

Placental Mucormycosis of an IVF-Induced Pregnancy in a Diabetic Patient

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Mucormycosis is a lethal fungal infection, rarely seen in immunocompetent hosts. It has been commonly known to cause aggressive fungal infection in pulmonary and paranasal sinuses. Placental fungal infection caused by Zygomycetes has rarely been described.

We present a case of a thirty-year-old pregnant woman with in-vitro fertilization (IVF) twin pregnancy aborted at 16 weeks of gestation due to incidental finding of placental mucormycosis. The patient was treated by evacuation and antifungal treatment. She had uneventful recovery.

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Mucormycosis is an uncommon, rapidly progressive fungal infection characterized by large areas of tissue necrosis and the presence of angio-invasion. It is considered as one of the infections occurring mainly in immunocompromised individuals and caused by a number of molds classified in the order Mucorales of the class Zygomycetes¹⁻⁴.

Involvement of the lungs and paranasal sinuses are considered the most common clinical form of the infection, followed by rhino-cerebral region, cutaneous, and gastrointestinal infections. The source of such infections is decaying materials, soil and plants¹⁻³. Mucormycosis is rarely reported in the female genital tract. However, placental infection has been reported occasionally with a good prognosis for the mothers only, and poor outcomes for the fetuses⁵⁻⁸.

The aim of this report is to present a case of placental mucormycosis infection after in-vitro fertilization (IVF) with twin pregnancy in a diabetic mother.

THE CASE

A thirty-year-old woman, G2P1, known case of diabetes mellitus (DM) on insulin treatment and hypothyroidism on thyroxin therapy presented at 16 weeks of gestation with twin pregnancy after IVF performed at a private clinic. The patient presented with four days per vaginal (PV) bleeding. The patient was afebrile and had no history of drug abuse.

Laboratory data revealed hemoglobin of 10.2g/l, white cell count of $9.12 \times 10^9/L$ and platelet count of $308 \times 10^9/L$. Her blood group was O-positive. G6PD and sickling tests were negative.

The electrolytes, renal and liver function tests were within normal limits. High vaginal swab culture at 12 weeks was negative. Serology for Hepatitis B and C, HIV and TORCH screen were negative.

Clinical examination revealed a bulky uterus of 14 weeks gestation, the cervix was open and the placenta was seen at cervical os with mild bleeding. She underwent evacuation of retained products of conception (ERPCS) under general anesthesia. The placenta was sent for histopathology examination. The specimen was a twin placenta composed of two separate discs. The placental disc (A) measured 13x7x2cm and weighed 245g and had a central umbilical cord measuring 17cm long. The placental disc (B) measured 8x7x2cm and weighed 123g and had a central umbilical cord measuring 10cm long. No gross abnormality was seen in disc (A). However, disc (B) was soft and necrotic. The membranes and umbilical cord of disc (B) were yellowish-white and lusterless.

Microscopically, placental disc (A) showed second-trimester villous maturation and the attached umbilical cord and membranes were within normal limits. The disc (B) showed marked acute villitis with large areas of necrosis and micro abscess formation. The placenta, membranes, and cord showed many broad, non-septate branching fungal hyphae and spores were morphologically compatible with the mucormycosis (zygomycosis), confirmed by Gomori methenamine silver stain (GMS) and periodic acid Schiff (PAS) special stains, see figures 1-4. The organisms were high in the placenta, moderate in the membranes and the low in the umbilical cord. Vascular invasion was noted.

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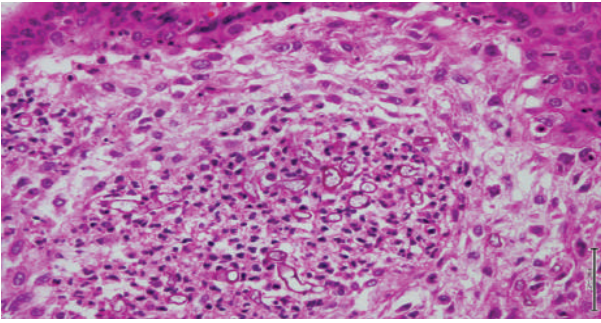


Figure 1: Placental Villus Showing Acute Villitis with Hyphae and Spores of Broad Non-Septate Mucormycosis (H&E 40X)

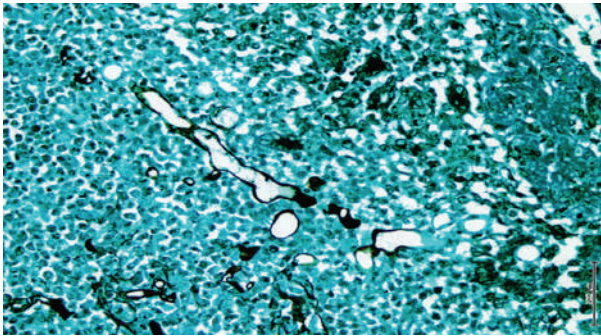


Figure 2: Placental Villus Showing Acute Villitis with Hyphae and Spores of Broad Non-Septate Mucormycosis. Silver Stain Highlighting the Organisms (GMS stain 40X)

