their entire length. The patient also underwent a right maxillary antrostomy, right anterior and posterior ethmoidectomy, as well as right sphenoidotomy. The wound was subsequently managed with wet-to-dry dressings using amphotericin-soaked gauze, and was otherwise allowed to granulate without additional grafts or flaps. Postoperatively, the patient suffered stroke in the distribution of the right middle cerebral artery secondary to intracranial angioinvasion. Fortunately, no major neurologic sequelae were noted. He was hospitalized for 5 weeks, and required 1 additional surgical debridement his second week for persistent necrotic tissue. He was treated with high dose intravenous liposomal amphotericin B (5 mg/kg/daily) for 4 weeks, along with posaconazole (200 mg PO tid) for 12 months, and systemic anticoagulation for 6 months. Final culture results did not show growth, but characteristic histopathologic findings were felt to be diagnostic. He remains disease free and without significant neurologic deficits 2 years later.

DISCUSSION

Cutaneous mucormycosis, accounting for 11–19% of all cases, is the third most common form after ROCM and pulmonary mucormycosis.[3,4] Direct fungal inoculation of the skin has been reported after wound trauma, lacerations, punctures by tree thorns, surgical injuries, burns, abrasions, insect bites, tattoos, contaminated adhesive tapes and dressings, and puncture sites from arterial lines and insulin injections.[3–5] Patients may present with lesions localized to the skin (56%), deep extension into subcutaneous tissues (24%), or disseminated infection (20%).[2,3]

Mucormycosis rarely develops in immunocompetent hosts as spores are readily phagocytosed by neutrophils and macrophages.[6,7] Immunocompromised patients, including those with acidosis, have impaired fungicidal activity resulting in spore germination and subsequent infection.[6] Of note, however, mucormycosis has been reported in patients with no underlying systemic disease, and cutaneous mucormycosis is most common in these instances.[2,6]

Mucor is an angiotropic fungus with a predilection for the internal elastic lamina of the blood vessels, often invading neighboring tissues via direct extension along vessels and nerves.[8,9] Orbital extension following cutaneous inoculation of the fungus has never been described, and likely occurred in this case via direct extension along the supratrochlear and supraorbital neurovascular bundles. Mortality from mucormycosis is estimated at 30% with cutaneous disease,[3] and reaching as high as 80% or more in ROCM cases with cerebral involvement.[7] In these cases, death usually results from intracerebral extension causing fatal cerebrovascular thrombosis or meningoencephalitis.[10]

The signs, symptoms, and radiographic findings of cutaneous and orbital mucormycosis are nonspecific, requiring histopathologic evidence or culture for diagnosis.[1] The aggressive nature of this disease requires rapid diagnosis, early intervention with antifungal therapy, and the reversal of the underlying immunocompromising conditions—in this case strict glycemic control and underlying acidosis.[5,9] The role of surgical debridement, and specifically the role of exenteration in ROCM, is considered controversial but may control extension and facilitate better penetration by antifungal medications.[9] Existing systemic antifungal treatments include intravenous liposomal amphotericin B and oral Posaconazole.[9,11]As was done in this case, following debridement of necrotic tissue local amphotericin dressings may be applied.[9] Other treatment modalities discussed in the literature include the use of hyperbaric oxygen, and treatment with 5-fluoro-cytosine therapy.[6,9]

Mucormycosis must remain on the differential of any immunocompromised or diabetic patient with nonspecific orbital findings,[12,13] even in the absence of naso-canthal eschar and sinus disease. As demonstrated above, secondary orbital mucormycosis may occur via direct extension following periorbital cutaneous inoculation. We attribute our patient's successful outcome to aggressive surgical debridement, prompt antifungal administration, and rapid reversal of underlying ketoacidosis.

