Mycetoma was first described by Dr. John Gill, while working in Madura, India, in 1842 (as recounted by Ahmed et al.\textsuperscript{1}). This disease is subclassified into 2 categories (“actinomycosis” and “true mycetoma”) according to the type of causative agent. Mycetoma is a pathological process in which eumycotic (fungal) or actinomycotic (bacterial) causative agents from an exogenous source produce grains. It is a localized, chronic, and deforming infectious disease of subcutaneous tissue, skin, and bones. It occurs in the so-called mycetoma belt stretching between the latitudes of 15°S and 30°N, and is endemic in relatively arid areas.\textsuperscript{4} The organisms are present in the soil and may enter the subcutaneous tissue by traumatic inoculation. The infection then spreads through the fascial planes and destroys connective tissue and bone. In the bone, the cortex is invaded and masses of grains gradually replace osseous tissue and marrow. Poor personal hygiene, malnutrition, any history of trauma, wounds on bare feet, and multiple systemic infections may predispose an individual to the development of mycetoma, and it occurs mainly among farmers, herdsmen, field workers, and those who walk barefoot.

The clinical manifestation of mycetoma includes a triad of tumefaction, draining sinus tracts, and grain formation and extrusion. The most commonly affected site is the foot (70%); however, other exposed body parts such as the hand, leg, knee, arm, thigh, and perineum can be infected occasionally.\textsuperscript{7} Craniofacial mycetoma is extremely rare, especially that caused by fungi, and is the most difficult form to treat.\textsuperscript{7} Gumaa et al.\textsuperscript{5} showed that mycetoma involving the head and neck accounted for 15 (3.75%) of 400 cases. An investigation by Lynch\textsuperscript{10} indicated that the rate of cranial infection was only 3 of 317 cases in eumycetoma and 15 of 233 cases in actinomyce-toma; that is, 15 of 18 mycetoma infections of the head were due to actinomycetes.

Craniofacial mycetoma is extremely rare; only 2 cases have been reported so far in the world literature. We describe a case of maduromycetoma involving the right parietal cortex, overlying bone, and subcutaneous tissue. Interestingly, the previous 2 reports also involved the parietal lobe.

**Case Report**

**History and Examination.** This 17-year-old girl, who belonged to a farm family, presented with a 2-year history of recurrent generalized seizures, a progressively increasing right parietal scalp swelling for 3 months, and discharging sinus in the right parietal scalp wound for 2.5 months. There was no history of any obvious trauma or injury to the head or scalp. However, the patient reported a history of carrying wooden sticks on her head as a daily household routine. She also gave a history of incision and
The results of routine laboratory investigations were within normal limits, and the Western blot test was negative for HIV. Findings on the chest radiograph were normal, but the skull radiograph showed 2 well-defined radiolucent osteolytic areas in the right parietal region (Fig. 1A). A CT scan of the brain obtained with contrast material revealed 2 well-defined, hyperdense, enhancing extraaxial lesions measuring 19 × 18 mm and 12 × 10 mm in the right parietal lobe, with scalloping and erosion of overlying parietal bone (Fig. 1B) and perilesional vasogenic edema. The patient underwent surgery for gross-total removal of the lesion, along with the involved dura mater, bone, and scalp.

**Operation and Postoperative Course.** Subcutaneous pus and necrotic tissue with thick adhesions were noted intraoperatively. A black, well-defined lesion was noted to infiltrate the bone and dura mater and was invading the cerebral tissue. A craniotomy was done. The bone was thinned out and fragile and was infiltrated at some places. The dura was incised 2 cm away from the lesion. There was a good plane of cleavage between the lesion and the brain, except at some places the lesion was infiltrating the cerebral tissue. Gross-total excision of the lesion was done, along with the involved dura and the bone. Duraplasty was performed and the bone flap was replaced after obtaining a clean margin. The involved scalp was excised, and primary closure of the healthy scalp margins was done. Immediate and delayed postoperative periods were uneventful.

