

Brucellosis in adolescent pregnancy – case report and review of literature

Brucelloza w ciąży – przypadek kliniczny i przegląd literatury

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Abstract

Brucellosis is a zoonotic disease that can be encountered during pregnancy, especially in endemic areas such as Latin America, Africa, Asia, Mediterranean countries and eastern region of Turkey.

We present a case of a 19-year-old pregnant woman of 19-20 weeks gestation diagnosed with brucellosis. Main presentation at admission were hematuria and nausea. Advanced investigations revealed blood culture positive for brucella. Abortion occurred in the course of medical therapy.

Key words: **Brucellosis / pregnancy / abortion /**

Streszczenie

Brucelloza jest chorobą odzwierzęcą, która może wystąpić w ciąży szczególnie w rejonach endemicznych, takich jak: Ameryka Łacińska, Afryka, Azja, kraje śródziemnomorskie i zachodnie regiony Turcji.

Prezentujemy przypadek 19-letniej ciężarnej w 19-20 tygodniu, u której rozpoznano brucellozę. Głównymi objawami przy przyjęciu do szpitala były krwimocz i nudności. Szczegółowe badania diagnostyczne wykazały pałeczki brucelli w posiewie krwi. W przebiegu leczenia wystąpiło poronienie samoistne.

Słowa kluczowe: **brucelloza / ciąża / poronienie /**

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Introduction

Brucellosis is a zoonotic disease that can be encountered during pregnancy, especially in endemic areas such as Latin America, Africa, Asia and Mediterranean countries [1]. It is one of the most common bacterial zoonoses in the world, with 500.000 new cases reported annually and incidence in some countries of more than 10/100.000 [2]. Several endemic areas (France, Israel and Latin America) achieved control of the disease in the past [2]. Yet the disease remains to be endemic in many developing countries.

Brucella is a gram-negative coccobacile, non-motile, intracellular aerobic bacterium. It has four types: Brucella Melitensis, Canis, Suis and Abortus [3]. Brucella melitensis seems to be the most virulent to human body. Brucella can be found in both domestic and wild animals and is transmitted to humans through direct contact with infected animals, consumption of their infected and unpasteurized dairy products or inhalation of aerosols. Portals of entry of the organism are the conjunctiva, respiratory mucosa and damaged skin [4].

Laboratory technicians and veterinarians in the endemic areas are at greatest risk of transmission. Interestingly enough, physicians who treat patients with brucellosis do not experience increased risk because person-to-person transmission is uncommon. Acquisition of the infection from human sources may occur in the following ways: vertical transmission with placental circulation, breast feeding, blood transfusion, bone marrow transplantation and sexual contact.

Brucella species cause abortion in animals such as sheep, cattle, goats or dogs. In literature there have been numerous reports about complications in pregnancy of humans, such as abortion, intrauterine fetal death, preterm birth. There is no clear evidence about congenital anomalies [2, 3, 4].

The disease should be treated as soon as it is diagnosed but there are no randomized trials for brucellosis treatment in pregnancy. Nevertheless, antimicrobial therapy has been proven to have protective effect against abortion and to prevent the transmission of the disease to the fetus. Rifampicine and trimethoprim/sulfamethoxazole combination is the most commonly used regimen. Treatment for six weeks or more is offered as it has an advantage over shorter treatment regimens [4].

We present the clinical course of an adolescent pregnant patient with brucellosis whose pregnancy ended with abortion.

Case

A 19 year-old pregnant woman at 19 weeks gestation (gravida 1, para 0) was referred to our clinic with hematuria and nausea. The patient lives in Izmir, a large metropolis in the Western region of Turkey. Her past medical history was not significant. Physical examination was unremarkable. Blood and urine tests were performed. 6-7 erythrocyte and as many calcium oxalate crystals were seen in the urine examination and liver enzymes were mildly elevated. Hematocrit: 28% (36%-46%), Hemoglobin: 9.1g/dL (12-16g/dL) and C reactive protein (CRP) were 5.29mg/dl (<0.5). Tests of serum markers obtained for hepatitis A, B and C viruses were negative. Urinary ultrasonography was performed and bilateral grade 1 hydronephrosis was found. Hyperemesis was severe and she was hospitalized. Thyroid function test was performed and found to be normal. On the third day of

hospitalization she had a temperature of 38,6 °C. Blood and urine samples were taken for culture. Urine and blood culture were negative. She had no fever then and was discharged.

A few days later she returned to the same clinic with nausea, fever and malaise. Hemogram was abnormal, Hematocrit: 21%, Hemoglobin: 5.29g/dl and C reactive protein was 3.75mg/dl. Hepatic enzymes were still mildly elevated and her temperature was 38,8°C. She was hospitalized. Blood and urine samples were taken for culture. Blood culture was positive for Brucella melitensis. Blood samples were taken for brucella agglutination testing and treatment with trimethoprim/sulfamethoxazole (400mg b.i.d., per oral), rifampicine (300mg b.i.d, per oral) and ceftriaxone (1 g, intravenously) were started. On the second day of the treatment membrane rupture occurred and vaginal examination revealed 2cm cervical dilatation. Patient aborted within 10 hours. The umbilical cord culture for brucella was negative.

Discussion

Brucellosis is a systemic disease with acute and chronic forms and any organ or system can be affected. It is a serious public health issue in many developing countries. Most patients complain about fever, sweat, malaise, nausea, headache, anorexia, arthralgia and the disease can be very debilitating.

Our patient presented with nausea, malaise and fever. At first we did not suspect brucellosis and the diagnose was made unexpectedly with the detection of brucella in blood culture.