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Increased Incidence of Rhino-Orbital-Cerebral Mucormycosis After Colorado Flooding

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Abstract: **In September 2013, central Colorado experienced a record amount of rainfall resulting in widespread flooding. Within 1 month of the flooding, 4 patients presented to the authors' institution with rhino-orbital-cerebral mucormycosis. This represents the largest number of cases ever recorded over a 1-month period. The authors hypothesize that the combination of immunocompromised status and environmental exposure resulted in the increased incidence.**

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Rhino-orbital-cerebral mucormycosis (ROCM) is a relatively rare fungal infection with severe morbidity and high mortality. An analysis of the largest reviews of ROCM shows an average incidence of less than 1 case a year.[1–3] An unusually high incidence of ROCM after severe local flooding is reported. This case series adheres to the principles of the Declaration of Helsinki and is in full compliance with Health Insurance Portability and Accountability Act standards.

CASE SERIES

In September 2013, record-breaking rainfall caused widespread flooding in the Denver-Boulder metropolitan area. Over the next month, 4 patients with ROCM presented to the authors' institution. Each case is specifically discussed below; the Table summarizes the clinical findings for each patient.

PATIENT 1

A 66-year-old man with recently diagnosed acute myelogenous leukemia status postinduction chemotherapy with cytarabine/clofarabine developed neutropenic fever on October 12. He initially presented to an outside hospital, where his workup was concerning for sinus disease. He underwent sinus debridement at that facility, then was transferred to the authors' institution for further management of presumed invasive fungal sinusitis involving the right maxillary and ethmoid sinuses. White blood cell count on arrival was <100 cells/μl. He was intubated and sedated, and immediately started on amphotericin B 5 mg/kg intravenously (IV) every 24 hours and anidulafungin 100 mg IV every 24 hours. Initial antifungal treatment for all patients in this series was based on a presumed diagnosis of mucormycosis and determined with the help of the infectious disease specialists. MRI at that time revealed continued right maxillary and ethmoid sinus disease, without evidence of orbital involvement. Repeat sinus debridement and culture revealed *Mucormycosis* (*Rhizopus oryzae*) with vascular invasion as the cause. Despite aggressive surgical debridement and antifungal therapy, the infection progressed. Follow-up MRI showed a new frontal cerebritis and right orbital involvement, but ophthalmic examination could not be completed due to his condition. His hospital course was complicated by transfusion-related lung injury and sepsis secondary to *Vancomycin-resistant Enterococcus*. Eleven days after admission to the hospital, the patient went into cardiac arrest and could not be revived.

PATIENT 2

A 42-year-old man with poorly controlled diabetes mellitus (DM) presented to an outside hospital on October 23 with skin changes on his left cheek after finishing a course of Augmentin and nasal rinses for presumed sinusitis. He underwent endoscopic sinus biopsies but developed complete ophthalmoplegia with no light perception (NLP) vision in the OS 1 day later. He was then transferred to the hospital where MRI showed involvement of his left orbit, maxillary, and ethmoid sinuses. On presentation, his glucose was 259 mg/dl and glycated hemoglobin (HbA1c) was 13.7%. He underwent urgent eyelid-sparing left orbital exenteration, sinus debridement, and resection of soft tissue facial necrosis. Medical therapy included amphotericin B 5 mg/kg IV every 24 hours and posaconazole 200 mg by mouth every 8 hours, and biopsy specimens from facial soft tissue were positive for M*ucormycosis* (*R. oryzae*). The patient continued to show necrosis of his facial soft tissues, and repeat MRI indicated involvement of his left cavernous sinus. He underwent subsequent soft tissue debridement including removal of his eyelids and medial brow (Fig. 1) and had an endoventricular drain placed for intrathecal amphotericin B. These treatments were able to control the infection, and 1 month later, the patient underwent facial reconstruction with an anterior lateral thigh free flap (Fig. 2).

PATIENT 3

A 52-year-old man with poorly controlled DM was initially admitted to the institution on October 30 with altered mental status, headache, right eye pain, and blood glucose of 598 mg/dl. Ophthalmic examination revealed right periorbital edema, a right afferent pupillary defect (APD), decreased motility, and visual acuity of 20/200 OD. MRI showed right-sided maxillary, ethmoid, and sphenoid sinusitis with orbital involvement. Urgent sinus biopsy and debridement were performed, which showed *Mucormycosis* (*R. oryzae*), and the patient was started on amphotericin B 5 mg/kg IV every 24 hours, posaconazole 200 mg by mouth every 8 hours, vancomycin, and piperacillin/tazobactam. The following morning, he was noted to have complete ophthalmoplegia and NLP vision OD. He underwent emergent eyelid-sparing orbital exenteration and repeat sinus debridement, but an MRI on the same day showed evolving cerebritis. Neurosurgery was consulted, but CNS involvement was determined too extensive to surgically debride. He was placed on comfort care and passed away 1 week later.

