SHORT REPORTS

Outbreak of *Paecilomyces variotii* Peritonitis in Peritoneal Dialysis Patients after the 2010 Chilean Earthquake

Fungal peritonitis (FP) accounts for 3 – 6% of all peritonitis episodes in chronic peritoneal dialysis (PD), being associated with high morbidity and mortality. Mortality rates are in the range of 15 – 50%, and loss of the peritoneal membrane function can be over 40% (1). The most common cause of the disease is *Candida* species (*C. albicans*, *C. parapsilosis*, *C. glabrata*). Other yeasts and filamentous fungi such as *Aspergillus*, *Paecilomyces*, *Penicillium*, and *Zygomycetes* are found less frequently. The strongest risk factors for FP in PD patients are prolonged use of antibiotics and previous bacterial peritonitis (2). Other suggested risk factors are immunosuppression, malnutrition, bowel perforation, diverticulitis, and, possibly, certain comorbidities such as diabetes or neoplastic diseases (1).

Paecilomyces spp is a filamentous fungus like the genus *Penicillium* and *Aspergillus*. It is found in soil and water and is one of the main dwellers of house dust. It is rarely associated with human infections. When a disease does occur, it is more often related to foreign bodies or immunosuppressed patients (3,4).

After the earthquake of February 27, 2010, in Chile, there was an increase in the rate of FP from 1% to 6%, due to the appearance of 6 cases caused by *Paecilomyces variotii* (5).

Here we describe the clinical characteristics and outcomes of 3 of these patients. Although there was no proof of the precise route of infection in our patients, in all 3 cases there was a major alteration in the storage of the PD fluid bags, resulting especially in exposure to excessive dust and destruction of the architecture of the storage holds. It is quite possible that in the context of a natural disaster like a big earthquake, the risk of infections associated with this fungus could increase because of the excessive dust in the environment.

CASE 1

A 58-year-old female living in Santiago, with end-stage chronic kidney disease (CKD) of unknown etiology

had been using continuous ambulatory PD (CAPD) for 4 years. She had had 1 episode of peritonitis 1 year prior to admission. On March 26, 2010, she consulted for difficulty at the entrance and drainage of peritoneal fluid, abdominal pain, cloudy fluid, and liquid stools. Peritoneal fluid analysis showed 815 cells/mm³, 60% polymorphonuclears. We performed the diagnosis of peritonitis associated with PD so she was treated with intraperitoneal vancomycin and amikacin plus oral metronidazole. Ninety-six hours later the abdominal pain persisted and increased peritoneal cellularity. Abdomen and pelvis computer tomography (CT) scan ruled out secondary peritonitis. The patient was diagnosed with refractory peritonitis, followed by catheter removal, and transferred to hemodialysis (HD). Her condition worsened, with fever and abdominal pain. The peritoneal fluid culture at 10 days of incubation was positive for *Paecilomyces variotii*. She began treatment with intravenous amphotericin B plus oral itraconazole. The abdominal pain continued so she needed laparotomy at 3 weeks of evolution with the finding of tabicated collections. Her condition improved and she completed 8 weeks of antifungal therapy (800 mg cumulative amphotericin B). Peritoneal biopsy showed encapsulating peritoneal sclerosing (EPS). Now she is currently asymptomatic, maintaining on HD.

CASE 2

A 46-year-old male living in Santiago, diagnosed with CKD of unknown etiology had been on automated PD (APD) for 7 years with 5 episodes of previous peritonitis, the last one 3 months prior to admission. On April 1, 2010, he presented pain and bloating, cloudy peritoneal fluid, fever, and diarrhea. Analysis of peritoneal fluid showed 3,340 leukocytes, 91% of them polymorphonuclear. A CT scan of the abdomen and pelvis ruled out secondary peritonitis. He was treated with intraperitoneal cefazolin and amikacin. He developed acute abdominal pain, so a laparotomy was performed, revealing multiple adhesions. The peritoneal catheter was removed and he began HD. Cultures of peritoneal fluid on admission and peritoneal fluid taken intraoperatively at 7 days of incubation were positive for *Paecilomyces variotii*. He

started therapy with amphotericin B intravenously plus oral itraconazole for 4 weeks. He completed 750 mg of cumulative dose of amphotericin B, with the result that the periods of abdominal pain and loose bowel movements were declining steadily. Peritoneal biopsy showed EPS. He is currently in good conditions, asymptomatic.

