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Placental and fetal candidiasis

Presentation of a case of an abortus

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Abstract

The authors present a case of intrauterine fetal infection by candida, in an abortion of four months, associated with an I.U.D. In the placenta and adnexa we observed an acute inflammation consisting of extraplacental membranitis, omphalitis, chorio-amnionitis and choriovasculitis with a marked villitis and intervillitis. In the fetus, involvement of the skin, lungs and pharynx was observed.

This case represents, probably the 15th reported instance of congenital fetal candidiasis, and the first case of a candida hematogenic placental infection acquired from the fetal blood. The fetus undoubtedly acquired its infection by an ascending route, through the contamined amniotic fluid.

Introduction

Candidiasis of the placenta and adnexa is rarely described (1–7, 10, 11, 16–22); it is the result of an ascending infection from the vagina. Congenital fetal involvement, however, was not proven in all these cases, and we were only able to find 15 cases of congenital fetal candidiases in a review of the literature (2, 3, 6, 7, 11, 12, 13, 16, 18–20, 22–24) (summarized in Table 1). Cases with late appearance of lesions are not included in Table 1 because they may be caused by contamination of the fetus in the birth canal, during delivery (14, 15, 18, 20).

In this paper we present an abortus with widespread fetal and placental lesions due to candidiasis. It represents the first reported instance of candidiasis of the placenta (villi and intervillous space) through an hematogenic route from the fetus.

Case report. M.B.S., 29-year-old, IV-para, V-gravida. After successfully using an intra-uterine contraceptive device (I.U.D.) of the 'Lorena's Cross' type for 2 years she became pregnant (last menstrual period, June 6, 1981). She sought medical advice in her third month of gestation (September 1981) because of a whitish vaginal discharge. A vaginal smear revealed many hyphae and spores consistent with candida. She was treated with Gyno-Daktarin. On October 19, she was hospitalized with an open cervix and recently ruptured membranes. On the same day, she expelled the fetus, placenta and I.U.D. About two weeks later, she was submitted to a clinical and laboratory investigation that revealed no abnormalities. Her blood sugar was within normal limits, and she was not taking any immunosuppressive drug. At this time a culture of the vagina was negative for candida.

Pathological report. The fetus was a severely macerated male with a crown–heel length of 18 cm and weight of 110 g. An attached three-vessel cord was present. There was a severe involvement of the fetal skin with extensive, whitish and elevated patches, sometimes coalescent, involving thorax, abdomen, sacral area, buttocks, neck and upper and lower extremities (Fig. 1). There were no other gross abnormalities at autopsy. Histological examination was partially compromised because of autolysis but even so sections from lungs, digestive tract, pharynx, brain and skin were submitted to histopatho-

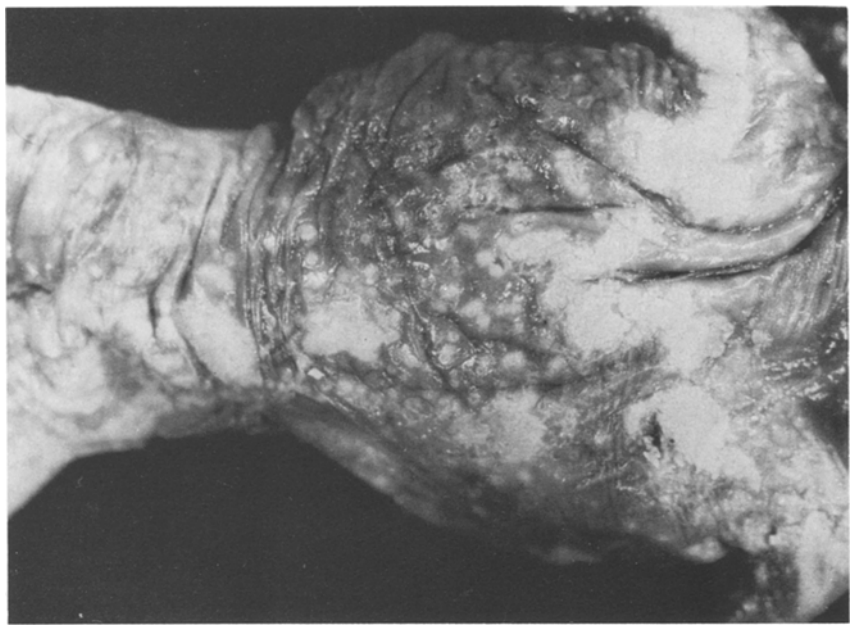

Fig. 1. See the extensive and multiple white lesions in the fetal skin.

