Visceral leishmaniasis, caused by protozoan parasites of the Leishmania genus, is very rare cause of postpartum pyrexia. It is also known as kala-azar, black fever, and Dumdum fever. Signs and symptoms include fever, weight loss, mucosal ulcers, fatigue, anemia, and substantial swelling of the liver and spleen. Case report: We represent a very rare case of the septic form of visceral leishmaniasis in a thirty-year-old woman during puerperium, 31 days after vaginal delivery. Her continuously febrile state, splenomegaly, and laboratory findings characteristic of a febrile state meant that the disease at the beginning was understood and treated as a puerperal sepsis. The patient's condition worsened continuously, despite treatment with wide spectrum antimicrobial agents. Expert advice at the Clinic decided that hysterectomy was necessary. After a short remission, her febrile state returned; we decided to transfer the patient to the Clinic for Infectious Diseases for further evaluation and diagnosis. Microscopic analyses of a sternal biopsy showed polymorphic forms of Leishmania chagasi, confirming the diagnosis of visceral leishmaniasis. After adequate the patient recovered completely. Conclusion: Only careful examination, close observation, and prompt treatment performed by a multidisciplinary team of specialists can lead to a good outcome for the patient. Bone marrow biopsy remains the gold standard in the diagnosis of Visceral leishmaniasis.

Keywords: *Fever of unknown origin • Postpartal period • Sepsis • Puerperium • Visceral leishmaniasis • Kala-azar*

1. Introduction

Postpartum pyrexia and sepsis are among the leading causes of preventable maternal morbidity and mortality not only in developing, but also in developed, countries [1-3]. Most postpartum infections take place after hospital discharge, which is usually 24 hours after delivery.

The World Health Organization (WHO), defines puerperal sepsis as "infection of the genital tract occurring at any time between the onset of the rupture of membranes or labor and the 42nd day postpartum in which fever and one or more of the following are present: pelvic pain, abnormal vaginal discharge, abnormal odor of discharge and delay in the rate of reduction of size of the uterus" [2]. The febrile parturient presents a unique diagnostic dilemma and therapeutic challenge to all who are involved in her care, especially the obstetrician.

After delivery, the placental bed, caesarean section and episiotomy wounds, cervical and vaginal lacerations are all highly vulnerable to infection [3]. The risk of postpartum infection is increased by a number of factors: prolonged rupture of membranes more than 18 h before delivery; pre-existing vaginal infection or history of Group B Streptococcal infection; wound haematomas; retained

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pieces of placenta or membranes or intrauterine clot; or retained swabs. Some conditions such as anaemia, an impaired immune system, impaired glucose tolerance or diabetes mellitus, reduce resistance to infection.

However, infection is by far the most common cause of pyrexia in the parturient. Special attention should be paid to women who may be infected with Leishmania chagasi during pregnancy, because little information is available regarding the proportion of infected pregnant women or their geographical distribution [4]. Visceral leishmaniasis, also known as kala-azar, is considered to be a rare in pregnancy occurrence in view of the cases reported in the literature.

The epidemiology of leishmaniasis is extremely diverse, with 12 million people infected worldwide. In the Mediterranean basin, visceral leishmaniasis is caused by Leishmania infantum, known as 'Mediterranean kala-azar' [5]. The diagnosis of Mediterranean kala-azar is complex and requires detection of parasites in bone marrow smears [5,6]. Visceral leishmaniasis is a chronic systemic disease that is characterized by persistent pyrexia, weight loss, asthenia, adynamia and anemia, among other clinical manifestations. The disease is fatal when untreated, with death generally occurring 1 to 2 years after the onset of clinical manifestations.

Visceral leishmaniasis is usually transmitted by phlebotomine sandflies. Nonvector transmission occasionally occurs through blood transfusions, contaminated needles of drug users, organ transplants, or laboratory infection [5]. Only a few cases of congenital transmission have been reported. The etiological agent of this zoonosis is the protozoan Leishmania chagasi, genus Leishmania, family Trypanosomatidae. Its evolutive cycle is characterized by two forms: the amastigote form (without flagellae), an obligatory intracellular stage in vertebrates; and the promastigote form (flagellated) found in the digestive tube of the insect vector and in artificial culture media [5]. In the Mediterranean, where the incidence is estimated to be at least 1000 cases per year, the disease affects patients of all ages, but children and the immunosupressed are more frequently involved. In our country, Republic of Serbia, leishmaniasis is very rare disease presented in few studies in the literature. For this reason, including leishmaniasis in differential diagnosis of postpartal pyrexia and sepsis is of great importance, considering the very severe consequences.

Normal pregnancy is accompanied by changes in immune response, mainly a decrease in cellular immunity and a proportional increase in humoral immunity [7,8]. These physiological events result in an increase in the risk for infections sustained by some parasitic agents whose immunity is based on a T-helper 1 predominant response [7]. However, on the basis of this immunological evidence, the risk of visceral leishmaniasis during pregnancy may be higher. During pregnancy, the disease may have negative consequences for the fetus and is life-threatening for the mother in the postpartum period.

