

Ustilago as a Cause of Fungal Peritonitis: Case Report and Review of the Literature

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Fungal peritonitis is an uncommon complication of ambulatory peritoneal dialysis in children and often necessitates catheter removal, prolonged hospitalization and conversion to hemodialysis. The majority of these infections are due to *Candida albicans* and related species. We present an uncommon case of peritonitis due to the unusual plant pathogen *Ustilago*.

CASE

A 3-year-old Latin American male with a complex medical history notable for hypertension, end-stage renal disease secondary to posterior urethral valves and obstructive uropathy and chronic peritoneal dialysis (PD) presented with abdominal pain, vomiting and diarrhea. The patient was found to be hypovolemic and hyperkalemic and was admitted to the nephrology service for rehydration and correction of electrolyte derangements with a working diagnosis of viral gastroenteritis. At home his mother was responsible for performing his PD. The patient did not have a history of foreign travel. His diet included traditional Mexican foods, but he denied consumption of unpasteurized dairy products. On hospital day 5, he uncapped his PD catheter and inserted a yellow crayon on which he had been chewing. The crayon was extracted without difficulty and did not enter the peritoneal cavity; the crayon was discarded and not sent for culture.

The following day, the patient developed fever to 101° F along with worsening abdominal pain, vomiting and diarrhea. During dialysis, the peritoneal fluid was noted to be cloudy and was sent for cell count and culture. Peritoneal fluid white blood cell count was 1530 cells/mm³, with 43% neutrophils, 16% lymphocytes, 39% monocytes and 2% eosinophils. The patient was given intraperitoneal vancomycin and ceftazidime pending culture results. His past medical history was significant for three previous episodes of documented infectious peritonitis with *Candida parapsilosis* (3.5 years prior), *Staphylococcus epidermidis* (3 years prior) and group A

Streptococcus (1.5 years prior). Due to persistent fever and symptoms, intraperitoneal fluconazole was added to the patient's regimen on hospital day 8.

The initial peritoneal fluid culture grew a fungus that contained both hyphae and yeast forms, and peritoneal fluid cultures continued to grow fungus for 11 consecutive days. The patient continued to have fever, abdominal pain and diarrhea despite intraperitoneal fluconazole. Blood aerobic, anaerobic and fungal cultures did not yield a pathogen. Serum was sent for the 1,3 β -D-glucan assay and was negative.

The infectious diseases service was consulted to assist with management on hospital day 19 and recommended liposomal amphotericin B 5 mg/kg/dose intravenously once daily and PD catheter removal. The patient underwent removal of the PD catheter on hospital day 20 and was started on intermittent hemodialysis. An abdominal ultrasound was performed which revealed no evidence of abscess.

The fungus identified in peritoneal cultures produced very mucoid colonies on Sabouraud dextrose agar (Figure in supplemental content). It was urease positive and initially identified by Vitek 2 (Biomérieux, Sweden) as a *Cryptococcus* species. Based on morphology, however, it was felt that the organism more closely resembled one of the smut fungi. The fungus was sent to the Fungal Identification and Susceptibility Laboratory at the University of Texas Health Science Center at San Antonio for further identification. DNA was isolated and subjected to sequencing studies which revealed the organism belonged to the *Ustilago* genus 20 days after the

culture was initially obtained. The isolate was not viable for further studies and susceptibility testing.

Upon learning of the identification of the fungus, our consult service recommended stopping amphotericin and starting itraconazole 5 mg/kg/d on hospital day 27 to complete a 21-day course post-catheter removal. Of note, the patient had pronounced improvement in symptomatology following catheter removal even prior to changing antifungal agents. He continued on intermittent hemodialysis and was discharged to home in good condition. He underwent reinitiation of peritoneal dialysis approximately 1 month later and is currently doing well.

DISCUSSION

Infectious peritonitis is a known complication of ambulatory peritoneal dialysis in children. Fungi accounted for 2.9% of cases of peritonitis in children in one large series, with previous episodes of peritonitis being a well-described risk factor [1]. Among the 51 episodes of fungal peritonitis in this series, 79% of cases were caused by *Candida* species. A number of other clinically important fungi have been noted to cause peritonitis in the setting of peritoneal dialysis, notably *Rhodotorula*, *Rhizopus*, *Aspergillus* spp., *Cryptococcus neoformans* and *Histoplasma capsulatum* [2, 3]. *Ustilago* spp. are a particularly unusual cause of fungal peritonitis, to the best of our knowledge, being described only once in a series of 51 patients [1].