logic examination. The sections were stained with hematoxilin-eosin and with the method of periodic-acid Schiff (P.A.S.). Silver impregnation (Grocott's technique) was performed on all sections. Despite autolysis an inflammatory infiltrate of mononuclear cells was seen in the interductal septa of the lungs (Fig. 2, right panel) with hyphae and spores of candida present in the septa and in the lumen and wall of bronchia (Fig. 2, left panel). The pharyngeal mucosa exhibited necrosis and heavy fungal contamination. In the intestines, fungi were seen only in the lumen. The most severe lesions were found in the skin. There were extended areas of necrosis involving the upper dermis and epidermis with

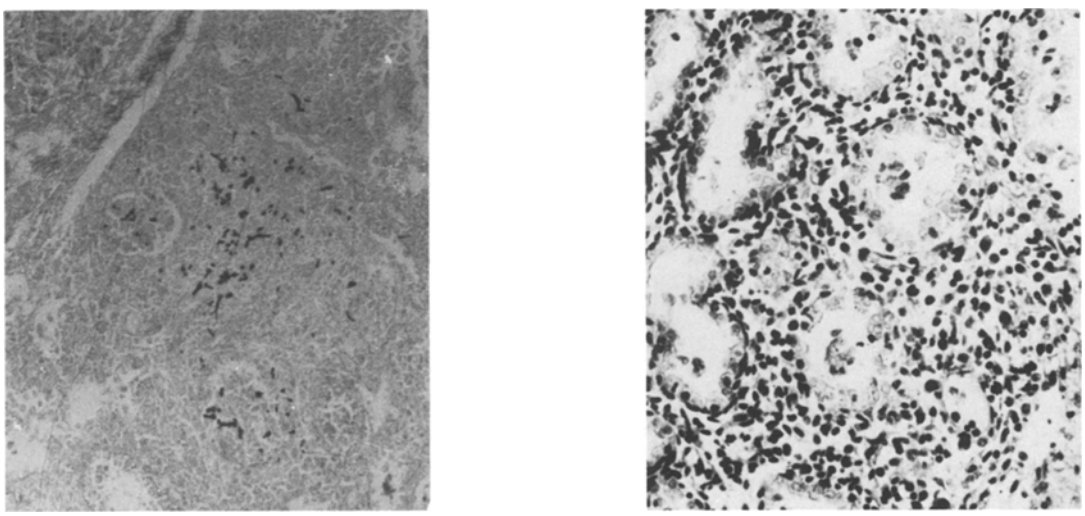

Fig. 2. Lung: *Left panel.* Hyphae and spores in the interductal septa and the wall of bronchia. Grocott's method. ×100. *Right panel.* Alveolar ducts lined by cuboidal cells. See a mononuclear infiltrate in the septa. H.E. ×200.

many fungal hyphae. No fungal contamination was seen in the other organs studied microscopically. The placenta weighed 30 g. The fetal surface showed loss of the normal translucency and many pin-point whitish lesions. The cut surface exhibited a spongy and pale tissue. The extraplacental membranes were friable, edematous and opaque and showed very tiny yellow-white nodules which were also present on the surface of the umbilical cord.

Microscopically, the chorionic plate was markedly thickened and edematous with a heavy infiltration of polymorphonuclear leukocytes. There were many areas of necrosis in the amnion with heavy invasion of fungi. The same aspect was observed in the amnion of the extraplacental membranes and on the surface of the umbilical cord. Fungi and a heavy infiltration of neutrophils were also seen in the vessels of the chorionic plate (Fig. 3) and the umbilical vessels (Fig. 4). In the intervillous space of the placenta there was a heavy inflammatory exudate of neutrophils sometimes forming abscesses (Fig. 5). Frequently, villi showed necrosis and infiltration of neutrophils (Figs. 6 and 7). Less frequently, hyphae and spores were seen in the lumen of villous vessels (Fig. 8). No fungus was seen in the decidua.

