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Mucormycosis: A Fatal Case by *Saksenaea vasiformis*

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A fatal case of mucormycosis in a previously healthy 26-year-old woman who developed a progressive necrotizing lesion is presented. Histopathological and mycological studies revealed the presence of a Zygomycete, which after several cultures proved to be *Saksenaea vasiformis*. No underlying pathological condition was detected. This case might prove to be the first one of fatal *Saksenaea vasiformis* infection reported in Latin America, and only the 4th one in the world literature. The relevance of mucormycosis in the diagnosis and management of necrotizing cellulitis is stressed.

Mucormycosis is a particularly aggressive entity caused by saprophytic fungi of the class Zygomycetes, order Mucorales, which can cause fulminant necrosis of the skin and subcutaneous tissues, difficult to differentiate from necrosis due to anaerobic and aerobic bacteria. This entity, because it is so infrequent, tends to occur only in hosts whose immune system is compromised by conditions that create a state of total or partial immune incompetence [1, 2].

In 1976 Wilson et al. [3] called attention to the need for including zygomycetic gangrenous cellulitis as a real possibility in the differential diagnosis of progressive, gangrenous and necrotizing lesions of the skin, especially in diabetics. These authors reported 2 cases, one of them fatal, and presented a review of the literature that included 9 additional patients.

This form of mycosis tends to remain unsuspected and, because of the usual concomitant infection by a multitude of microorganisms, is difficult to identify, and a late diagnosis is common. Because of the fulminating nature of this necrotizing mycotic infection, the chance of cure resides in an early diagnosis that allows prompt radical debridement and resection. Early diagnosis is possible only if, under a high index of suspicion, a biopsy is performed, which is the only effective and rapid means of establishing the diagnosis.

Our case is reported with the purpose of underlying the importance of this entity in the differential diagnosis and management of gangrenous fasceitis and necrotizing cellulitis. Because of its etiologic agent, *Saksenaea vasiformis*, it may prove to be the first case of its kind reported in Latin America and the 4th case anywhere in the world [4]; only 2 former cases appear in the published world literature [5, 6].

Case Report

A 26-year-old woman was admitted with massive necrosis of the right gluteal region, of an aggressive and rapidly progressing nature, following an intramuscular injection. The necrotizing lesion extended to cover the entire sacro-lumbar region and the right flank, leaving the muscular layers denuded (Fig. 1). She had been treated with gentamicin and clindamycin at another institution. The patient was extremely toxic; the widespread lesion presented purulent and fetid exudate and a white mold over the edges. A biopsy was taken, and the sections revealed the presence of a Zygomycete, confirming the diagnostic impression of a severe case of mucormycosis. The patient's condition continued to deteriorate with relentless progression of tissue necrosis, in spite of vigorous treatment with profuse lavage, resection, and debridements under general

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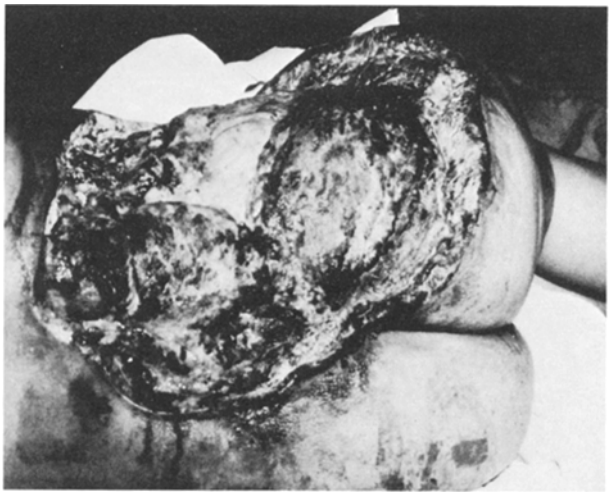

Fig. 1. Extensive destruction of gluteal, sacral, and flank regions by gangrenous cellulitis with purulent exudate and necrotic and violaceous margins.