The diagnose of acute brucellosis is based on detailed medical history, epidemiological information, clinical features, serum agglutinin titer of >1/160 or positive blood culture result. Blood culture is the gold standard in the diagnosis and positive results range from 15% to 80% of cases [2]. Bone marrow culture has higher sensitivity than blood culture [5].

In the absence of bacterial isolation serology is another way of diagnosing the disease. Tube agglutination is widely used as a serological test. A single titer of 1/160 or a fourfold rise in the titer is accepted as significant for the tube agglutination test. In our case contact with an infected animal or consumption of infected product was suspected. Serum agglutination titer was 1/320 and blood culture was positive.

Brucellosis effects all age groups. The main source of brucella are infected animals and their products. In most countries the incidence is unknown. A multicenter study in Turkey showed that seropositivity is 1,8% in healthy population and 6% in high-risk groups such as veterinarians or butchers. Another study in Saudi Arabia noted the incidence of brucellosis in pregnant women. In rural areas of Saudi Arabia, pregnant women without any symptoms were screened and 3.5% showed positive titer [2]. In Egypt between 2005-2007, the incidence of brucellosis among pregnant women was found to be 12.2% [3]. However, in many developing countries the incidence of brucellosis in pregnancy is unknown [2].

Effects of brucellosis in pregnant women are not clear. In case of infected pregnant animals such as cattle, dogs, sheep, goats, the organism frequently transmits the fetus by transplacental way what results in contagious abortion. Brucella organisms reproduce in placental trophoblasts. Erythritol is the key element produced by animal placenta and brucella utilize erythritol which appears to be the growth factor for brucella.

In human placenta brucella species were isolated in many studies but the absence of erythritol and the anti-brucella activity of the amniotic fluid have been thought to be the protective mechanism. However, there are several case report and studies about abortion and preterm delivery associated with active brucellosis. Infection with brucella in pregnant women leads to abortion, premature delivery and in utero fetal death but there is no association between brucellosis and congenital anomalies. In PubMed, many cases reported effects of brucellosis in pregnant women. (Table I).

Several case reports have shown an increased abortion rate. A study by Khan et al [5] demonstrated a significantly high incidence (43%) of first and second trimester abortion among pregnant women with active brucellosis. Intrauterine fetal death rate was 2% in the third trimester. No association has been found between spontaneous abortion and the antibody titer. Another study by Elshamy et al [3] pointed that the incidence of abortion was 27.27% among pregnant women with active brucellosis and in utero fetal death and preterm labor incidence were 12.72% and 10.90% respectively. There was a significant difference between the patients with a titer of more than 1/160 and less than 1/160 in terms of abortion rate. In the article, it was concluded that the frequency of fetal loss among patients with brucellosis is very high. However Kurdoglu et al [1] showed that there is no correlation between antibody titer and pregnancy outcomes. In our case the agglutination titer was 1/320 and spontaneous abortion occurred in the second trimester, 2 days after hospitalization.

There is no consensus on treatment regimens for brucellosis during pregnancy but brucella infection should be treated both for maternal and fetal well being [6, 7, 8].

The disease should be treated as soon as it is diagnosed but there are no randomized trials for brucellosis treatment in pregnancy. Antimicrobial therapy has been shown to have protective effect against abortion and to prevent the transmission of the disease to the fetus. The best choice drugs for treatment have to be effective and have minimal adverse effects on the fetus. Rifampicine and trimethoprim/sulfamethoxazole combination is the most commonly used regimen [9, 10].

Monotherapy regimen using either rifampicine or trimethoprim/sulfamethoxazole is inadequate, with high relapse rates. Potential adverse effects of antimicrobials on fetus needs monotherapy for brucellosis in pregnancy. In literature there have been successfully treated cases with monotherapy [11]. Treatment for six weeks or more is offered and has an advantage over shorter treatment regimens.

In conclusion, brucellosis is a major public health problem in endemic developing countries. Infection with brucella in pregnant women may lead to abortion, premature delivery and in utero fetal death. Brucella should always be taken into account in the event of undiagnosed high fever.

Table 1. Clinical course of pregnant women infected with brucellosis reported in *PubMed*.

Author	Year	Number of patients with brucellosis	Clinical course
Poole et al. [15]	1972	1	Abortion
Saram et al [17]	1974	6	Abortion
Porreco et al. [10]	1974	1	Abortion
Schreyer et al. [11]	1980	1	Intrauterine death
Lulu et al. [12]	1988	35	11 abortions
Sharif et al. [16]	1990	42	6 abortions
Seoud et al. [18]	1991	6	1 voluntary termination 1 abortion at 12 weeks
Figueroa Damian et al. [19]	1995	4	4 continued with no adverse effects
Malone et al. [13]	1997	1	Abortion at 25 weeks
Makhseed et al. [14]	1998	25	Acute or chronic Brucella infection was found in 8% of preterm, 10% of intrauterine fetal death, and 7% of abortion cases
Hacmon et al. [8]	1998	7	1 second trimester abortion 2 preterm delivery and 4 term delivery
Khan et al. [5]	2002	92	The incidence of spontaneous abortion 43%, and the incidence of intrauterine fetal death was 2%
Ozbay et al. [7]	2006	1	Twin pregnancy, no adverse effects
Elshamy M et al [3]	2008	55	15 Abortion, 7 intrauterine death 6 Preterm labour
Karcaaltincaba D et al [2]	2009	2	One of them delivered normally and the other patient had an abortion.
Kurdoglu M et al. [1]	2010	29	3 spontaneous abortion in first trimester 4 spontaneous abortion in second trimester 1 Intrauterine fetal death, 2 Preterm delivery

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