Discussion

In the present case there was a cytologically-proved candida vaginitis in the third month of gestation that was treated at that time. One month later the patient aborted an infected fetus and placenta. After the abortion a culture of the vaginal secretion did not reveal candida, showing that the infection was successfully treated. This fact indicates that the infection had occurred with intact membranes. There are also a few cases in the literature of congenital candida infection without premature rupture of the membranes (6, 17, 19–21, 24). In these cases, the fungus penetrated through the extraplacental membranes and infected the amnionic fluid. The contaminated fluid spread the infection to the membranes (placental and extraplacental), to the umbilical cord surface and to the fetal skin. The infection of the lungs, pharynx and the presence of fungi in the digestive tract seen in our case was due to inhaling and swallowing infected amnionic fluid. In seven cases in the literature of fetal candida infections (Table 1), the lesions were restricted to the skin. The majority of cases with visceral lesions corresponded to fetuses of very low weight (2, 3, 11, 16, 18, 22). Probably the low immunological res-

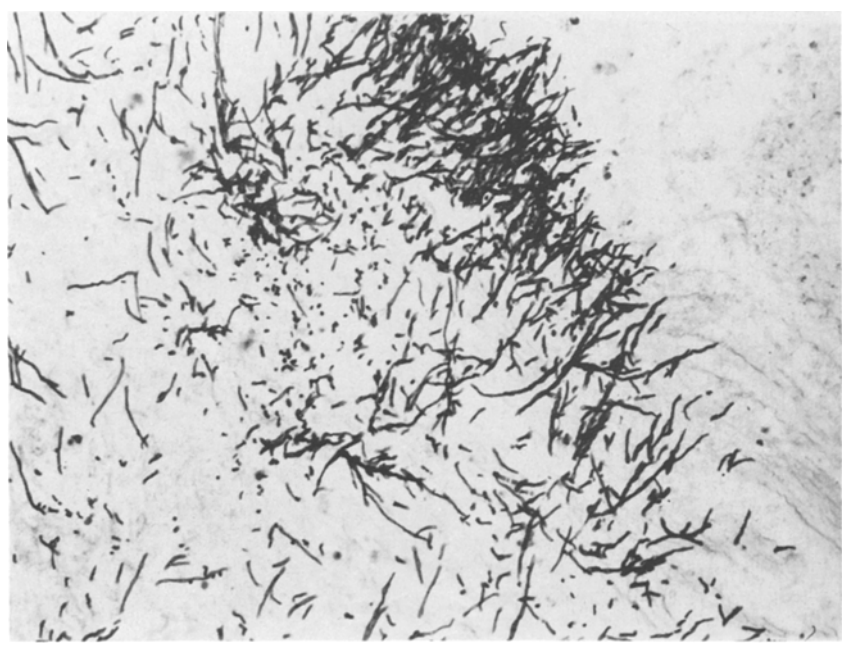

Fig. 3. Placenta (chorionic plate). A heavy invasion of fungi is seen in the wall of a chorionic vessel. Grocott's method. ×200.

