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Transabdominal collection of amniotic fluid “sludge” and identification of *Candida albicans* intra-amniotic infection

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Abstract

A G3P2 patient who conceived while using an intrauterine contraceptive device presented at 20 weeks of gestation with mild irregular uterine contractions and vaginal bleeding. Sonographic examination at admission showed the presence of dense amniotic fluid “sludge” and a long sonographic uterine cervix (42 mm). To assess the microbiologic significance of amniotic fluid “sludge,” we performed a transabdominal amniocentesis. The procedure was performed under real-time ultrasound, and fluid resembling pus at gross examination was noted. Rapid amniotic fluid analysis showed the presence of a high white blood cell count and structures resembling hyphae. Amniotic fluid cultures were positive for *Candida albicans*. Treatment was begun with broad-spectrum antibiotics, including Fluconazole, upon the visualization of pus in the “sludge” material because of the presence of hyphae in the Gram stain. Despite treatment, the patient went into spontaneous preterm labor and delivered five days after admission. Placental examination

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revealed acute fungal histologic chorioamnionitis and funisitis. This represents the first report of transabdominal collection and analysis of amniotic fluid “sludge” and the microbiologic detection of *Candida albicans* in this material. This report provides evidence that transabdominal retrieval of “sludge” is possible and may be of significant value for patient management and selection of antimicrobial agents.

Keywords

amniocentesis; biofilms; chorioamnionitis; funisitis; intra-amniotic infection/inflammation; intrauterine contraceptive device; microbial invasion of the amniotic cavity; preterm prelabor rupture of the membranes; spontaneous preterm labor; transvaginal ultrasound

Introduction

Conception while using an intrauterine contraceptive device (IUD) is a risk factor for adverse pregnancy outcome, including intrauterine infection often due to fungi [1–4], spontaneous preterm labor/birth (with or without ruptured membranes) [1, 5–14], maternal sepsis [6, 7, 15], and even death [16]. Amniotic fluid “sludge” is frequently detected in patients who present with an episode of suspected preterm labor [17–19], cervical insufficiency [20, 21], and an asymptomatic short cervix [20, 22–26]. The presence of “sludge” is a risk factor for preterm delivery, histologic chorioamnionitis, and intra-amniotic infection [19, 21–24, 27–29]. Although originally thought by some to represent a blood clot in the amniotic fluid [30], “sludge” is now known to represent intra-amniotic inflammation/infection due to microbial biofilms in patients with preterm parturition [31].

Previous cases of “sludge,” which have been the subject of studies using microbiologic techniques, have been retrieved transvaginally from patients who have inevitable preterm delivery [31, 32]. However, it is technically feasible to retrieve “sludge” by transabdominal aspiration. This would allow the analysis of the material in the context of an ongoing pregnancy.

We report herein the first transabdominal collection of “sludge” and identification of *Candida albicans* in a patient who conceived with an IUD.

Case Report

A 34 year-old Hispanic woman, gravida 3 para 2, who had two previous term deliveries (one vaginal, one Cesarean), was admitted at 20 weeks of gestation due to vaginal bleeding and irregular uterine contractility that did not meet the criteria for preterm labor because there were no changes in her cervix. The patient had conceived despite having a T380A copper IUD. A vaginal speculum examination revealed a few blood clots with no active bleeding. Transvaginal ultrasound showed a cervical length of 42 mm and floating, dense hyperechogenic particulate matter, amniotic fluid “sludge,” in close proximity to the internal cervical os (Figure 1 and Videoclip 1). After obtaining written informed consent from the patient, a transabdominal amniocentesis was performed using a 20-gauge needle to exclude intra-amniotic infection [1–15, 33–7] based on the combination of amniotic fluid “sludge”

[17, 18, 21, 22, 28, 31, 32], idiopathic vaginal bleeding [48, 49], and pregnancy co-existing with an IUD [1]. The tip of the needle was directed toward the “sludge” and allowed aspiration of this material (Videoclip 2). The gross characteristics of the amniotic fluid and “sludge” are depicted in Figure 2 and Videoclip 3.