**Histopathological Examination.** On gross examination, the biopsy material was composed of brown-black, 2- to 4-mm grains admixed with pieces of gray-white, soft tissue. On microscopic examination, the grains were seen as rust-brown, oval colonies of long interfacing filamentous fungi (seen as negative shadows on H & E staining) embedded in a brown matrix (uniform cement-like material) and surrounded by neutrophilic exudates. The Splendore-Hoeppli phenomenon was not prominent. The gray-white, soft tissue showed brain parenchyma with fibrosis and dense inflammatory cell infiltrate on the meningeal surface. The inflammatory infiltrate was composed of neutrophils, lymphocytes, plasma cells, histiocytes, and foreign-body giant cells. Microabscess formation was also seen. The fungal hyphae were better seen in specimens prepared with PAS staining. Gomori methenamine-silver stain demonstrated the fungal colonies to be composed of radially arranged, septate filamentous hyphae, which were distributed throughout the grains. The dura mater and bone had similar histopathological results. The gross and microscopic findings in the lesion we describe are characteristic features of eumycotic mycetoma, which is also known as maduromycosis (Fig. 2).

At her 6-month follow-up visit, the patient had no neurological deficits, she was seizure free on oral phenytoin therapy, and there was no discharging sinus. Postoperative MRI studies of the brain (obtained with contrast at 4 months) revealed gliosis at the surgical site (Fig. 3).

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**Fig. 1.** A: Skull radiograph showing radiolucent osteolytic areas in the right parietal region (arrows). B: Head CT scan, bone window, showing osteolytic area in the right parietal region. C and D: Coronal and sagittal reconstructed brain CT scans obtained with contrast material showing 2 dense, nonenhancing extraaxial lesions (arrows) in the right parietal region and erosion of overlying skull bone.

**Fig. 2.** Photomicrographs showing biopsy specimens. A: Black-brown grains appearing as rust-brown colonies surrounded by acute inflammatory exudates. Inset: Within the grains, fungal hyphae are seen as negative shadows (black arrows). B: Adjacent brain parenchyma with inflammatory infiltrate and fibrosis on the meningeal surface. Inset: Giant cells and histiocytes are seen. C: Section showing long filamentous fungal hyphae (blue arrow) within the grains. D: Section showing filamentous septate hyphae (black arrows). H & E (A and B), PAS (C), and Gomori methenamine-silver (D). Original magnification × 40 (A), × 100 (B), and × 400 (insets [in A and B], C, and D).
Craniocerebral maduromycosis

Discussion

Hickey\(^8\) reported 3 instances of cranial maduromycetoma without penetration of the dura mater in 1950. One case involved the cranial vault quite extensively in a 20-year-old shepherd, and only a biopsy procedure was done (not excision). The other 2 cases, which occurred in a 30-year-old farmer and a 24-year-old shepherd, were sinocranial and involved the orbits and paranasal sinuses. In both cases, the lesion was surgically removed, necessitating enucleation of the eyeball in the farmer. Lynch\(^{10}\) reported in 1964 that 3 of 18 mycetoma infections of the head were due to eumycetoma, of which only 1 was caused by \textit{Madurella mycetomatis}.

The first reported case of eumycetoma (maduromycosis) involving the cerebral cortex in the English literature was reported by Natarajan et al.\(^{13}\) in India in 1975. Their patient had a pyogenic brain abscess at the site of the cranial mycetoma (Table 1); the causative organism was \textit{M. mycetomatis}. Eumycetoma presenting as a tumor of the mandible was reported in 1975 by Gumaa and colleagues;\(^6\) the causative organism was \textit{M. mycetomatis}. Gumaa et al.\(^4\) reported in 1986 that only 2 of 15 mycetomas involving the head and neck were caused by \textit{M. mycetomatis}. Eumycetoma presenting as a cerebellopontine lesion was reported by Sai Kiran et al.\(^{14}\) in India in 2007; the causative organism was \textit{Pseudallescheria boydii}.

The second reported case of maduromycosis involving the cerebral cortex was reported by Beeram et al.\(^2\) in India in 2008; the causative organism was \textit{M. mycetomatis}. Oral cavity mycetoma was reported by Nai et al.\(^{12}\) in 2011.