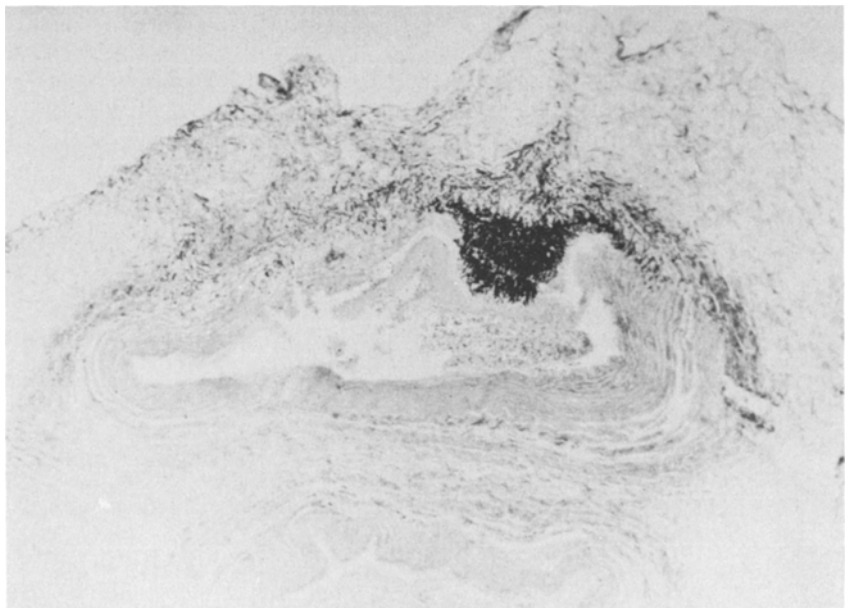

Fig. 4. Umbilical cord. Umbilical vein showing an area of necrosis and heavy invasion of fungi, protruding in the vessel's lumen. Grocott's method. ×40.

ponse of these immature conceptuses might be responsible for the severity of the disease.

In our case, despite maceration, a mononuclear infiltrate was seen in the interalveolar spaces (pneumonitis) and also around the bronchia. It is generally accepted that pulmonary candidiasis causes a bronchopneumonia or bronchitis, as was observed in three cases in the literature (7, 11, 18).

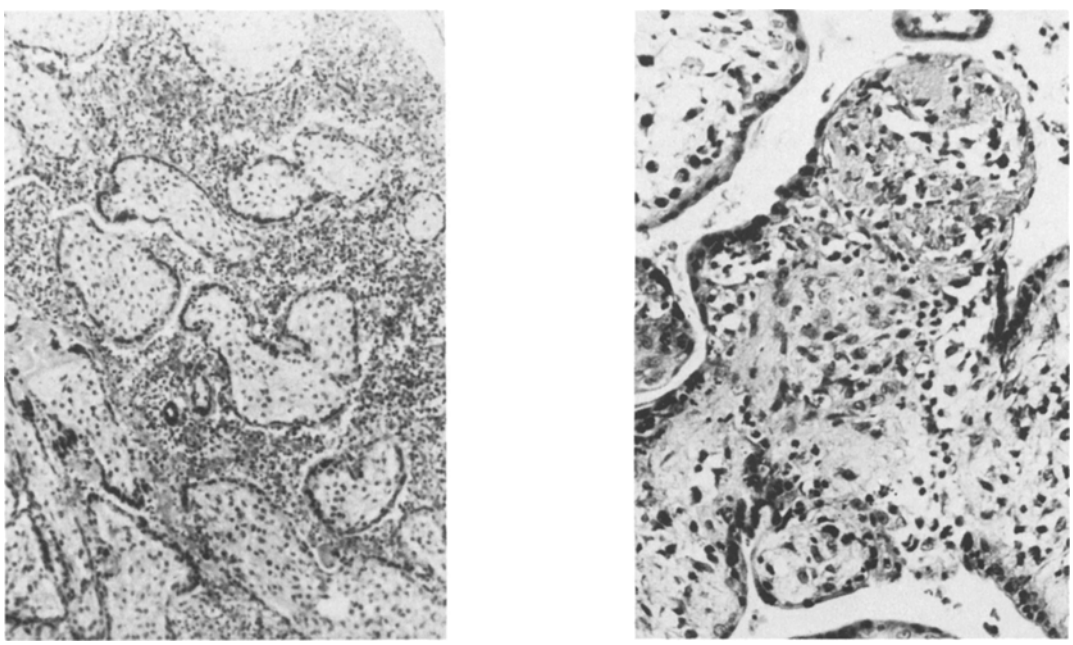

Fig. 5. Placenta: *Left panel.* See an exudate of neutrophils in the intervillous space. H.E. ×100. *Right panel.* Focal necrosis of the trophoblast and chorium and infiltration of neutrophils is observed in one villi. H.E. ×200.

