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Invasive fungal infection caused by *curvularia* species in a patient with intranasal drug use: A case report

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ABSTRACT

Chronic invasive fungal sinusitis (CIFS) is an invasive fungal infection that can occur in immunocompetent individuals and is typically caused by *Aspergillus* species. Although many reported cases are unable to identify an etiology for the infection, certain risk factors such as chronic intranasal cocaine use can make patients susceptible to CIFS. This case report describes a unique case of CIFS secondary to *Curvularia* species in an immunocompetent patient with intranasal drug use.

1. Introduction

Invasive fungal infections (IFIs) are uncommon infections that currently account for approximately 27.2/100,000 cases per year in the United States [1–3]. IFIs are distinguished from superficial infections by being characterized as serious, deep, or disseminated, and are frequently associated with poor outcomes [4]. Patients at higher risk for IFI include those with hematologic malignancies, prolonged antibiotic use, increased number of chemotherapy cycles, and immunosuppression. However, immunocompetent patients have also been reported to have fungal infections.

One form of IFI is chronic invasive fungal sinusitis (CIFS). Unlike other invasive fungal infections, CIFS may present in immunocompetent individuals. These infections progress slowly over weeks or months without a clear diagnostic picture, which can delay necessary intervention. If untreated, invasion into neighboring structures may cause altered mental status, seizures, strokes, proptosis, and intracranial complications [5,6]. These infections are most frequently caused by *Aspergillus* species. Few cases in the literature have reported the cause due to *Curvularia* species [7–9]. In this case report, we describe an immunocompetent patient with intranasal cocaine and perfume inhalant use who developed invasive fungal sinusitis due to *Curvularia* species with disseminated disease.

2. Case presentation

On day 0, a 43-year-old female with a history of bipolar disorder, anxiety, and polysubstance abuse presented to the emergency department due to altered mental status, right sided weakness, and slurred speech. Twenty five days prior to presentation (day −25), she was found to have a 6.8 × 6.7 × 6.2cm left superior pole kidney mass and a left-sided enlarged periaortic lymph node (Fig. 1). A kidney biopsy revealed multiple noncaseating granulomas and GMS stains positive for fungal hyphae. However, no speciation was obtained and she had not received any treatment.

On presentation, the patient was afebrile, somnolent but arousable to stimuli, and appeared acutely ill with a National Institutes of Health stroke scale of 14. She was able to follow commands and had a dysarthric speech. Other neurologic deficits included a dysconjugate gaze with left sided facial droop and right sided hemiparesis. Otherwise, the patient had unremarkable findings on cardiovascular and pulmonary exams. As she was not able to provide history, the patient's mother reported a history of chronic perfume inhalant use and cocaine abuse, which was confirmed on urine toxicology. A CT head and neck with contrast on day 0 revealed a subacute to chronic basal ganglia lacunar infarcts and a left sphenoid opacity with scattered hyperintensities and erosive changes (Fig. 2). Additionally, CT angiogram showed basilar artery and left internal carotid artery stenosis and right internal carotid artery outpouchings. MRI brain with contrast on day 1 revealed multiple infarcts (Fig. 3).

The patient received blood cultures and serum fungal testing on day 1. Serum fungal testing revealed a positive Fungitell Beta-D Glucan assay (>500pg/mL), but was negative for *Aspergillus* antigen (Galactomannan) testing. Bacteria and fungal blood cultures were negative throughout the hospital duration.

Due to concern for an invasive fungal process, the patient underwent

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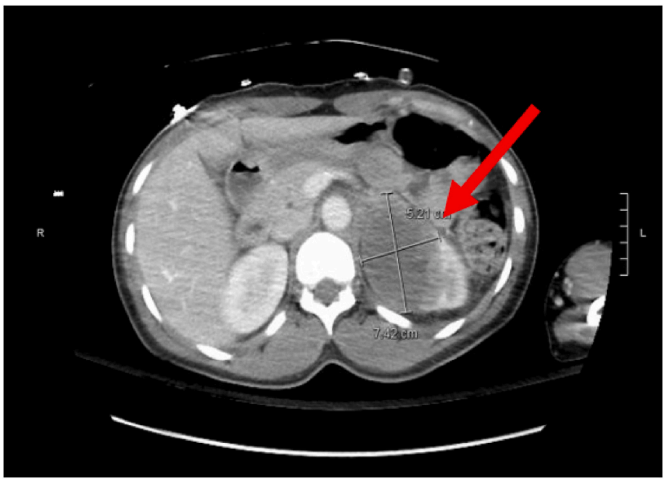

