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## A "Kelp-Like" Microorganism Within the Belly

Marie-Alix de Kyvon, Claudia Carvalho-Schneider, Adrien Lemaigen, David Dussart, Mathilde Barbaz, Pierre-Guillaume Barbe, Philippe Lanotte, Louis Bernard, Éric Bailly, J Chandenier, et al.

► **To cite this version:**

Marie-Alix de Kyvon, Claudia Carvalho-Schneider, Adrien Lemaigen, David Dussart, Mathilde Barbaz, et al.. A "Kelp-Like" Microorganism Within the Belly. *Clinical Infectious Diseases*, 2018. hal-02443964

**HAL Id: hal-02443964**

**<https://hal.science/hal-02443964>**

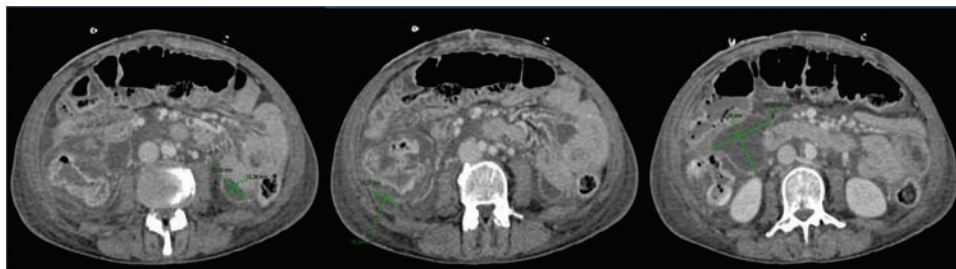
Submitted on 17 Jan 2020

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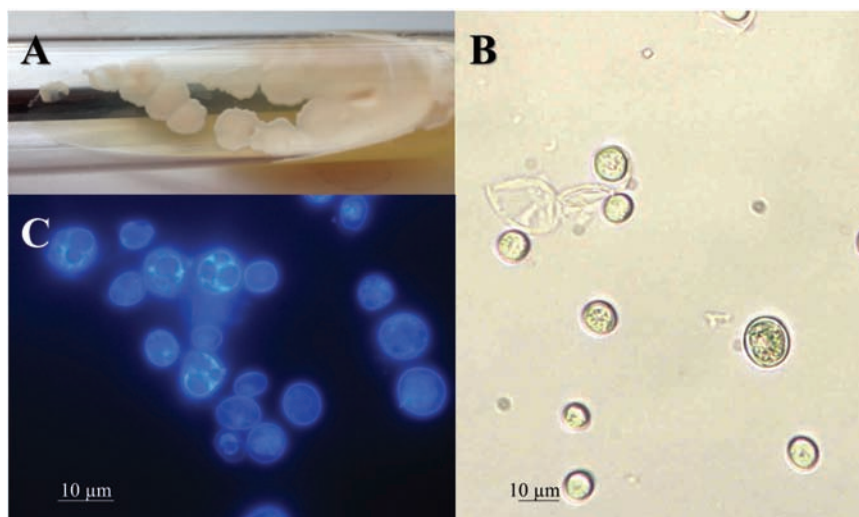
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Anthony Amoroso and Ajit P. Limaye, Section Editors

## A “Kelp-Like” Microorganism Within the Belly



**Figure 1.** Medical imaging of abdomen. Noncontrast computed tomography scan showed 3 large abscesses within the peritoneum on day 3 (abscesses' sizes = 29.3 × 15.4 mm, 28.4 × 15.2 mm, and 82.2 × 47.1 mm).



**Figure 2.** Microbiological findings from the abscess aspirate. *A*, After 6 days of culture, creamy, pale (instead of “whitish”), yeast-like colonies with flat rough texture. *B*, Microscopic observation of positive culture through fresh mounting (magnification ×400). *C*, Microscopic observation of positive culture according to calcofluor method (magnification ×400).