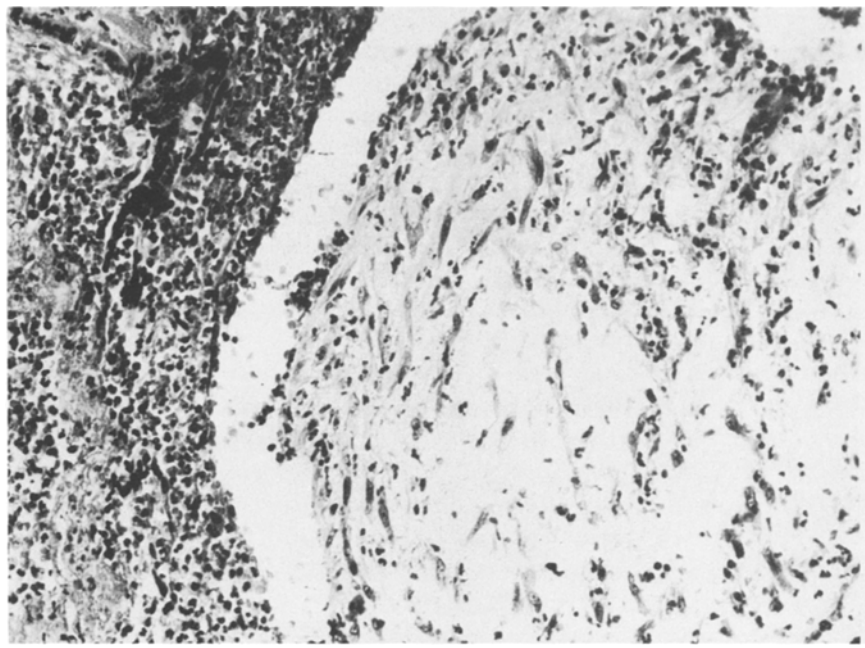

Fig. 6. Placenta. See a villus with total destruction of the trophoblastic epithelium, edema and infiltration of neutrophils. H.E. ×200.

As we found fungi in the lungs, it seems to us improbable that this pneumonitis was caused by another pathogen.

The skin lesions of fetal congenital candidiasis are generally described as a diffuse macular erythematous rash or as disseminated very small papular, vesicular or pustular lesions (7, 12, 13, 19, 20, 23, 24). In the case studied there were very extensive

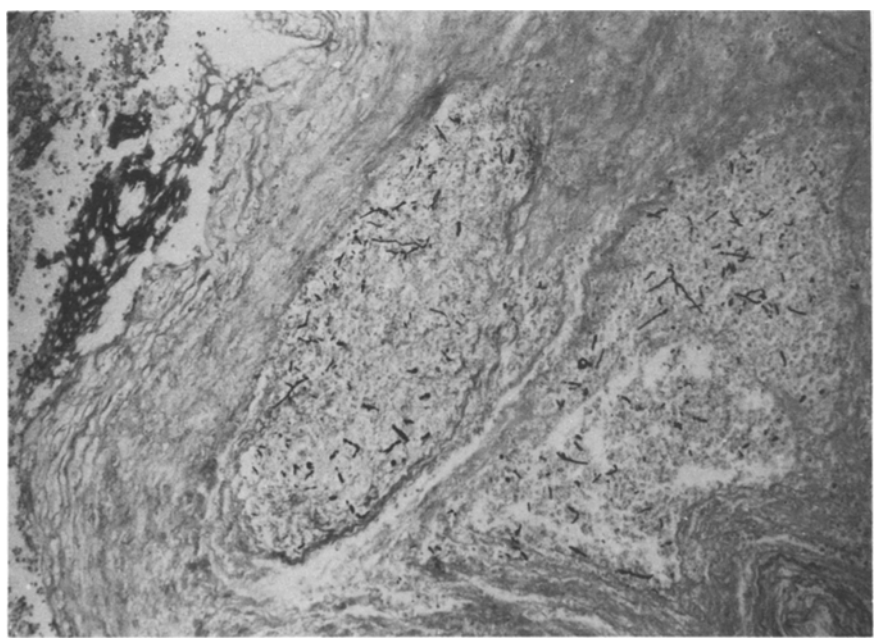

Fig. 7. Placenta. Fungi were seen in the lumens and also in the wall of villous vessels. Grocott's method. ×100.

Table 1. Cases of intrauterine fetal infection by candida.