Amniotic fluid analysis revealed a white blood cell count of 1627 cells/mm³ (under normal circumstances, there are no white blood cells in the amniotic fluid, and a nucleated cell count above 50 is considered indicative of intra-amniotic inflammation). Amniotic fluid glucose was not detectable (under normal circumstances, a concentration below 14 mg/dl is suggestive of intra-amniotic infection/inflammation), and a Gram stain of the amniotic fluid revealed fusiform structures consistent with hyphae (Figure 3).

Broad-spectrum antibiotic treatment was initiated, including Clindamycin 900 mg IV every 8 hours, Ceftriaxone 1 g IV every 12 hours, Azithromycin 1 g PO once a day, and Fluconazole 400 mg IV once a day. Two days after the amniocentesis, cultures from the amniotic fluid and “sludge” were positive for *Candida albicans*. Five days after admission, the intensity and frequency of uterine contractions increased, and the patient progressed into well-established preterm labor, delivering a non-viable male fetus weighing 421 grams. Histological examination of the placenta revealed acute chorioamnionitis and severe funisitis. The umbilical cord presented several small, well-circumscribed white nodules—fungal infection microabscesses—on the surface [50] (Figure 4).

Discussion

Amniotic fluid “sludge” as a sonographic sign of intra-amniotic infection/inflammation

Amniotic fluid “sludge” is particulate matter attributed to bacterial biofilms [32] floating in close proximity to the cervix. “Sludge” was reported in asymptomatic patients at risk for preterm delivery [20–22, 24, 28] and those with preterm labor [17, 27] and/or acute cervical insufficiency [20, 21, 29]. Indeed, this particulate matter was reported as a risk factor for spontaneous preterm delivery [17, 19, 22, 25–29], preterm prelabor rupture of the membranes (PROM) [17, 22], acute histologic chorioamnionitis and funisitis as well as intra-amniotic infection/inflammation [17–26, 28, 32, 51] in asymptomatic women [28], patients with spontaneous preterm labor with intact membranes [17–19], asymptomatic women at high risk for spontaneous preterm delivery [22, 26], singleton and twin pregnancies with a sonographic short cervix [20, 22–26], acute cervical insufficiency [21], and in cases with a subchorionic hematoma [51].

Microorganisms isolated from the amniotic fluid in patients with “sludge” include the following: *Ureaplasma* spp., *Mycoplasma hominis*, *Fusobacterium nucleatum*, *Candida albicans*, *Peptostreptococcus* spp., Group B *Streptococcus*, *Gardnerella vaginalis*, *Acinetobacter* spp., *Streptococcus mutans*, *Aspergillus flavus*, and *Staphylococcus warneri* [17, 18, 21, 22, 28, 32].

Retrieval of “sludge”

Thus far, the retrieval of “sludge” from the intra-amniotic cavity has only been performed vaginally [31, 32]. Therefore, the available information regarding the microbiology and the

nature of “sludge” is confined to these patients. This case report is the first to demonstrate a transabdominal collection of amniotic fluid “sludge” (Videoclip 2). This is important because women with amniotic fluid “sludge” may have negative amniotic fluid cultures, despite the presence of microorganisms within the particulate matter, as is typical in biofilms [31, 32]. This information has the potential to impact the clinical management of patients; for example, those with cervical insufficiency and “sludge” who have an amniocentesis with negative amniotic fluid cultures may undergo placement of a cerclage, a procedure that would not have occurred in the presence of known microbial invasion of the amniotic cavity.

A previous report demonstrated that women with a cerclage who have “sludge” are at a substantially greater risk for preterm birth [52], intra-amniotic infection/inflammation, and clinical chorioamnionitis compared to those without this particulate matter [22]. The feasibility of collecting amniotic fluid “sludge” transabdominally will provide physicians with more accurate information regarding the microbiological status of the amniotic cavity, enabling a tailored patient management, e.g., the placement of a cerclage in women with cervical insufficiency or the administration of antibiotic treatment that may eradicate microbial invasion in the amniotic cavity [53–58].

In the case presented herein, the identification of *Candida albicans* in the amniotic fluid and the demonstration of hyphae in the sample of “sludge” changed patient management by adding antifungal agents.