A 50-year-old woman suffering from paranoid schizophrenia with carelessness symptom was referred on day 0 for peritonitis caused by a perforated gastro-duodenal ulcer. In her recent medical history, anorexia, constipation, and impairment of general health condition were reported. A biological inflammatory syndrome was noticed at admission, with C-reactive protein of 320.1 mg/L, procalcitonin of 216.68 μg/L, and

polymorphonuclear neutrophil count of  $16.4 \times 10^9/L$ . To note, blood calcium, total serum protein, and hemoglobin were low at 1.77 mmol/L, 40 g/L (including 16 g/L for albumin), and 81 g/L, respectively. Several intraperitoneal abscesses were detected by computed tomography on day 3 (Figure 1). Abscess aspirate showed a moderately inflammatory liquid with no malignant cells (day 4). On the third day following

the sampling (day 7), flat colonies started growing in vitro at 30°C on Sabouraud dextrose agar (BD Sabouraud Glucose Agar, Becton-Dickinson, Pont-Le-Claix, France) (Figure 2). Broad-spectrum antibiotic therapy (initially based on intravenous ceftriaxone, metronidazole, and fluconazole; amoxicillin

and erythromycin were added on day 4 and on day 9, respectively) was inefficient. Noteworthy, on day 18, measurement of (1,3)- $\beta$ -D-glucan antigen was positive at 474 ng/mL in serum. All blood cultures remained sterile.

What is your diagnosis?

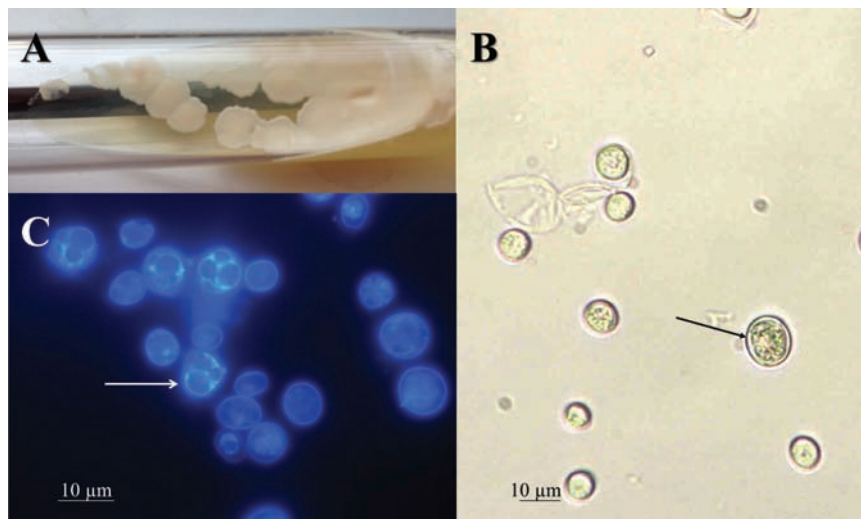
## A “Kelp-Like” Microorganism Within the Belly

Diagnosis: *Prototheca zopfii* peritonitis.

Macro- and microscopic observations were suggestive of *Prototheca* spp. (Figure 3), an achlorophyllous unicellular alga that has been previously described as being ubiquitous in sewage, ponds, plants, soil and mud, fresh-water aquariums and marine waters, cow milk, fruit bats, animal waste, and so on. *Prototheca* spp. colonies could be easily mistaken with yeasts, especially with *Candida krusei*, but microscopic examination usually highlights round, thick-walled sporangia containing mulberry-shaped sporangiospores (also referred to as endospores or autospores). *Prototheca* spp. must be differentiated from other endospore-forming microorganisms that undergo internal septation (eg, *Coccidioides immitis* and *Rhinosporidium seeberi*); asexual multiplication in mature *Prototheca* cells begins with the nuclear division of the mother cell, followed by cleavage of the cytoplasm surrounding each daughter cell. Thereafter, sporangia are lysed and shed free sporangiospores. Two *Prototheca* species are involved in human medicine, *Prototheca wickerhamii* and *Prototheca zopfii*. Distinguishing one from the other is challenging [1]: *P. zopfii* sporangiospores are more spherical and bulkier than those of *P. wickerhamii* [2]. Moreover, *P. zopfii*

sporangia are more subdivided than those of *P. wickerhamii*, but not so symmetrical regarding the internal segmentation. In this case, carbohydrate assimilation profile identified *P. zopfii* (score of Api20C AUX system, bioMerieux, Craponne, France: 87.6% probability; no identification incompatibility). Sequence of D1/D2 variable domain of the 28S large-subunit ribosomal DNA gene confirmed *P. zopfii* var. *hydrocarbonea* (99% identical, 537 nucleotides/540; 100% query cover; GenBank accession number issued: MF421524). *Prototheca zopfii* was shown in vitro to contain approximately 10% glucose residues that are (1,3)- $\beta$ -linked in the polymerized oligosaccharides of its cell wall [3], which is likely the reason why measurement of (1, 3)- $\beta$ -D-glucan antigen was positive in the patient's blood [4].