CASE 3

A 61-year-old male living in Navidad town, near San Antonio City, with CKD due to diabetic nephropathy, on APD for 3 years, with no history of peritonitis prior to admission, was hospitalized on June 12, 2010, with a 3-day history of abdominal pain, cloudy peritoneal fluid, and diarrhea. Analysis of peritoneal fluid showed 8,960 leukocytes, 99% polymorphonuclear cells. Treatment was initiated with cefazolin associated with amikacin, with no clinical improvement. A CT scan of the abdomen and pelvis ruled out secondary peritonitis. He continued to experience persistent abdominal pain and increased cellularity of the peritoneal fluid so the PD catheter was removed and he began HD. The catheter had visible fungal colonization. The peritoneal fluid culture at 11 days of incubation was positive for *Paecilomyces variotii*. The culture of the tip of the peritoneal catheter was also positive for the same agent. He completed treatment with 900 mg cumulative dose of amphotericin B. The patient

had a positive initial response with antifungal therapy, but 2 weeks later he died from severe pneumonia with multiple organ failure.

LABORATORY STUDY OF *PAECILOMYCES VARIOTII*

To assess whether the patients had a common source of infection, microbiological testing was conducted to search for filamentous fungi in 2 unused bags of PD solution belonging to patients 1 and 2 (6). Direct sowing was performed for aliquots of each bag in MacConkey agar plates, and Sabouraud 5% sheep's blood. A total of 200 mL of each bag in sterile chambers with filter paper with 0.2 micron pore was also filtrated, then the filters were seeded in MacConkey agar plates, and Sabouraud 5% sheep's blood, under aerobic incubation at 35°C for 14 days, with visual reading until the end of incubation. There was no bacterial or fungal development at 14 days of incubation.

A study was performed with polymerase chain reaction (PCR) fingerprint to assess whether different strains found in the patients had a common origin. The strain of patients 2 and 3 are closely related and probably come from the same clone. However, the strain of patient 1 was unrelated to the other 2 (Figure 1).

The Public Health Institute of Chile, on the other hand, undertook a microbiological study of 24 series of bags

Figure 1 — A. Culture of *Paecilomyces variotii*. B. PCR fingerprint of strains obtained from the 3 cases (trials 1, 2, 3) and from a control strain. C. The strains from patients 2 and 3 are related, and could come from a same clone. The strain from patient 1 is not related to the other 2. PCR=polymerase chain reaction.

out of 49 dialysis solution bags belonging to the series of Dianeal line imported by Industrial Comercial Baxter Chile Ltda. and manufactured in Mexico or Brazil. No bag had fungal growth.

DISCUSSION

Fungal peritonitis corresponds to 3 – 6% of PD-associated peritonitis. It is mainly caused by *Candida* species, with few cases corresponding to filamentous fungi. It is both a rare and severe illness, with a mortality rate between 15 and 50% and technique failure over 40% (1). The genus *Paecilomyces* is a saprophytic airborne fungus of soil, water, and decaying organic material. It has also been reported as a contaminant in laboratory cultures, and as one of the main pollutants of house dust (3), wooden shelves where the PD solutions are kept, and even as a contaminant in bags of unused PD solutions (4). It is rarely implicated in human infections, and when it is, it is primarily in immunocompromised patients or patients with prosthetic material, and rarely in PD (4,7).