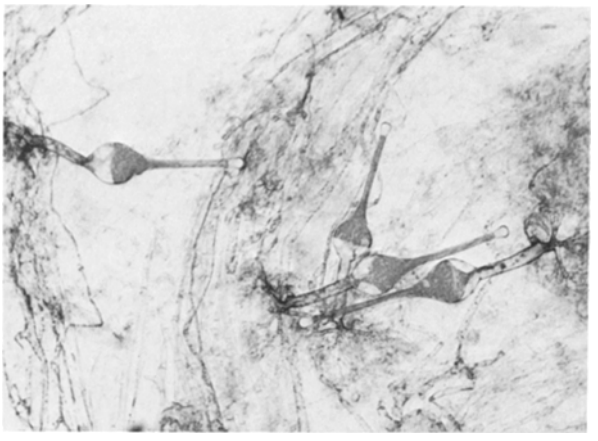

Fig. 2. Typical vase-like sporangia which identify the fungus as *Saksenaea vasiformis* (40 ×).

anesthesia, amphotericin B, and parenteral nutritional support; pulmonary infiltrates appeared over the left lung, and the patient died on the 5th hospital day, the 12th of her illness. Permission for autopsy was denied.

Direct examination of the necrotic material showed abundant hyphae that signaled the presence of a Zygomycete. Cultures on Sabouraud medium yielded a grayish mycelial growth. Microcultures with prolonged incubation and culture in bread-containing media [7] were negative, pointing toward a very uncommon fungus species. Considering the possibility of the genus *Saksenaea,* recently recognized as pathogenic, the culture from a Sabouraud-agar plate was placed in sterile water, a method that promotes the formation of fungal reproductive structures [6]. Three days later the typical vase-like

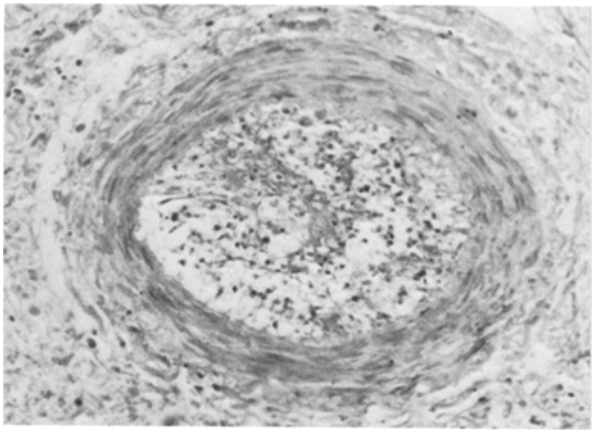

Fig. 3. Small-calibre vessel with thrombus formation composed of inflammatory cells and scarce hyphae whose walls stain weakly with Schiff (PASH ×150).

sporangia appeared, allowing the identification of this Zygomycete as *Saksenaea vasiformis* (Fig. 2).

Sections processed with special fungal stains showed the invasive trend of the lesion with penetration of the Zygomycete into the lumen of arterioles, with thrombi formation, findings that are quite characteristic of mucormycosis (Fig. 3).

Discussion

It is well known that certain primarily nonpathogenic fungi, when located in a favorable environment, acquire unusual pathogenicity, thus behaving as opportunistic organisms. Such is the case with fungi of the Zygomycetes class, Mucorales order, and Mucoracae, Cunninghamellaceae, Mortierellaceae, and Saksenaeceae families, organisms that are commonly encountered as natural saprophytes, but which in immunologically compromised hosts can give rise to acute clinical pictures that are rapidly progressive and often fatal [2, 8].

Invasion of arterial vessels is a prominent feature of the lesions caused by these Zygomycetes; this results in embolization, ischemia, and necrosis of surrounding tissues. Ischemic necrosis of the skin is typical, as is the usual dissemination and extension to other organs. Bruck et al. [9] has noted this occurrence in up to 27% of patients with extensive burns. The genera that are most commonly isolated from human lesions are *Rhizopus, Mucor,* and *Absidia,* with the recent addition of *Saksenaea* [5, 6] and *Cunninghamella* [10]. These entities can occur both in humans and animals, with members of the *Absidia* genus prominent as infecting agents in small animals [8].

Four main clinical presentations are distinguish-

able in humans: rhinocerebral, pulmonary, cutaneous, and visceral. Rhinocerebral mucormycosis is commonly caused by *Rhizopus oryzae* species; the mortality rate is high, up to 80% to 90% [11]. Pulmonary mucormycosis is progressive and often fatal [12], although some cases have been cured by pulmonary resection [13]. It has no specific roentgenographic characteristics, and diagnosis is difficult [1, 2, 14].