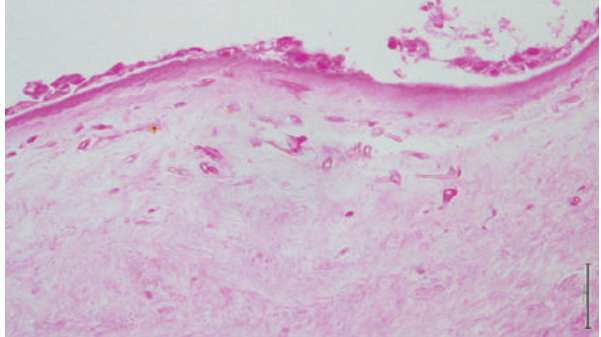


Figure 3: Placental Membranes Showing Necrosis with Hyphae and Spores of Broad Non-Septate Mucormycosis (H&E 20X)

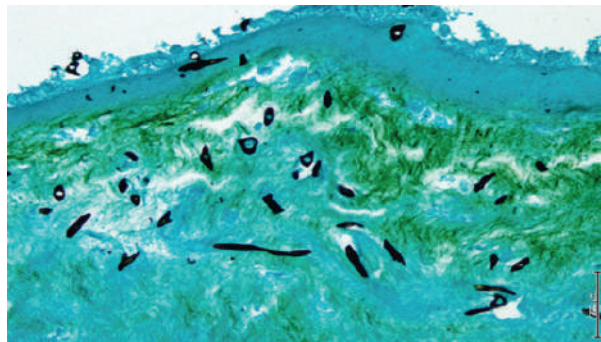


Figure 4: Placental Membranes Showing Hyphae and Spores of Broad Non-Septate Mucormycosis. Silver Stain Highlighting the Organisms (GMS stain 20X)

The specimen in the paraffin block was tested for molecular identification and confirmation; however, the result was unrewarding (see details in discussion).

The patient was discharged after three days on oral Metronidazole and analgesics. However, the patient presented one week later with PV bleeding of dark red tissue and severe abdominal pain; she was found to have retained products of conception (RPOC), which was evacuated and the specimen was sent to the lab for histology examination. Again, the examined tissue revealed RPOC with focal mucormycosis. The patient was discharged in a stable condition and no antifungal therapy was prescribed. The patient did not receive antifungal therapy due to the complete evacuation of the infected placental tissue. The patient was followed up closely in the outpatient clinic. She continued to be in a good health condition; however, she was not able to conceive.

DISCUSSION

Mucormycosis has been encountered as one of the most common invasive fungal infections in immunosuppression by prolonged courses of corticosteroids, severe burns and hematological malignancies. Diabetes mellitus has been recognized to be one of the major risk factors due to the impaired phagocytic functions^{1,2,8}.

Mucorales are commonly found in the environment such as soil, plants and decaying materials³⁻⁴. The route of transmission is mainly through air-borne spores or through percutaneous routes¹. Mucorales can be grown on sheep blood agar and Sabouraud dextrose agar (SDA) as fluffy white, grey, brownish colonies⁴. The definitive diagnosis of mucormycosis relies on directly examining and identifying the fungal elements in the biopsy³. Morphologically, they appear as broad, non-septated hyphae with right-angle branching, which typically invade the blood vessels, causing necrosis, thrombosis and ischemia³⁻⁴. In this case, the fungus was identified by studying the aborted placental tissue specimen with H&E, GMS and PAS. However, because there was no clinical suspicion of such an infection, no samples were sent for microbiological studies. Therefore, we lack the confirmation of the diagnosis by culturing the organism from the placental tissue due to the formalin fixation, which inhibits the fungal growth. Nevertheless, the morphological appearances were consistent with Zygomycetes. Furthermore, the paraffin block was tested for molecular identification and confirmation. The polymerase chain reaction result was negative for fungal DNA. However, the negative result might be a result of poor tissue fixation, especially if PBS-buffered formaldehyde was used for fixation as this will result in DNA fragmentation within the tissue due to acidic hydrolysis. It might also be due to low load of fungi in the tissue. Therefore, the diagnosis was made based solely on the characteristic morphology of the fungus on histological examination.

To the best of our knowledge, only a few cases of female genital tract mucormycosis have been reported in the literature. Sobel described a case of vaginal mucormycosis in a non-pregnant woman⁹. Three cases of placental mucormycosis were reported; they could present either as abortion, as in our case, stillbirth or as an incidental finding after normal vaginal delivery⁵⁻⁷.

The source of the infection in our case was most likely the ascending IVF-induced procedure, as the load of the organisms was the most in the placental villi and least in the umbilical cord. This explains why the patient was otherwise normal with no further worsening of the symptoms even after the abortion.

Treatment of mucormycosis is challenging. It requires a combination of radical surgical debridement of the infected tissue and aggressive antifungal therapy. Amphotericin B is the first-line against mucormycosis²⁻⁴.

CONCLUSION

This is a rare case of IVF-induced placental mucormycosis in a diabetic patient leading to abortion. In our opinion, IVF procedures should be performed in a well-established assisted reproductive technology unit to avoid nosocomial infectious hazards due to unhygienic practices. The clinicians and pathologists should be aware of this condition. Thereby, careful placenta examination in aborted patients after IVF procedure is recommended to exclude such type of infection with subsequent complications.

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