Mycetoma is more common in males; the male/female ratio ranges between 3:1 and 4:1.\(^3\) This disease occurs mainly among farmers, herders, field workers, and those who walk barefoot. In the 2 previously reported cases, the patients were young male farm laborers. Our patient was a young female belonging to a farm family in a rural area with an arid climate. Black-grain fungi cause eumycetoma in arid regions, whereas white-grain fungi cause eumycetoma in regions with higher rainfall and without a significant dry season.\(^3\) In our case and in the 2 previously reported cases, maduromycoses (black-grain fungi) were present.

In addition, in our case and in the 2 previously reported cases, a history of seizure was present, whereas neurological deficit was only present in the case reported by Natarajan et al.\(^{13}\). Seizures seem to be the most common symptom of craniocerebral maduromycosis. In the present case and in the previously reported ones, the lesion involved the parietal region; this seems to be the most common site of craniocerebral maduromycosis.

There are some conflicting reports about the role of the immune status of the susceptible population. Some investigators have reported partial impairment of the cell-mediated immune response in severely infected patients or in those who do not respond to medical treatment. Eumycetoma has not been reported in HIV-infected patients.\(^7\) The patient in our study was immunocompetent.

### TABLE 1: Literature review with demographic data, treatment, and outcome in 3 patients with craniocerebral maduromycetoma*

<table>
<thead>
<tr>
<th>Demographic Data</th>
<th>Natarajan et al.</th>
<th>Beeram et al.</th>
<th>Present Study</th>
</tr>
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<tr>
<td>condition on follow-up</td>
<td>discharging sinus</td>
<td>discharging sinus</td>
<td>no discharging sinus</td>
</tr>
</tbody>
</table>

* neuro = neurological; NR = not reported.

Fig. 3. Postoperative T1- and T2-weighted MRI studies of the brain (axial sections) showing gliosis at the surgical site (arrows).
In the maduromycoses, osteolytic changes predominate on radiographs, and although some sclerosis occurs around the lacunae produced, osteogenesis is usually not marked. The area of bone destruction characteristically forms circles or segments of circles simulating Gruyère cheese. In contrast, the bone lesion associated with actinomycosis shows a reticulated appearance due to osteolysis, but there is also marked osteogenic activity and often periosteal formation.\textsuperscript{10} Purely osteolytic lesions with sclerotic changes are seen in the foot, whereas in the skull, changes are mainly sclerotic, with few osteolytic areas.\textsuperscript{5} In our case, there were osteolytic lesions. A “dot in circle” sign on MRI studies is considered specific for mycetoma.\textsuperscript{7} In the present case, a preoperative MRI study was not done.

In the past, the recommended treatment for localized eumycetoma due to \textit{M. mycetomatis} was excision supplemented by griseofulvin and penicillin G procaine.\textsuperscript{11} In the 2 previously reported cases of cranio-cerebral maduromycoses, neither streptomycin with penicillin (advocated by Natarajan et al.\textsuperscript{13}) nor itraconazole (advocated by Beeram et al.)\textsuperscript{2} could eliminate the fungus completely, and both patients continued to have discharging sinuses at follow-up. In his time, Hickey\textsuperscript{8} had no medical treatment available at all. In our case, however, the patient was given voriconazole and terbinafine, and there was no discharging sinus on follow-up. The treatment of mycetoma is difficult, and failure is not uncommon. Generally, the response is better in cases of actinomycetoma than in eumycetoma. Early diagnosis followed by antifungal treatment in combination with excision appears to be a reasonable treatment.

\section*{Conclusions}
Maduromycetoma involving the cranio-cerebral [cranio-cerebral] is extremely rare. We report the third case of cranio-cerebral maduromycetoma. Although \textit{M. mycetomatis} is the major cause of eumycetoma, little is known about its ecology, the most susceptible hosts, and host-pathogen interactions. This disease should be discussed by public health authorities and the scientific community, which can help in its early diagnosis and treatment.

\section*{Disclosure}
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Goel, Gupta. Acquisition of data: Goel, Gupta, Jain. Drafting the article: all authors. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Kataria. Study supervision: Sinha.

\section*{References}


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