



Case Report

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Case Report – Endometrial TB

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Introduction

Tuberculosis remains one of the main causes of infection-related deaths worldwide, especially in developing countries. For the first time in two decades, the global incidence rate rose again between 2020 and 2022 by 3.9%, causing 1.3 million deaths in 2022 [1]. Miliary tuberculosis is a potentially fatal form caused by disseminated lymphohaematogenous spread of *Mycobacterium tuberculosis* bacilli. This form is more common in people with a compromised immune system, such as HIV-positive people. Pregnant and postpartum women also have an increased risk of developing miliary tuberculosis [2,3]. This risk is particularly high for women who have undergone in vitro fertilization (IVF) due to genital tuberculosis and infertility [4,5]. So far, there have only been a few reports of this disease following IVF treatment, with most cases coming from China, where tuberculosis is more common [6]. Here we present the case of a 30-year-old Kosovar woman who underwent a medically induced abortion after IVF. Subsequently, she developed miliary tuberculosis, which is rare in Austria.

Case

A 30-year-old woman presented to our clinic in October 2023 with vaginal bleeding at 18 weeks' gestation in her second pregnancy after IVF procedure in which one embryo was transferred. The first pregnancy was a miscarriage in the sixth week of pregnancy. The patient had already undergone first trimester screening in the 13th week of gestation, which showed a pre-eclampsia risk of 1:39 before the 37th week. She was advised to take acetylsalicylic acid 150 mg until the 36th week of pregnancy. In the 18th week of gestation, the patient presented with light vaginal bleeding. Ultrasound was

performed and showed anhydramnios and suspected polycystic kidney disease. A test to detect premature rupture of membranes was negative. Laboratory results showed high infection parameters, so the patient was treated with amoxicillin for a suspected infection. Due to the high risk of intrauterine and extrauterine death due to pulmonary hypoplasia, after careful consideration the patient and her partner decided to terminate the pregnancy. The patient underwent a medical abortion procedure using mifepristone and misoprostol, followed by a curettage. She was discharged the next day without any complications. Histologic examination of the curettage specimen showed exaggerated placental site and granulomatous endometritis with multinucleated giant cells of the Langhans type and extensive necrosis. Ziehl-Nelsen stain was negative for acid-fast bacilli; however, a mycobacterium-specific polymerase chain reaction was positive for *Mycobacterium tuberculosis* complex (IS6110-sequence). Histologic examination of the placenta revealed chorangiomas, subchorionic and necrotizing amnionitis. Fetal autopsy and histology examination revealed a eutrophic male fetus with oligo-/anhydramnios sequence (contractures, lung hypoplasia) and neutrophil-rich stomach contents as sign of amnion infection syndrome. Granulomatous inflammation was not found in the placenta or the fetus. Ziehl-Neelsen stain and PCR for *Mycobacterium* was not performed on fetal or placental tissue. After consultation with the pathologist, the following progression was suspected: The urogenital tuberculosis caused endometrial necrosis, leading to premature rupture of the membranes with subsequent anhydramnios, leading to pulmonary hypoplasia and amnion infection syndrome.

Clinically, one month after the abortion, the patient had a daily fever, nocturnal cough without sputum and pain in her back. For further diagnosis, a CT scan of the chest and abdomen was performed and showed multiple disseminated nodular lesions <3 mm in both lungs as well as calcifications of the pleura and spleen, indicating miliary tuberculosis. The patient's menstrual blood tested positive for tuberculosis by PCR. Mycobacterium tuberculosis was also detected in the urine and menstrual blood culture. Anti-TB medication with isoniazid, rifampicin, pyrazinamide and ethambutol was started for treatment. One week later, the patient presented again due to severe headaches and

photophobia. A CT scan of the head showed no abnormalities. The patient was admitted to the emergency ward and a lumbar puncture was performed, which revealed a high cell count, high protein and glucose, suggesting tuberculosis meningitis. However, the liquor's PCR test was negative. The anti-TB therapy was supplemented with adjuvant corticosteroid therapy. On the same day, the patient was admitted to a specialized tuberculosis centre for further treatment. An MRI of the brain revealed signs of tuberculosis meningitis. After one month of hospitalisation, the patient was discharged with anti-TB medication (Figures 1a & 1b).

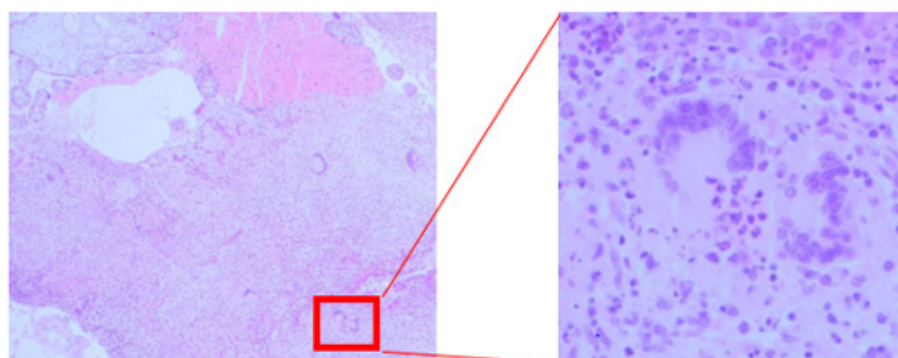


Figure 1a: curettage specimen with granulomatous endometritis (HE, 40x)

Figure 1b: multinucleated giant cell of the Langhans type (HE, 200x).

Discussion

Active tuberculosis in pregnancy is highly related with increased maternal and fetal morbidity and mortality. Due to delayed diagnosis and treatment in pregnancy, tuberculosis is associated with miscarriages, induced abortions, premature births and increased maternal morbidity, including respiratory disease [7]. Reactivation of latent tuberculosis is probably one of the main causes of miliary tuberculosis in pregnancy. During pregnancy hormonal changes such as increased levels of estrogen, progesterone, and glucocorticoids modulate the immune system, which leads to a decrease in the activity of macrophages, NK cells, and T helper cells [8]. Studies have shown, that there is a higher incidence of military tuberculosis in pregnant women who have undergone in vitro fertilization and embryo transfer (IVF-ET) [9]. The use of glucocorticoids, progesterone and estrogen during IVF is associated with suppression of the immune system, thus leading to reactivation of TB and progression to disseminated infection [10,11]. This case report demonstrates the fulminant progression of miliary tuberculosis after an IVF-ET pregnancy and following medically induced termination due to endometrial tuberculosis and subsequent anhydramnios. Retrospective anamnesis revealed that the patient is originally from the Republic of Kosovo but has been living in Austria for the past three years. There is no known history of tuberculosis in her family or contacts. In retrospect, it is likely that chronic endometrial tuberculosis caused the first miscarriage in her medical history and subsequent infertility due

to genital tuberculosis led to IVF treatment. Our case supports the recommendation that patients originating from countries with a high incidence of tuberculosis should be screened before undergoing IVF treatment due to infertility.

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