

Secondary Peritonitis Caused by *Streptomyces viridis*

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***Streptomyces* organisms are soil inhabitants rarely causing nonmycetomic infections. We describe a case of secondary peritonitis caused by *Streptomyces viridis* in a chronic alcoholic patient who presented with fever, abdominal distension, and pain in the abdomen. The most likely source of infection was by inoculation through multiple paracenteses, done for treatment of ascites, before the patient came to our health care center. This is the second case report of *Streptomyces* peritonitis and the first case caused by *Streptomyces viridis*, which is usually found in the soil in our geographic region.**

CASE REPORT

A 53-year-old male presented to the medical emergency room with complaints of fever, abdominal distension, and pain in the abdomen for 7 days. He was a chronic alcoholic, taking around 214 g of alcohol daily for the past 10 years. There was no history of melaena or hematemesis. There was also no history of any headache, rhinorrhea, sore throat, cough, dysuria, or bowel complaints. The patient gave a history of multiple paracenteses, done outside our hospital, for management of abdominal distension.

On examination, the patient was febrile (38°C) and was in mild distress due to dyspnea and abdominal pain. His sclerae of both sides were icteric. On palpation, his abdomen was firm, distended, and diffusely tender. The rest of the systemic examination was within normal limits.

On admission, the peripheral leukocyte count was 17,000/mm³, with 84% neutrophils and 12% lymphocytes. The platelet count was adequate. The serum creatinine level was 1.5 mg/dl, and the sodium level was 135 mmol/liter. The total bilirubin level was elevated, at 4.4 mg/dl, as were the alanine aminotransferase and aspartate transaminase levels (93 and 105 U/liter, respectively) and the international normalized ratio (1.1). The test for HIV was nonreactive. Upper gastrointestinal (GI) endoscopy revealed grade II esophageal varices, and ultrasonography of the abdomen showed signs of chronic liver disease with gross ascites. To rule out any infectious cause, specimens of blood and ascitic fluid were submitted for culture before the patient was started on ceftriaxone.

Ascitic fluid collected was pale yellow and turbid in appearance. It showed a white blood cell count of 5,600/mm³, with a differential count of 80% neutrophils and 20% lymphocytes. Gram staining showed the presence of pus cells with long, filamentous, extensively branched, Gram-positive structures. Aerobic culture on blood agar showed a significant number of large, folded, glabrous colonies with an earthy odor. Gram staining from blood agar showed Gram-positive, branching, filamentous bacilli. Partial acid-fast staining was negative. Based on culture characteristics, Gram staining, and acid-fast staining, the isolate was presumptively identified as belonging to a *Streptomyces* species and was sent to the Department of Medical Microbiology and Infectious Diseases, Erasmus MC University Medical Center, Rotterdam, The Netherlands, for sequencing and final identification. 16S rRNA gene PCR amplification was performed using the primers EUB-L (5'-CTTTACGCCCATTTAATCCG-3') and EUB-R

(5'-AGAGTTTGATCCTGGTTCAG-3') (17). This amplified only about 600 bp of the 16S rRNA gene, not the whole gene. A total of 480 bp of this product was analyzed, and the isolate was identified as *Streptomyces viridis*. The sequence homology was 99%; only 1 bp differed from the reference sequence in GenBank (accession number [AB184361.2](https://www.ncbi.nlm.nih.gov/nuccore/AB184361.2)).

Based on the CLSI microdilution and breakpoint guidelines for nocardiae and other aerobic actinomycetes, the isolate was susceptible to trimethoprim-sulfamethoxazole, ceftriaxone, imipenem, erythromycin, tetracycline, amikacin, and clarithromycin but was resistant to penicillin (3). All anaerobic, fungal, and mycobacterial cultures of ascitic fluid were negative. The blood culture was also found to be negative.

The patient was started on intravenous ceftriaxone at 1 g every 12 hours. A proton pump inhibitor, diuretics, and lactulose were also given to alleviate the symptoms. After 4 weeks of treatment with ceftriaxone, the patient became afebrile, and a repeat culture was negative. The patient was discharged and was advised to take oral trimethoprim-sulfamethoxazole (double strength three times a day [TID]) for 5 months. The patient's clinical condition improved, and treatment for his liver disease was continued.

The aerobic actinomycetes consist of a large, diverse group of obligate aerobic and relatively slow-growing Gram-positive bacilli with a tendency to form chains or filaments. They are found as saprophytes in soil and other natural habitats. These organisms are categorized on the basis of their acid fastness: *Nocardia* and *Rhodococcus* species are weakly acid fast, while *Streptomyces* and *Actinomadura* species are non-acid fast (11).