Fig. 1. CT abdomen and pelvis with contrast showed 7.4 × 5.2 × 6.3 cm heterogenous left upper pole kidney mass with perinephric fat stranding after biopsy and a 2.6 cm left periaortic lymphadenopathy, not shown. Mass was site of kidney biopsy showing fungal hyphae.

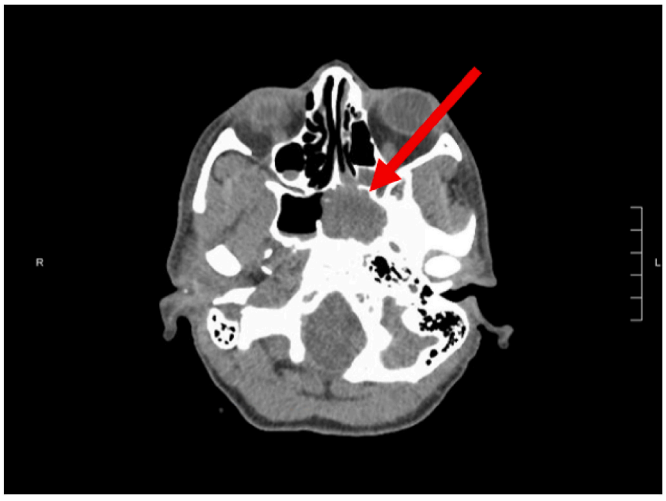

Fig. 2. CT head and neck with contrast in axial plane showed tissue attenuation bulging from the left sphenopalatine foramen to the left pterygopalatine fossa.

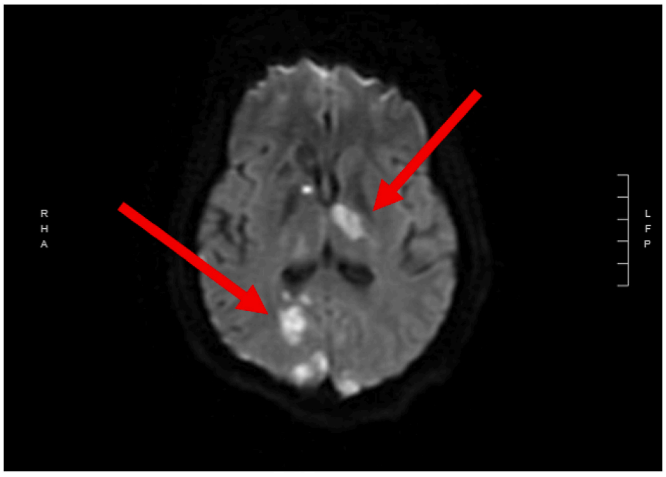

Fig. 3. MRI brain with contrast, axial diffusion weighted image showed extensive acute infarctions in the right and left occipital lobes and basal ganglia, and a subacute caudate lesion.

diagnostic nasal endoscopy with tissue biopsy on day 5. Sphenoid tissue revealed necrotizing invasive fungal sinusitis with granuloma formation and foreign-body giant cell reaction. Tissue culture was positive for *Pseudomonas putida*, *Staphylococcus epidermidis*, and *Bipolaris* species. The culture was sent to an outside fungal testing laboratory, which found that it most closely resembled *Curvularia buchloes* (formerly *bipolaris buchloes)*. The species was found to be sensitive to amphotericin B with a minimum inhibitory concentration (MIC) of 0.03 mcg/mL, caspofungin with MIC of 0.25 mcg/mL, fluconazole with MIC of 32 mcg/mL, and posaconazole and voriconazole both with MIC of 0.125 mcg/mL. For *Curvularia* species however, there are no establish breakpoints for the minimum inhibitory concentration.