Cutaneous mucormycosis has acquired increasing importance in skin lesions and infections in surgical patients. It has been reported in association with certain elastic adhesive tapes [15, 16] and in ischemic ulcers of the legs [17]. Cutaneous forms tend to occur most frequently as secondary invasion in patients with extensive burns [9], with rapid conversion to ischemic necrosis and systemic dissemination [18] as a noteworthy feature; widespread tissue destruction is frequent [19]. It is possible that this infective complication may remain undisclosed in many patients with burns and other gangrenous lesions; surgeons must maintain a high index of suspicion when treating burns, ischemic ulcerations in diabetics, or necrotizing cellulitis, for mucormycosis may be gestating. In many cases, these forms of skin lesions may represent disseminated manifestations of mucormycosis [20].

Visceral mucormycosis, although scarce, has been reported occurring in the gastrointestinal tract [21–23], kidney [24], brain [25, 26], recipients of organ transplants [27, 28], and even in vascular grafts [29].

The case herein reported exhibits some interesting aspects. There was no antecedent evidence pointing to the presence of an underlying condition that could explain the extreme aggressiveness of the clinical course; apparently the fungus was deposited deeply in the muscular mass by injection, and this originated the entire process. Another outstanding aspect in this reported case is the etiologic agent, *Saksenaea vasiformis,* an infrequent Zygomycete but one that has recently ascended as an important pathogen [4–6]. Its isolation and identification, although not difficult, confront problems when its presence is not suspected, since it does not give rise to reproductive structures in the habitual culture media, as happened in this instance. Few cases of mucormycosis have been reported in the Colombian literature [30], this patient representing the first one due to *Saksenaea vasiformis* reported in this country. To our knowledge this is one of the very few cases reported in the world literature: 2 in the United States, 1 by Ajello et al. [6], 1 by Torell et al. [5]; one will soon be reported from Wisconsin, and there has been 1 case from Iraq, but diagnosed in London [4].

In conclusion, it must be stated that mucormycosis is a particularly aggressive and malignant form of fungal infection which causes fulminant necrosis of the skin and subcutaneous tissues, difficult to differentiate from the gangrenous and necrotizing lesions [3] that surgeons must confront as result of synergistic infections by aerobic and anaerobic microorganisms [30, 31]. Prognosis is ominous, considering that there is usually a serious underlying condition and that invasion is by a fungus singularly resistant to amphotericin B, the only therapeutic agent of any reliable activity against systemic mycosis [2]. This drug has shown benefit only in exceptional instances [11, 12] and was of no avail in our case.

Résumé

Un cas fatal de mucormycose concernant une femme de 26 ans en bonne santé et qui développa des lésions nécrotiques progressives est présenté. L'étude histopathologique et mycologique révéla à leur niveau la présence d'un zygomycète qui après plusieurs cultures s'avèra être un *Saksenaea vasiformis*. Aucune autre lésion sous-jacente ne fut décelée. Cette observation concerne le premier cas d'infection fatale par *Saksenaea vasiformis* rapporté en Amérique latine et le quatrième des cas publiés dans la littérature mondiale. L'implication de la mucormycose dans le diagnostic et le traitement de la cellulité nécrosante est soulignée.

Resumen

La mucormicosis es una entidad particularmente agresiva, causada por hongos saprofitos de la clase Zigomicetos, orden Mucorales, capaz de producir necrosis fulminante de la piel y de los tejidos subcutáneos difícil de diferenciar de las lesiones por infecciones bacterianas anaeróbicas y aeróbicas. La celulitis gangrenosa zigomicética debe ser considerada en el diagnóstico diferencial de las lesiones necrosantes de la piel, especialmente en diabéticos y en pacientes en estado de incompetencia inmunológica. En virtud de la naturaleza fulminante de este tipo de infección necrosante micótica, la posibilidad de curación depende de un diagnóstico precoz que haga posible realizar pronta resección y debridación radical.

Se presenta un caso de mucormicosis en una mujer de 26 años de edad, previamente sana, quien desarrolló una lesión necrosante progresiva y fatal. Los estudios histopatológicos y micológicos revelaron la presencia de un zigomiceto, que en cultivos probó ser *Saksenaea vasiformis*. Este caso puede ser el primero de infección fatal por *Saksenaea*

vasiformis informado en América Latina y el cuarto en la literatura médica mundial. Se hace énfasis sobre la relevancia de la mucormicosis en el diagnóstico y manejo de las celulitis necrosantes.

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