2. Case report

G.S., a thirty-year-old woman, (gravida 3, para 1), was referred to our tertiary care hospital 31 days after a vaginal delivery as a transfer from the Clinic for Infectious Diseases; her symptoms were weakness, fatigue, fever, and diarrhea of fifteen days' duration. Before admission to our our tertiary care hospital, she had been hospitalized in the Clinic for Infectious Diseases for a period of 7 days because of similar symptoms, predominantly a high fever (max. 40.7°C).

Her vaginal delivery went quite well with an episiotomy; she gave birth to a healthy child, and until the day of admission to our clinic, she was visited twice by her gynecologist. During the second visit, cephalexin at 500 mg 4x1 in combination with acetaminophen were prescribed. On admission to our clinic, her temperature was 37.6°C, blood pressure 110/70 mmHg, pulse rate 80 per min, and respiration rate, 16 per min. Physical examination revealed a palpable spleen up to 4 cm below the left subcostal margin. Neither lymphadenopathy or hepatomegaly was evident.

A complete blood count showed anemia (red cell 2,27/ml, hemoglobin 62 g/L) and thrombocytopenia (platelet count 69,000/ml): the hematocrit was 19,5%, the white cell count 3,1/ml (lymphocytes 39,6%, monocytes 6,7%, and granulocits 53,7%). Her C-reactive protein was 41,6 mg/L, and erythrocyte sedimentation rate was 83 mm in first hour. Biochemical tests, liver test, and urine analysis were within normal limits.

An abdominal ultrasound revealed an enlarged uterine cavity with some contents inside it. We took a swab of the uterus cavity and sent it for microbiological examination; we then did a curettage of the uterine cavity, as we suspected a residual piece of the placenta. Both the swab and material from curettage were negative. We prescribed vancomycin hydrochloride 1g x 2, meropenem 1g x 3, and 2 units of fresh frozen plasma because of extreme anemia and thrombocytopenia.

As the fever and diarrhea persisted, we decided to draw blood for a blood culture and a sample for coprocultures. The hemoculture was negative, but the coproculture was positive for the fungus Candida spp.; therefore, we continued with the above-referenced antibiotic therapy but with the addition of fuconazole sol. a 100 ml. After two days, fever still persisted. We decided to do a hysteroscopy with a multiple biopsy. Histopathological

findings showed that the biopsy specimens had no trace of residue or an inflammatory tissue reaction.

Diagnostic attempts continued; her chest X-ray and an electrocardiogram were normal. An abdominal ultrasound confirmed persistent splenomegaly. We decided to do pelvic computerized tomography, which showed a moderately enlarged uterus, inadequate involution relative to the time elapsed since birth, a small amount of hemorrhagic contents in the cavity, free fluid in the Douglas recesus as a result of acute pelvic inflammation.

After this finding and the persistence of fever, expert advice decided that hysterectomy was necessary because it was thought that the uterus was the focus of infection. The operation went well and histopathological examination of the uterus did not show any specific findings. Two days after surgery, the fever was significantly reduced and subfebril temperatures appeared up to 37.6°C, that persisted until she was relocated to the Clinic for Infectious Diseases on the sixth postoperative day.

A biopsy of sternum was done.; microscopic analyses showed polymorphic forms of Leishmania chagasi, confirming the diagnosis of Visceral leishmaniasis.

Emergency Call (EC) data were collected from the database of the EC Service of Florence (118 Firenze Soccorso). The total number of ECs during the study period (summer 2005: 1st June-31st August) was 13,354. The EC Snoon (12:30:01-18:30:00); 4 - evening (18:30:01-00:30:00 next day). This was carried out for the total number of ECs and for each single type of disease (Figure 1).

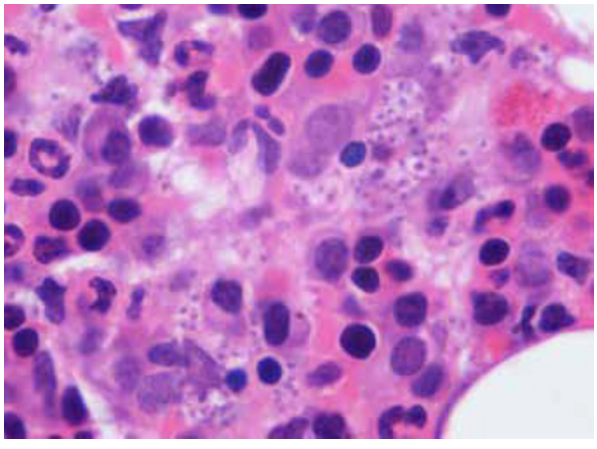

Figure 1.