PATIENT 4

A 48-year-old man with poorly controlled DM was admitted to the authors' institution on November 4 with left-sided facial numbness and pain. On presentation, blood glucose was 152 mg/dl, and HbA1c was 7.5%. MRI showed left maxillary and ethmoid sinusitis, and the patient was diagnosed with invasive fungal sinusitis (*Mucormycosis*, *R. oryzae*) after bedside punch biopsy of the palate. He was started on amphotericin B 5 mg/kg IV every 24 hours, posaconazole 200 mg by mouth every 8 hours, and anidulafungin 100 mg IV every 24 hours, and underwent emergent left radical maxillectomy and left total ethmoidectomy. The next day, ophthalmology was consulted for decreased vision OS. Examination revealed vision of 20/100 OS, with a left APD and

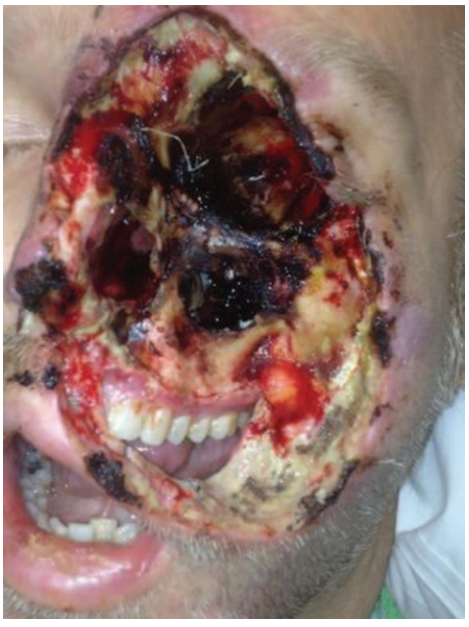

FIG. 1. External photograph of the patient after left exenteration and debridement of infected soft tissues.

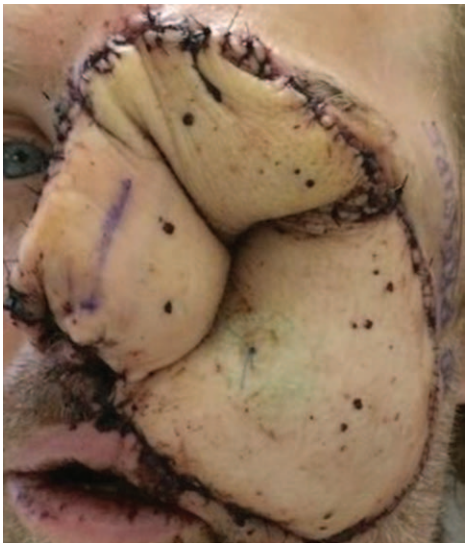

FIG. 2. External photograph of the same patient 1 week after reconstruction with free flap.

restricted motility. Repeat MRI showed left orbital involvement, and the patient was subsequently taken for left eyelid-sparing orbital exenteration and further sinus debridement. The infection was controlled with these treatments, and 3 weeks later, he was transferred to a skilled nursing facility on posaconazole for life. Plans for further orbital reconstruction are pending.

DISCUSSION

This case series of 4 patients with ROCM over a 1-month period represents the highest incidence of cases over a short time period reported in the literature. Over the previous 10 years at our institution, the senior author (V.D.D.) treated on average 1 patient with ROCM a year. This experience is consistent with some of the largest reviews of ROCM in the literature. Abedi et al.[1] reviewed 18 patients over a 25-year period, González et al.[2] reviewed 16 patients over an 18-year period, and Thurtell et al.[3] reviewed 14 patients over a 17-year period. These series combined average 1 patient every 15 months. In a recent review out of India, Bala et al.[4] reviewed 38 patients with mucormycosis over an 18-month period. Twenty-three of these patients presented with ROCM, giving an incidence of 1 patient every 24 days. In the post-flood period of the current series, the authors averaged 1 patient every 5.75 days.