Mycetoma, the most common manifestation of *Streptomyces* infection, usually involves the subcutaneous tissue of legs and feet and occurs due to the direct inoculation of the microorganism through an injury caused by a thorn (5). Invasive *Streptomyces* infections, defined as infections other than mycetoma or superfi-

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cial skin infections, are extremely rare. These infections occur most often in immunocompromised patients such as those with HIV infection and those on immunosuppressive drugs such as corticosteroids and anticancer drugs (11).

The clinical significance of recovering these organisms is often unclear, as there have been many reports of isolation of *Streptomyces* species without definitive proof of their pathogenic role. Therefore, the role of *Streptomyces* species in visceral infections has been controversial, particularly in a polymicrobial setting (4). Diagnosis of invasive *Streptomyces* infection is made by clinical (i.e., immune status of the patient and infection other than superficial skin infection) and microbiological correlation. Isolation of the organism in pure culture and from a sterile site, direct examination of infected tissue (by Gram staining or biopsy), and exclusion of any other pathogen will confirm true cases caused by *Streptomyces* species. Earlier identification to the species level was based on morphological features and rapid enzyme tests of fluorophores (4). Currently, 16S rRNA gene sequencing is considered the best method for species identification (9).

To identify all cases of invasive infection due to *Streptomyces*, we performed a PubMed search and also reviewed the references from previous publications on *Streptomyces* infection. Only those cases which represented true invasive infections were included (using the criteria given above). A total of 23 reports of *Streptomyces* species causing infection other than mycetoma have been documented to date.

The majority of invasive *Streptomyces* infections were bacteremia and lung infections (pneumonia, abscess, and pneumonitis) (4, 9). All of the species identified have been different, showing the opportunistic potential of this pathogen. Most of the patients had some underlying immunosuppressive condition, such as HIV infection, cancer, systemic lupus erythematosus (SLE), Crohn's disease, etc. *S. pelletieri*, *S. griseus*, *S. lanatus*, and *S. albus* have been isolated from various patients with lung pathology (7, 9, 10, 16).

Streptomyces spp. causing bacteremia were linked to central venous catheter (CVC) use and the immune status of the patient (4, 9). Carey et al. reported an unusual case of catheter-related bacteremia due to *Streptomyces* in a female patient with breast carcinoma who was receiving injectable holistic preparations (1). Moss et al. described the isolation of *S. bikiniensis* from an osteosarcoma patient without any overt clinical symptoms (12). Joseph et al. reported an unusual case of bacteremia due to *Streptomyces* spp. in a pregnant female secondary to subcutaneous mycetoma of the scalp (8). Kapadia et al. reviewed 3 cases of CVC-related bacteremia in cancer patients; for all three patients, removal of the CVC line led to resolution of signs and symptoms in patients (9).

The present case was unusual, as only one case of *Streptomyces* peritonitis, caused by *S. somaliensis* and with no underlying condition reported, has been described previously (6). The patient we describe here represents the first reported case of secondary peritonitis caused by *S. viridis* in a patient with chronic alcoholic liver disease and gross ascites. The *Streptomyces* isolate was considered the primary pathogen because it was seen on the direct smear and isolated in pure form on culture media. Also unique to this case is the likely mechanism by which this infection occurred. Most cases of secondary peritonitis are caused by bacteria which arrive in the peritoneal cavity from a gut source, most often due to rupture of abdominal viscera. In contrast, for our patient the likely source of peritoneal infection was direct inoculation into the peritoneal cavity during paracentesis done in the past. *S. viridis* is found in the soil in various parts of India (15).

Streptomyces species rarely cause atypical visceral infections. Mossad et al. reported an atypical case of *Streptomyces* endocarditis in a patient with a prosthetic heart valve (13). *S. griseus* was isolated from a patient with a brain abscess by Clarke et al. (2). Rose et al. also discussed a case of brain abscess caused by *Streptomyces* infection following penetration trauma (14).

Based on various *in vitro* results, the best treatment options for visceral *Streptomyces* infection include macrolides, minocycline, doxycycline, ceftriaxone, amikacin, and imipenem. Cotrimoxazole is not the drug of choice for treating invasive *Streptomyces* infection, in contrast to the treatment of nocardiosis (4). A variety of antimicrobial regimens were used in the previously reported cases, and in most cases the outcome was good, with resolution of infection. However, the optimal choice of antimicrobial agent and duration of therapy for treating *Streptomyces* visceral infections remain to be determined (9).

Conclusions. Though *Streptomyces* species are not commonly recovered from clinical specimens, these organisms can cause invasive infections. The present case illustrates the potential of *Streptomyces* spp. to cause invasive infection.

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