Pregnancy conceived with an intrauterine contraceptive device: a risk factor for intra-amniotic infection

Conceiving in the presence of an IUD is associated with increased risk for maternal and fetal morbidity. In cases where the IUD cannot be removed in the beginning of pregnancy, there are increased rates of complications, including: intrauterine infection often due to fungi [1–4], late spontaneous abortion [6, 8], spontaneous preterm labor/birth (with or without ruptured membranes) [1, 5–14], histological chorioamnionitis/funisitis [50], abruptio placentae [1], adverse neonatal outcome [1–15, 33–45], maternal sepsis [6, 7, 15], and even death [16]. Indeed, in a large cohort study including 12,297 patients of whom 196 conceived with an IUD, the rate of preterm birth in the latter group was 56.1%, and approximately two-thirds of these births were due to preterm PROM [1]. Women who conceive with an IUD have a 5-fold higher risk of having an intra-amniotic infection than those who conceived without an IUD [1]. The prevalence of a positive amniotic fluid culture in patients who had an IUD was 45.9%, and 31% of them had *Candida* spp., a rate 5 times higher than in patients without an IUD [1].

Conclusion

We report, for the first time, the transabdominal collection of “sludge” material, which made possible the diagnosis of intra-amniotic infection due to *Candida albicans*. This observation is important because it indicates that, in selected cases, amniotic fluid “sludge” can be retrieved without rupturing the membranes. This would allow assessment of the inflammatory and microbiologic status of the amniotic cavity and create opportunities for tailored treatment and patient management.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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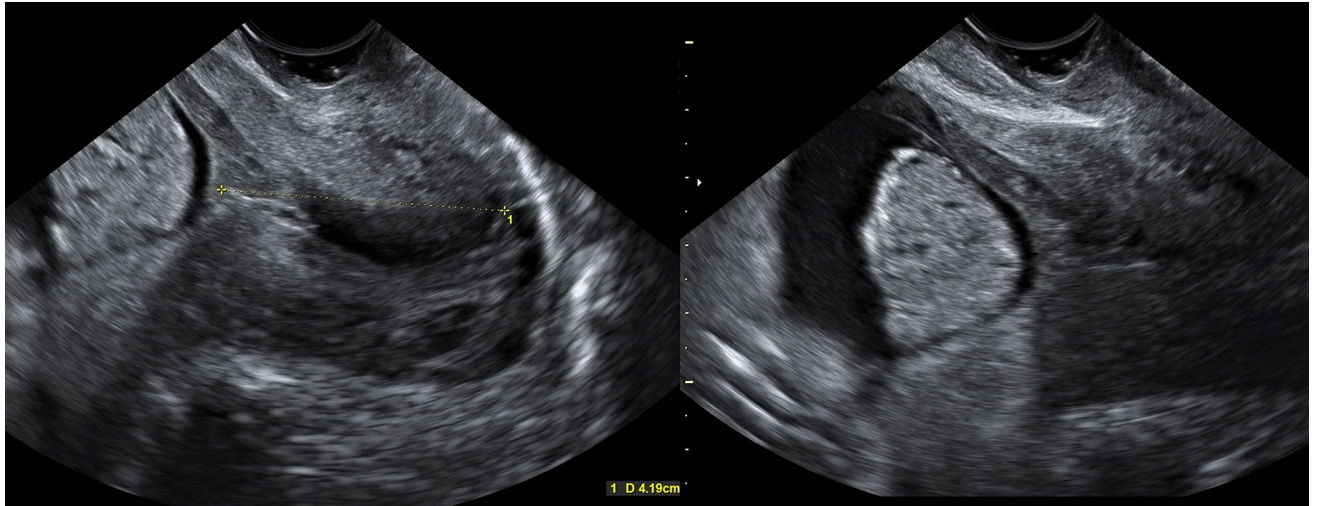


Figure 1. Two-dimensional transvaginal ultrasound showing amniotic fluid "sludge" in a patient with an intrauterine device, vaginal bleeding, and a long cervix at 20 weeks of gestation.



Figure 2. Amniotic fluid samples collected during the transabdominal amniocentesis: **a)** from the lower uterine compartment and **b)** directly from the "sludge." The amniotic fluid looks turbid, while the "sludge" was thick and dense.

