Arthritis Caused by *Nannizziopsis obscura*, France

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Nannizziopsis spp., fungi responsible for emerging diseases, are rarely involved in human bone and joint infections. We present a rare case of septic arthritis with necrotizing cellulitis caused by *N. obscura* in a patient in France who had undergone kidney transplant. Rapid, aggressive medical and surgical management led to a favorable outcome.

Nannizziopsis spp. are keratinophilic fungi that can cause aggressive pyogranulomatous lesions affecting the skin, integument, and musculoskeletal systems of reptiles. The ecology of these fungi is not well known, and human infections are rarely. We report a case of septic arthritis caused by *N. obscura.*

In April 2019, a 56-year-old man, originally from Senegal and a former taxi driver in France, was hospitalized in the intensive care unit of Ambroise-Paré Hospital, Boulogne-Billancourt, France, for renal failure and sepsis. He had a prior diagnosis of diabetes mellitus, had undergone kidney transplant 6 years earlier for interstitial kidney disease, and had been undergoing dialysis during the prior year. His usual medication regimen included tacrolimus (4 mg 2×/d), prednisolone (5 mg 2×/d), and mycophenolate mofetil (250 mg 4×/d; stopped at admission).

At admission, the patient was hypothermic (34.9°C) and had moderate impaired consciousness. Blood pressure was 152/85 mm Hg and heart rate 95 bpm. No septic shock was observed. The patient's right leg showed swelling, redness, and tenderness. Testing revealed creatinine level of 333 μmol/L, leukocyte count of 5.6 G/L, neutrophil count of 4.77 G/L, and creatine phosphokinase level of 26 IU/L. A computed tomography scan of the right lower limb revealed ankle joint effusion associated with gas, compatible with septic arthritis (Figure). On the basis of these findings and the observance of concomitant necrotizing cellulitis, the patient underwent immediate surgery, which involved debridement of the skin and subcutaneous tissues of the dorsal face of the right foot and the medial face of the distal tibia, including excision of necrotic tissue (fascia and muscle). Abundant purulent discharge was observed during surgery.

Because direct histologic examination of intraoperative samples revealed several septate and arthrosporous mycelial filaments, we prescribed empiric treatment that included liposomal amphotericin B and broad-spectrum antibiotics. Because no bacteria were isolated, we stopped antibiotic therapy 5 days after surgery. The patient underwent additional surgeries 48 and 96 hours after initial surgery based on a diminishing clinical course and persistence of the previously observed fluid collections and air pockets on computed tomography scan, revealing effusion of the right tibio-talar joint and arthritis.

A subculture on Sabouraud dextrose agar with chloramphenicol yielded white, cottony colonies after 3–5 days. Using molecular identification by PCR amplification and sequencing of internal

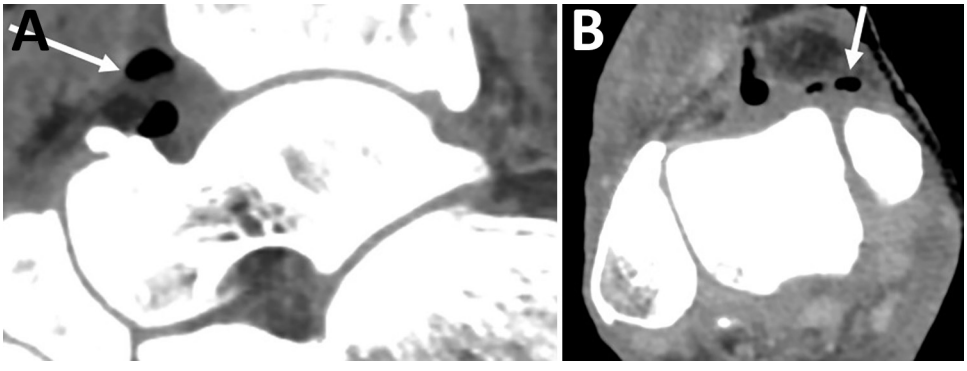

Figure. Sagittal (left) and axial (right) contrast-enhanced computed tomography images demonstrating ankle joint effusion associated with gas (arrows) in an immunocompromised man in France who had septic arthritis and soft tissue infection caused by *Nannizziopsis obscura.*

transcribed spacer (ITS) regions (ITS1–5,8S -ITS2), the clinical isolate was identified as *N. obscura,* confirmed by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. An antifongigram revealed a strain sensitive to azole antifungals (itraconazole [MIC 0.380 µg/mL], isavuconazole [MIC 0.064 µg/mL], voriconazole [MIC 0.008 µg/mL], and posaconazole [MIC 0.190 µg/mL]), micafungin (MIC 0.023 µg/mL), and amphotericin B (MIC 0.125 µg/mL). Serum β-D-glucan level was elevated (>500 pg/mL).

Because the *Nannizziopsis* strain was sensitive to voriconazole, we prescribed an initial oral regimen of the drug (3 mg/kg 2×/d) on day 6 of the initial intervention, without a loading dose. Drug monitoring revealed a plasma drug concentration of 0.7 mg/L, which was below the therapeutic threshold (1–2 mg/L), due to an ultra-rapid metabolizer profile after the genotyping of CYP2C19*17/*17. Voriconazole was then stopped and replaced by a regimen of posaconazole (loading dose, 300 mg 2×/d; maintenance dose, 300 mg/d) for a 1-year period. The patient's plasma drug concentration was 0.6 mg/L, above the therapeutic threshold (0.5 mg/L).