Authors	IUA (m)	Weight (g)	Death	Involved organs	Placenta and adnexal involvement
1. Sonnenschein *et al.*, 1960	7	2500	–	Skin	–
2. Blank, 1961	9	–	with 3 h	Lungs, stomach and ileum	Umbilical cord and EPM
3. Sonnenschein *et al.*, 1964	7	1700	–	Skin	–
4. John & Cherry, 1964	9	3200	–	Skin	–
5. Dvorak & Gavaller, 1966	8	2700	–	Skin and lungs	Umbilical cord and placental fetal surface
6. Albarracin *et al.*, 1967	6	800	with 63 h	Lungs	Umbilical cord, placental fetal surface and subcorionic IVE
7. Rhatigan, 1968	9	4300	–	Skin	Umbilical cord
8. Aterman, 1968	5	440	abortion	Skin and stomach	Umbilical cord
9. Schweid & Hopkins, 1968[a]	2.5	–	abortion	Lungs	Placental fetal surface
10. Misenheimer *et al.*, 1969 (case 1)[a]	6	1070	with 29 h	Lungs	EPM
11. Ho & Aterman, 1970[a]	4	75	abortion	Lungs, intestines and stomach	EPM
12. Rudolph *et al.*, 1977 (case 1)	9	3200	–	Skin	Umbilical cord and EPM
13. Levin *et al.*, 1978[b]	6	520	abortion	Brain	Placental fetal surface
14. Johnson *et al.*, 1981	6	1080	–	Skin	–
15. Johnson *et al.*, 1981	9	4300	–	Skin	–
16. Bittencourt *et al.*[a] (present case)	4	110	abortion	Skin, lungs and pharynx	Umbilical cord, EPM, placental fetal surface, villi and IVE

Legend: IUA = intrauterine age; EPM = extraplacental membranes; IVE = intervillous space; M = months.
[a] Pregnancy with I.U.D.
[b] Twin pregnancy.

plaques, sometimes confluent, with necrosis of the epidermis and upper dermis and with a heavy invasion of hyphae and spores. Probably, the intensity of these lesions was due to the immature immune response of this conceptus.

It is known that ascending infections, either bacterial or mycotic, can cause an inflammatory reaction in the placenta (chorio-amnionitis, subchorionic intervillitis and sometimes also a choriovasculitis) which neither involves the villi nor apparently interferes with the placental circulation and so does not impair the functional efficiency of the organ (8, 9). In the present case, however, aside from a marked necrotizing chorioamnionitis, a subchorionic intervillitis and a choriovasculitis, we observed a widespread necrotizing villitis and a marked and acute intervillitis sometimes forming true abscesses in the intervillous space. Furthermore, fungi were seen within the lumen of the villous vessels. Villitis and intervillitis always indicate an hematogenic infection and, generally, hematogenic infections are acquired from the mother's blood and are caused by viruses, bacteria and protozoa (9, 10). There is no reported case of placental hematogenic candidiasis (9, 10). This case is the first example of a candida hematogenic placentitis acquired by a retrograde route from the fetal blood, and the fetus acquired the infection by an ascending route through the placenta.

As in the other cases in the literature we did not observe any predisposing factor in the mother that could be responsible for the propagation of the fungus to the uterine cavity. The mother was a normal person and did not take any drug during gestation excluding the vaginal application of Miconazole. However, she used and I.U.D. for more than 2 years.

Similar associations of I.U.D. and pregnancy occurred in three other cases in the literature (11, 18, 22). We think that the possibility of a causal situation is difficult to prove. There are well-documented cases of ascending placental candida infection without association with I.U.D. On the other hand some authors believe in a possible fungal contami-

nation of the I.U.D. either during insertion or through the threads of the device that are present in the vagina (18). In the present case and in two other cases in the literature of this kind of association, the insertion of the I.U.D. was made many months before gestation and it is improbable that the fungi persisted for so long within the endometrial cavity. We believe that, if the amnionic sac is intact, there are no means to increase the possibility of infection by the mere presence of an I.U.D. in the neighbourhood. At least, in the case of Misenheimer & Garcia (18) and in our case the membranes had not yet ruptured at the time of placental infection.

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