3. Discussion

Postapartum infection is one of the main causes of maternal mortality worldwide, estimated to account for approximately 15% of all maternal postpartum deaths [2,3]. Postpartum infections are also an important cause of maternal morbidity, although accurate figures are difficult to find because of the variety of definitions used and the difficulty of obtaining data from the population at large, as many postpartum infections occur after discharge from hospital [2].

The principles of management in cases of postpartum infection include assessment of risk factors, a detailed history, detailed examination, and appropriate laboratory and radiologic tests. Treatment with a combination of high-dose broad-spectrum intravenous antibiotics, such as co-amoxiclav or cefuroxime and metronidazole, should be started immediately without waiting for microbiology results [3]. This is because septicaemia can have a very rapid and fulminating course, and adequate early intravenous antibiotic treatment may be life-saving.

Initial investigations should be carried out as soon as possible after admission. Observations of temperature, pulse, blood pressure, respiratory rate, quality and amount of lochia, pain score, fluid input and output, and level of consciousness should be made at regular intervals as dictated by the severity of the patient's condition.

The initial blood and microbiological investigations that should be performed in a woman presenting with postpartum infection include a vaginal swab, urine microscopy and culture, wound swab, rectal swab or other swabs as indicated, blood cultures (aerobic and anaerobic), sputum culture if there is a productive cough, full blood count, C-reactive protein, blood gases, lactate and coagulation screen if patient is clinically unwell, urea and electrolytes, liver function tests, and serum amylase D-dimer. Even if microbiological tests are negative, swabs and blood cultures should be repeated at intervals if the patient remains unwell. An ultrasound of abdomen and pelvis is indicated to assess uterine size and involution and whether any products of conception have been retained. Advice about possible causes and appropriate further investigations by physicians, microbiologists, specialists in infectious diseases or other specialists may assist diagnosis.

Additional investigations might include blood films, antinuclear antibodies and rheumatoid factor, as well as tests for infections such as hepatitis, HIV, tuberculosis, cytomegalovirus, glandular fever and Q-fever, abdominal X-rays, or ECG. A Doppler examination of leg and pelvic veins can show for evidence of venous thromboembolism; a CT of the abdomen may detect intraabdominal or renal abscesses; and transoesophageal echocardiography can detect bacterial vegetations on the heart valves. Visceral Leishmaniasis is included in the differential diagnosis of puerperal infection, especially when splenomegaly is present [4-9]. Visceral leishmaniasis is also known as kala-azar, black fever, and Dumdum fever is a endemic parasitic disease with

variable periods of incubation.

Immunocompromised patients and children frequently fall ill. During pregnancy, there is a change in the immune system that manifests as growth of humoral immunity and decline of cellular immunity [8]. Interestingly, it has recently been shown that pregnancy alters the equilibrium of cytokines towards the Th2 and away from the Th1 pattern during the antiparasite response in pregnant mice (T cell-mediated immune-response patterns, Th1 secreting IL-2, INF-g, and TNF-b, and Th2 secreting IL-4, IL-5, IL-6, IL-9, IL-10, and IL-13, identified among mouse CD4 Th clones) [7,8,10]. This shift in cytokine pattern provides an explanation for the increased susceptibility to Leishmania infection in pregnant mice, and possibly in pregnant women, as was the case with our patient [7,9]. The infection probably took place several months before delivery or much earlier, other such cases are described in the literature, and our patient was either asymptomatic during pregnancy or had a subclinical form of the disease [11,12]. The subclinical form of kala-azar is very common, according to WHO data, and its relation to the clinical form is 5:1 [7].

Many clinical entities can be confused with visceral leishmaniasis, among them a prolonged enterobacterial infection, the clinical manifestations of which overlap perfectly with the signs and symptoms of visceral leishmaniasis malaria, brucellosis, typhoid fever, acute Chagas disease, hepatosplenic schistosomiasis, lymphoma, multiple myeloma, sickle cell anemia, and leukemias [11]. In such cases, serological tests and bone marrow aspiration prove to be valuable tools for the diagnosis of the disease [5,7,12].

4. Conclusion

Postpartum pyrexia is a significant finding that requires a full history and examination, close observation, and prompt treatment. Most cases result from genital tract sepsis, but some are due to very rare disease such as visceral leishmaniasis. The incubation period of Visceral leishmaniasis is 3 to 8 months; our patient must have contracted the parasite during gestation. Thus, we report this case first, to underline the importance of bone marrow biopsy in the diagnosis of visceral leishmaniasis; second, to emphasize the possibility of presentation of the disease during the puerperium; and third, to draw attention to the possibility of infection with this rare disease in our area.

A multidisciplinary approach to every single patient, that includes colleagues in other specialties, particularly internal medicine, infectious disease, microbiology, haematology, anaesthesia and critical care, is of extreme importance for the treatment of patients with Visceral leishmaniasis during pregnancy, labor, and the postpartum period.

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