The primary pathogenic organism was believed to be the *Curvularia* species due to the patient's history of a kidney mass positive for fungal hyphae, negative Galactomannan testing to rule out *Aspergillus* species, and sphenoid tissue mass speciation. After initial broad-spectrum antibiotics from day 6 to day 8, the patient was placed on IV amphotericin B (2.5mg/kg body weight) on day 9 for approximately 22 days during her hospitalization. However, she was switched to 200mg PO voriconazole BID on day 30 for 2 days due to shortage of IV amphotericin B. While the patient's infection stabilized throughout her hospital course, her neurologic deficits did not significantly improve. Head and neck imaging was performed during her treatments on day 14 and day 22 of hospitalization, but did not show significant changes compared to admission. She was discharged to inpatient rehabilitation on day 32.

3. Discussion

While most cases of fungal infection occur in immunosuppressed patients, immunocompetent patients can also develop invasive fungal infections as in this case of chronic infectious fungal sinusitis. CIFS is infrequently diagnosed and its indolent nature with progression over weeks or months can make diagnosis and treatment difficult [5,10,11]. The most frequent fungal species identified are the *Aspergillus* species, but *Curvularia* species have been found as well [7–9,11]. Usually, *Curvularia* species is associated with less severe diagnoses, including allergic rhinosinusitis, onychomycosis, and dermatitis [7]. Previous studies have also associated intranasal illicit drug use as a potential cause of CIFS, however it is not well documented [5,12]. Notably, our patient had a previous history of cocaine abuse and perfume inhalant which could have contributed to her infection.

Intranasal use of cocaine causes vasoconstriction due to its sympathomimetic effects to elicit sinonasal tissue ischemia and cerebral vasospasm. With extended use, chronic mucosal inflammation can occur that can result in sinonasal osteocartilaginous necrosis [13,14]. Necrotic tissue can then serve as a nidus for invasive fungal organisms, which has been previously found in samples of cocaine [15]. The susceptibility of the damaged tissue can then result in CIFS. Additionally, intranasal cocaine use can induce cerebral vasospasm and platelet aggregation which can precipitate strokes [16]. Although our patient showed components of vascular disease in her posterior circulation that could be attributed to vasospastic etiology, given the severity of her fungal infection, it is more likely that her strokes were due to fungal infection. She likely developed CIFS as a result of cocaine and inhalant use, which ultimately led to fungal cerebrovascular disease and significant multifocal strokes. The presence of fungal elements in her kidney mass also raised concern for metastatic infection. However, blood cultures remained negative for fungemia.

The diagnosis of CIFS is dependent on histopathologic demonstration of fungal invasion of biopsied regions. Imaging modalities including CT and MRI scanning can be suggestive, but are not sufficiently specific or sensitive [17].

The main interventional modalities include surgical debridement and antifungal therapy to maximize survival [18]. Historically, patients required treatment for 5–18 months with amphotericin B or voriconazole [9,19]. However, studies now suggest that voriconazole may

be the drug of choice due to prevalence of Aspergillus species etiology [20]. Antifungals including amphotericin B, caspofungin, fluconazole, posaconazole, and voriconazole are shown to be effective against the *Curvularia* species. While some strains may be resistant to specific antifungal therapy, our patient was not resistant to any of the listed therapy. Overall survival rates are not well documented, but outcomes depend on prompt diagnosis and management. Suspicion for invasive fungal infection should be higher in patients with a history of intranasal drug or inhalant use, particularly if they have symptoms of nasal obstruction, infraorbital swelling, altered mental status or proptosis. While invasive *Curvularia* fungal infections in immunocompetent patients are very rare, treatment is similar to other causes of CIFS, including debridement and long-term antifungal therapy.

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Consent

Written informed consent was obtained from the patient or legal guardian(s) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of competing interest

There are none.

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