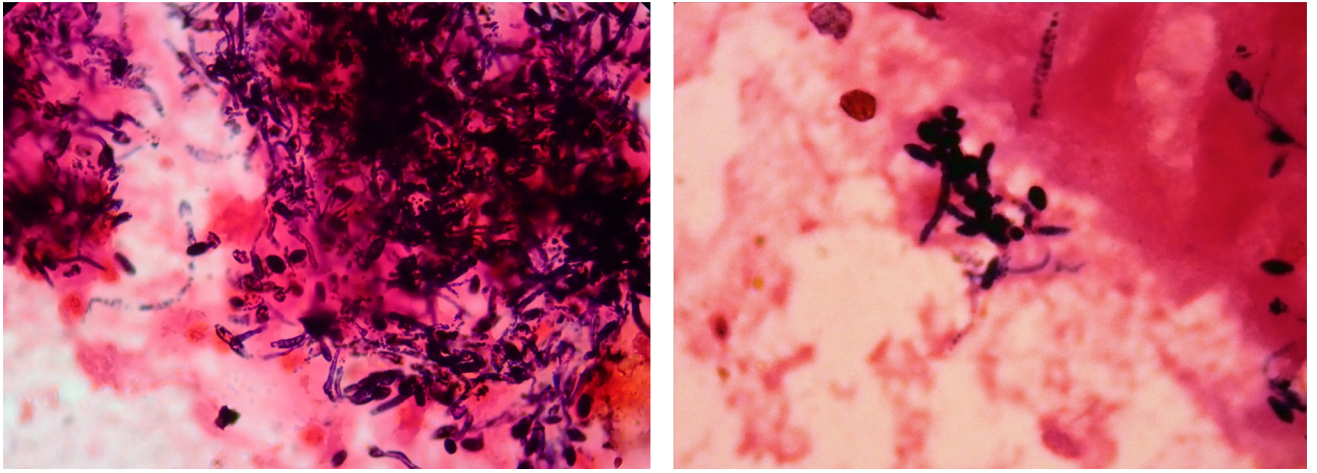


Figure 3.
Gram stain of amniotic fluid "sludge" showing the presence of fungal hyphae.

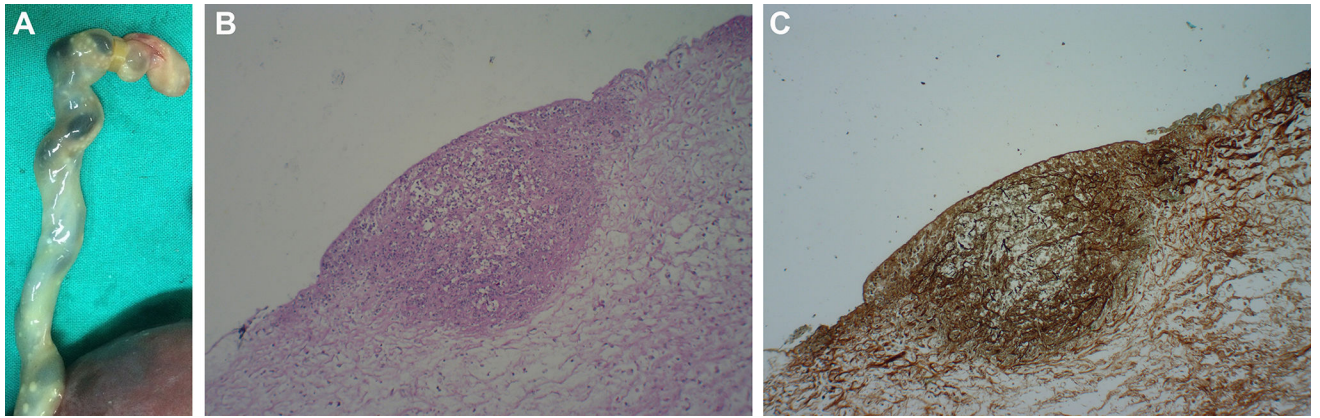


Figure 4.

a) Macroscopic examination of the umbilical cord revealed several small, well-circumscribed, white nodules on the surface. **b** and **c)** Histological section of the umbilical cord showing a microabscess in its surface with inflammatory cells (H&E) and fungal microorganisms (Grocott).