While each patient in this series was immunocompromised, the authors hypothesize that the severe local flooding a month earlier resulted in increased mucormycetes in the environment, resulting in the spike in cases. An after action review by the Colorado Department of Public Health found that all patients had environmental exposure, and 3 of the 4 patients had direct contact with the flood waters. Genetic sequencing of the mucor isolates was done and showed that the species of *R. oryzae* were not clones. This suggests that the infections did not come from a single source but rather were a result of widespread environmental exposure. During a disaster, pathogenic fungi can be displaced from their natural habitat, which can increase their environmental concentration and introduce them to areas where they would not normally be found.[5] Riggs et al.[6] studied mold growth in homes affected by hurricane Katrina. They found that visible mold growth occurred in 44% of homes and heavy mold growth occurred in 16% and concluded that these levels had the potential to cause health problems.

Fungal infections have been previously described after natural disasters.[5] Inhalational outbreaks of *Coccidioides* have been described after earthquakes[7] and severe dust storms.[8] After the 2011 tornado in Joplin, Missouri, 13 patients acquired necrotizing cutaneous mucormycosis infections of their wounds.[9] All patients were immunocompetent, and all cases were caused by *Apophysomyces trapeziformis*. These cutaneous infections occurred after multiple traumatic injuries and were acquired from the natural environment as a result of exposure to organic material and water.[9] Only one other previous case series has looked at the ophthalmic manifestations from fungal infections after flooding. Sridhar et al.[10] reviewed 3 patients with ophthalmic complaints after exposure to hurricane flood waters. Two of these patients had allergic fungal sinusitis with a return to normal ophthalmic function, and only 1 had invasive fungal sinusitis resulting in permanent vision loss. Given these health concerns, the Centers for Disease Control recommends that susceptible individuals avoid exposure to disturbed mold. If exposure cannot be avoided, personal protective equipment such as gloves and a mask should be worn.[11]

This series represents the largest number of cases of ROCM recorded over a 1-month period. The high mortality rate (50%) in this series is consistent with previous studies.[1,2] Given that all patients in this series had post-flooding environmental exposure, the authors hypothesize that increased mucormycetes in the environment resulted in the infection in susceptible persons. While ROCM is a relatively rare infection, environmental factors including natural disasters can affect the incidence. Clinicians practicing in parts of the country prone to flooding should keep it in their differential when immunocompromised patients present with symptoms of upper respiratory tract and sinus infection. Early signs and symptoms are not specific to ROCM, so a low threshold for biopsy is important to timely diagnosis and treatment.

Clinical summary for each patient

Patient	Date of admission	Underlying condition	Ophthalmic examination	Species	Surgical intervention	Outcome
1	October 12	AML	Intubated	*Rhizopus oryzae*	FESS × 2	Death
2	October 23	DM	L orbital apex syndrome, NLP OS	*Rhizopus oryzae*	FESS × 2, facial debridement × 2, Lexenteration	20/20 OD, L facial reconstruction with free flap
3	October 30	DM	R orbital apex syndrome, 20/200 OD	*Rhizopus oryzae*	FESS × 2, R exenteration	Death
4	November 4	DM	OS: 20/100,+ APD, restricted motility in all gazes	*Rhizopus oryzae*	FESS × 2, L exenteration	20/20 OD

AML, acute myelogenous leukemia; APD, afferent pupillary defect; DM, diabetes mellitus; FESS, functional endoscopic sinus surgery; L orbital, left orbital; NLP, no light perception; R orbital, right orbital.