Organisms of the genus *Ustilago* are often referred to as smut fungi, basidiomycete molds that are common environmental organisms. The basidiomycete fungi include the smuts which are well described as edible mushrooms, as well as pathogens of grain crops. Notably, this grouping also includes fungi of importance in human disease; the most clinically significant organism in this class is *Cryptococcus neoformans* [4]. These organisms are filamentous in nature, however, they can develop into haploid yeast forms in culture media; these factors likely contributed to the initial difficulty in identification of the pathogen in the case presented.

The Ustilaginales are specialized to parasitize a number of valuable crop species such as corn, sorghum, wheat and barley. Prominent among this group is *Ustilago maydis* (sometimes referred to as *U. zeae*), the etiologic agent of corn smut. *U. maydis* infection of corn leads to the development of tumor-like growths on the aerial portions of the plant, affecting the growth and viability of the crop [4, 5]. Furthermore, large consumption of contaminated corn has been associated with an alkaloid-like toxidrome in cattle, “the staggers.” *Ustilago*

spp., however, are often used in Latin American cuisine where it is better known as *huitlacoche* [6]; the fungus is frequently included as an ingredient in tortilla-based dishes.

There is a paucity of literature on the role that *Ustilago* spp. may play in human disease. A strong association has been described between skin hypersensitivity to spores of smut fungi, including *U. maydis*, and allergic rhinitis and asthma [4, 7]. Teo reported the case of a 23-year-old Chinese woman with a dermatitis whose skin scraping fungal cultures grew *Ustilago* spp.; the patient’s pet guinea pig was suffering from a scaly rash on its paws which also grew *Ustilago* spp. [8]. There are very few reports of invasive disease due to *Ustilago* in humans. One of the earliest cases was reported by Moore et al in 1946 in an adult farmer who died of chronic leptomeningitis; at autopsy fungal elements consistent with *Ustilago maydis* were found in brain tissue, however no cultures were available [9]. In addition there is a single case report of a central line associated bloodstream infection (CLA-BSI) due to *U. maydis* [10], and a report of hypersensitivity pneumonitis related to exposure to *U. esculenta* [11]. CLA-BSI due to *Pseudozyma aphidis*, a related *Ustilagomycete*, has been described in a child who consumed large quantities of corn tortilla chips [12]. Furthermore, there are additional reports of invasive disease in immunocompromised hosts due to other edible basidiomycetes, such as the mushroom *Volvariella volvacea* [13]. There are, however, limited data on invasive infections by organisms of the *Ustilago* genus in pediatrics. In terms of pathogenesis in the case presented, the most logical explanation seems that the child’s peritoneal cavity and catheter became contaminated from insertion of the crayon that may have been colonized with *Ustilagomycetes* from the environment and the child’s oral cavity. While our patient denied consumption of *huitlacoche*, he did consume other traditional Mexican foods including homemade corn tortillas which would be consistent with this mechanism.

Given the limited data on *Ustilago* in human disease, formulating specific recommendations for treatment are difficult. Based on the few reports of invasive infection due to *Ustilago* and related organisms, the minimum inhibitory concentrations tend to be lowest for itraconazole followed by amphotericin and fluconazole [10, 12]. There are no available data on the use of echinocandins in these infections. Itraconazole has been used in the few reports of human infection due to *Ustilago* spp. and related organisms for which specific antifungal therapy has been prescribed and this influenced our decision to change antifungal agents [8, 12]. It is worth noting that our patient

had prompt improvement in symptoms after removal of the peritoneal dialysis catheter, and that device removal may be necessary in the setting of infection with this organism. In addition, the reported case of *Ustilago* CLA-BSI was treated with catheter removal alone and not systemic antifungals with success [10].

In summary, we report an unusual case of peritonitis in a pediatric patient due to *Ustilago* spp. While traditionally thought of as only a plant pathogen, there continues to be emerging data that this agent can play a role in human disease. Moreover, this case highlights the importance of considering environmental fungi in clinical practice. Continued research into antifungal options for these organisms is warranted.

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Figure Legend: Panel A and B (close-up) Organism producing mucoid colonies on Sabouraud dextrose agar. Photographs courtesy of Dr. Paula Revell, Department of Pathology, Baylor College of Medicine