Although its pathogenicity was initially overlooked, *Prototheca* infection, so called protothecosis, is now clearly acknowledged as an opportunistic infection. It usually results from environmental exposure, through water or soiled vegetables/plants [1]. *P. zopfii* can cross natural barriers when the latter are impaired or after a trauma or surgery [2]. In our patient, the portal of entry was assumed to be digestive, starting from the perforated gastro-duodenal ulcer and inducing thereafter



**Figure 3.** Microbiological findings allowing definitive diagnosis of *Prototheca zopfii* peritonitis. *A*, Growth of *P. zopfii* strains is usually optimized at 25°C–37°C in aerobic or microaerophilic conditions, with proliferation starting within 48–72 hours of incubation. *B*, Microscopic observation of *P. zopfii* culture through fresh mounting (magnification  $\times 400$ ) showing numerous sporangia measuring 5–15  $\mu\text{m}$  ( $\rightarrow$ ) and containing sporangiospores in the interiors. There is neither budding nor hyphal formation. No capsule is visible. *C*, Microscopic observation of *P. zopfii* culture according to calcofluor method (magnification  $\times 400$ ) showing mulberry-like sporangia containing several ovoid-to-spherical sporangiospores ( $\rightarrow$ ).

peritonitis caused by *P. zopfii*. It was hypothesized that, because of her mental disorder, she might have ingested soil before hospital admission. Noteworthy, she was also receiving intramuscular injections of flupentixol decanoate antipsychotic and cyamemazine, which are both known to slow down the intestinal transit and may have played a role in the infectious process. According to the literature, protothecosis seems to be more common in immunocompromised patients [1, 5], especially when polymorphonuclear neutrophils have functional impairment. In the present case report, the patient was not highly immunocompromised but suffered from severe malnutrition underscored by important hypocalcemia, hypoalbuminemia, and anemia, as well as a body mass index of 17 kg/m<sup>2</sup>.

Prevalence of protothecosis is low: 140 human cases have been reported so far [6]. Peritonitis is very unusual. *Prototheca wickerhamii* was involved in five cases. Four of them were concomitant with peritoneal dialysis; only 1 case resulted in death (potentially because it was associated with bacterial superinfection [7]; indeed, *Prototheca* spp. are often isolated with other pathogens such as bacteria or yeasts [1], as in the present case, in which *P. zopfii* was concomitant with *Streptococcus salivarius* and *Escherichia coli*). In contrast, except for in our patient, no peritonitis was reported in the 17 human cases caused by *P. zopfii* species; most *P. zopfii* infections have involved skin and nails [4, 8–10] (Supplementary Data). The prognosis of deeply seated infection is poorer with *P. zopfii* species than with *P. wickerhamii* (23.5% vs 2.2% overall mortality, and even 100.0% when patients are immunocompromised).

In light of previous therapeutic successes against *P. wickerhamii* [1], and because *Prototheca* spp. possesses a plasma membrane with up to 4% ergosterol, amphotericin B is usually given for profound infection, but it remains a matter of debate, and there are currently no available therapeutic guidelines [7]. In vitro minimum inhibitory concentrations to amphotericin B and azole drugs were shown to be variable for *P. zopfii*, such that approximately 50% of isolates were assumed to be not susceptible to clinically achievable drug levels [11]. In our patient, intravenous treatment was initiated on day 15 based on a daily dose of 150 mg of liposomal amphotericin B and 500 mg of gentamicin. Although (1,3)- $\beta$ -D-glucan antigen was still elevated at 500 ng/mL on day 31, gentamicin was finally withdrawn on day 20 and amphotericin B on day 36. To date on day 410, the patient no longer reports any functional digestive disorders.

## Supplementary Data

Supplementary materials are available at <http://academic.oup.com/cid>. Consisting of data provided by the author to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the author, so questions or comments should be addressed to the author.

## Notes

**Acknowledgment.** We thank the patient for her cooperation. She did not object to the publication of this case report.

**Potential conflicts of interest.** All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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**Clinical Infectious Diseases**® 2018;67(9):1463–6

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