Computed tomography scans of the head, chest, abdomen, and pelvis and transesophageal cardiac ultrasound performed 2 months after admission revealed no lesion. The patient resumed immunosuppressive therapy with prednisolone (initiated after his kidney transplant) within 30 days of the last surgery for this soft-tissue infection. Tacrolimus, which was initiated at a reduced dosage (1.5 mg 2×/d) earlier in the patient's course of treatment, was then stopped. One year after his septic episode, the patient had no recurrence and had a partially functional lower right limb.

Only 14 cases of invasive *Nannizziopsis* infections in humans have been reported (*1*–*5*). These infections can be acute or chronic and usually occur in immunocompromised patients. Human infections caused by *Nannizziopsis* are generally cutaneous and subcutaneous, but some cases of pulmonary infection have been noted (*6*,*7*). Probabilistic treatment with azoles is recommended in the absence of a definitive diagnosis. Because serum β-D-glucans are typically very high during infections with *Nannizziopsis* spp., detection of a very high serum β-D-glucan level may guide the diagnosis of invasive fungal infection (*8*).

Given the wide variations in patient response and the potential impact of drug interactions, antifungal treatment should include serum drug monitoring to guide drug selection and optimize treatment dosage. Prognosis still largely depends on the underlying immunosuppression of the patient and the outcome of surgical management. This patient reported no recent travel to Africa, no history of cutaneous lesion or infection, and no recent contact with reptiles, which suggests that severe *Nannizziopsis* infection could occur several years after possible exposure among immunosuppressed patients.

This rare case of septic arthritis due to *N. obscura* occurred secondarily to a skin and soft tissue infection. Such severe infections require urgent medicosurgical treatment; the probability of a favorable outcome often diminishes when diagnosis and treatment are delayed. Medical treatment for infections caused by *N. obscura* is based on antifungals from the azole class, and dosages must be carefully monitored.

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Invasive Meningococcal X Disease during the COVID-19 Pandemic, Brazil

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Invasive meningococcal disease persists as a fulminant disorder worldwide. Although cases caused by *Neisseria meningitidis* serogroup X (MenX) occur infrequently, outbreaks have been reported in countries in Africa in recent decades. We report 2 cases of MenX invasive meningococcal disease in São Paulo, Brazil, in 2021 and 2022, during the COVID-19 pandemic.

Invasive meningococcal disease (IMD) is a severe disorder that is associated with high rates of morbidity and mortality worldwide (*1*). Although 12 serogroups of *Neisseria meningitidis* have been characterized based on their capsular polysaccharides, most IMD cases are caused by serogroups A, B, C, W, Y, and, more rarely, X (*1*).

N. meningitidis serogroup X (MenX) has been responsible for limited IMD cases in the United States and Europe, but since 1990, MenX isolates have emerged in some countries within the meningitis belt of Africa, causing outbreaks and epidemics in Burkina Faso, Togo, Niger, Kenya, and Uganda (*2*). In Brazil, only 6 cases of MenX IMD cases were reported in the last 15 years; the last one was isolated in the city of São Paulo in 2017 (http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sinannet/cnv/meninbr.def). We report 2 cases of MenX IMD that occurred in São Paulo in 2021 and 2022, during the COVID-19 pandemic. These isolates were identified during routine laboratory-based public health surveillance in the National Reference Laboratory at the Adolfo Lutz Institute in São Paulo.

Case-patient 1 was a 7-month-old boy who, in November 2021, was admitted to a São Paulo emergency department with fever, vomiting, bulging anterior fontanelle, stiff neck, and seizure. Cerebrospinal fluid collected at that time revealed a leukocyte count of 1,440 cells/mm^3 with a 73% proportion of neutrophils; protein level was 263 mg/dL, glucose 19 mg/dL, and lactate 80.5 mg/dL, and results of bacterioscopy and culture were negative. The patient was treated with ceftriaxone (100 mg/kg every 12 h) for 10 days, with a favorable outcome.

Case-patient 2 was a 6-year old boy who, in January 2022, was admitted to a São Paulo City emergency department with fever, headache, and vomiting. A sample of cerebrospinal fluid revealed a leukocyte count of 4920/mm^3 with a 96% proportion of neutrophils; protein level was 207 mg/dL, glucose 48 mg/dL, and lactate 82.3 mg/dL, and results for bacterioscopy and culture were negative. The patient was treated with ceftriaxone (100 mg/kg every 12 h), the recommended antibiotic, with a favorable outcome.

Because both patients were diagnosed with meningitis, chemoprophylaxis with rifampin was administered to all persons characterized as close contacts. Both patients resided in the city of São Paulo but in different regions, 40 km away from each other. Despite the short period between their illnesses, epidemiologic surveillance could not establish an obvious relationship between the 2 patients. Neither patient had traveled to countries with reported MenX disease, nor had they had known contact with other persons diagnosed with meningitis.

We extracted DNA from the cerebrospinal fluid samples obtained from the 2 patients using the Roche MagNa Pure LC 2.0 platform (https://lifescience.roche.com) according to the manufacturer's instructions. Both DNA samples were positive for *N. meningitidis* (*ctrA* gene) by multiplex real-time PCR (*3*), and these results were confirmed using another real-time PCR targeting the meningococcal *sodC* gene (*4*). Both samples were positive for genogroup X (*xcbB* gene)