The overall incidence of peritonitis in Chile dropped from 0.3 to 0.23 cases/patient/year between 2007 and 2009. During 2010, there was an increase in total peritonitis incidence that reached 0.263 cases/patient/year due to an increase in FP incidence from 1% to 6%, caused exclusively by the appearance of 6 cases never reported before of peritonitis from *Paecilomyces variotti* (5). In the year following the earthquake, despite a more targeted search of this agent, there were no cases identified of this fungi and the total incidence of peritonitis dropped again to 0.21 cases/patient/year (8) with a decrease in FP to 1% due to *Candida* species. Thus, the overall incidence of peritonitis during the year of the earthquake increased, not due to bacterial peritonitis, but to an outbreak of 6 cases by this filamentous fungus, never reported before or after the natural disaster (5).

Three of these patients were hospitalized at our hospital as described here. All of them had a severe progression requiring removal of the PD catheter and a shift to HD. The chosen treatment was the use of amphotericin B and itraconazole because of reports of resistance of *Paecilomyces variotti* to fluconazole (1). One of the patients died in septic shock due to pneumonia and the other 2 developed EPS, never returning to PD. Efforts to find a common origin with the stock cultures and genotyping of microorganisms did not provide conclusive evidence of a common source. However, in the second and third cases it could be considered that the contamination of the bags or lines occurred before delivery to patients.

The increase in incidence of peritonitis by this organism in relation to a natural disaster has never been described before. An earthquake, by interfering with the power supply and potable water, may be associated with a greater chance of breaking aseptic technique, which may predispose to these infections in PD patients (9). In Chile, the interruption of basic services was seen the first week and most patients did not experience building destruction (10). All the patients reported here had no problems in this respect: they did not wash their hands with contaminated water, they used alcohol the first days after the disaster, and bottled water to decrease the risk of peritonitis. It is also important to note that during the earthquake year the incidence of peritonitis produced by other microorganisms like gram-positive or gram-negative bacteria was the same, without cases produced by *Candida* species, arguing against a problem with bad hand washing (5).

All of our patients experienced a strong earthquake intensity (8.0 moment magnitude scale [MMS]). Two patients lived in Santiago, 500 kilometers from the earthquake's epicenter, and the other patient lived in Navidad town, 480 kilometers from the earthquake's epicenter. The intensity of the earthquake at its epicenter was 8.8 MMS, and 8.0 in Santiago and Navidad (see Figure 2).

Although none of them suffered the destruction of their home, there was a major alteration in the storage of the PD fluid bags, resulting especially in exposure to excessive dust and destruction of the architecture of the storage holds.

In the literature reviews, there are 17 cases of peritonitis by *Paecilomyces* spp reported in PD patients (4,7).

Figure 2 — Location of patients in relation to earthquake epicenter.

The largest group consists of 4 cases that occurred in Australia in 1990. That report included a search of a common source of contamination of the bags without finding any relationship (4). The spores of *Paecilomyces variotii* are ubiquitous and abundant. They are likely to be present in the environment at places of manufacture, storage, and use of the bags of PD fluid (4).

The present series of cases of peritonitis caused by *Paecilomyces variotii* and their clear relationship to the Chilean earthquake on February 27, 2010, suggest a relationship between the natural disaster and this unusual fungal infection in PD patients. It is worth noting that cases of peritonitis caused by this fungus in Chile were reported only that year, making it unlikely that this issue was just a coincidence.

Why peritonitis from *Paecilomyces variotii* occurred up to 4 months after the earthquake cannot be explained with certainty. This microorganism is a slow-growing fungus that usually lives in the soil and dust, and it is probable that after a massive dust release by an earthquake it could have colonized peritoneal fluid bags and connecting lines. Experiments on PD fluid bags have shown a slow growth rate from small inoculates of *Paecilomyces variotii*, suggesting that contamination of a bag should occur at least 2 to 3 weeks before fungal elements can be isolated from the fluid (4). Thus, we can speculate that the fungus contaminated the PD lines and bags because of the increase in dust released after the earthquake, and clinical evidence of this infection could take a long time to manifest in patients. However, there is no proof of the precise route of infection in our patients.

The present report suggests that in the context of a natural disaster like a big earthquake, the risk of peritonitis associated with *Paecilomyces variotii* could increase in PD patients, requiring a thorough study of atypical cases of peritonitis to identify and provide adequate therapy for this fungus.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

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