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Proliferative Fasciitis of the Orbit

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Abstract: **Proliferative fasciitis is a rare entity in the orbit. A 16-year-old boy presented with a growing right orbital mass, which was palpable just inferior to the medial right eyebrow. MRI demonstrated a 12 × 8 × 9 mm mass located medial to and slightly above the right globe within the subcutaneous soft tissues. An anterior orbitotomy with debulking of the lesion was performed. Histopathological examination confirmed a diagnosis of proliferative fasciitis. To the authors' knowledge, there is only one prior case in the literature demonstrating proliferative fasciitis of the orbit.**

Proliferative fasciitis can be found in the subcutaneous tissues of the extremities but is considered a rare entity in the orbit. Herein, the authors present a case of proliferative fasciitis originating in the orbit. This case report conforms to the tenets of the Declaration of Helsinki and is Health Insurance Portability and Accountability Act compliant.

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CASE REPORT

A 16-year-old boy presented with a mass, which was palpable in the medial aspect of the right upper eyelid. The patient denied any history of trauma or previous eye disease. The mass was first noticed by the patient approximately 5 months prior to presentation, and it had since increased in size, becoming more firm and somewhat uncomfortable. At the time of presentation examination, a 1.5 × 1 cm firm, nonmobile mass was noted just inferior to the medial right eyebrow (Fig. 1A). The patient described pain on palpation of the lesion. The patient's visual acuity was 20/20 OU. There was no proptosis, and extraocular movements were intact. MRI demonstrated a 12 × 8 × 9 mm focus of intermediate T1 signal that enhanced brightly and was located in the anterior superomedial orbit within the subcutaneous soft tissues of the medial brow (Fig. 1B). The lesion extended broadly to the bony orbit margin but without evidence of erosive changes to the adjacent bone. A right anterior orbitotomy with biopsy was performed for further evaluation and treatment of the lesion.

At the time of surgery, the lesion was noted to be pink-gray in color, poorly encapsulated, and adherent to the surrounding tissues, including those in the peritrochlear region. Most of the lesion was excised, with the exception of the immediate peritrochlear tissue, so as to minimize the risk of postoperative diplopia. Pathologic examination of the lesion showed a cellular but relatively bland spindle cell proliferation. The spindle cells were entrapped in hyalinized ropey collagen bundles. Mitotic activity was brisk. Scattered multinucleated giant cells were present, and of particular note, in some regions ganglion-like reactive cells admixed with entrapped muscle fibers were noted (Fig. 2). Immunohistochemical staining demonstrated occasional CD68-positive macrophages. The spindle cells were negative for S-100, desmin, and factor 13a. Smooth muscle actin was focally positive, supporting the diagnosis of a myofibroblastic proliferation. The final diagnosis was consistent with proliferative fasciitis. At most recent 6-month follow up, the patient was doing well but continues to be followed, understanding the potential need for additional treatment depending on his clinical course.

DISCUSSION

Prior to 1975, the term proliferative fasciitis was used synonymously with nodular fasciitis. At that time, Chung and Enzinger[1] first delineated proliferative fasciitis as an entity distinct from the nodular form. While both proliferative fasciitis and nodular fasciitis are benign fascial/subcutaneous lesions, proliferative fasciitis is more closely related to, and considered the cutaneous counterpart of, proliferative myositis.[2] Microscopically, proliferative fasciitis is characterized by a diffuse infiltrative fibroblastic growth associated with multifocal proliferations of large basophilic ganglion-like cells. This is in contrast to nodular fasciitis, which demonstrates a spindle cell proliferation lacking ganglion-like cells.[3] The tendency of proliferative fasciitis to grow rapidly in conjunction with its clinical and histologic features explain how this lesion has sometimes been confused with sarcoma, ganglioneuroblastoma, rhabdomyosarcoma, fibrosarcoma, and other malignant mesenchymal tumors.[1] Thus, awareness of the clinical presentation and microscopic features of this lesion can be helpful in making the correct diagnosis and guiding appropriate treatment.

The etiology of proliferative fasciitis is unknown, but in some cases, outside the orbit has been associated with preceding local trauma.[1,5] In a study reported by Chung and Enzinger,[1] 10 out of 53 patients had a history of trauma prior to presentation with proliferative fasciitis. Proliferative fasciitis occurs most frequently on the upper extremities, followed by the lower extremities and the trunk. It does not show a predilection for

