Cerebral mycetoma with cranial osteomyelitis

Case report

VAMSEEMOHAN BEERAM, M.Ch.,1 SUNDARAM CHALLA, M.D.,2 AND PRASAD VANNEMREDDY, M.D.1

Departments of 1Neurosurgery and 2Pathology, Nizam’s Institute of Medical Sciences, Hyderabad, India

Mycetoma is a chronic granulomatous infection caused by true fungi (eumycetoma) or bacterial actinomycetes (actinomycetoma). The first description of this disease is usually attributed to Dr. John Gill, who reported “Madura foot” in a dispensary report of the Madras Medical Service of the British Army in India, in 1842. Mycetoma is characterized by the presence of a subcutaneous mass and multiple sinuses draining pus, blood, and fungal grains. The grains, also known as sclerotia, are aggregates of the fungal hyphae or the bacterial filaments, sometimes embedded in a tough, cement-like material. The shape and color of the grains provide clues about the species of causative organism. The presence of the triad of tumefaction, draining sinuses, and sclerotia defines mycetoma. Usually the dorsal aspect of the foot is involved, but lesions of the hand, leg, torso, arm, and thigh have also been reported. When the scalp is involved, the infection usually starts in the back of the head and neck. The causative agents include a wide variety of filamentous bacteria (actinomycotic mycetoma) and fungi (eumycotic mycetoma). In the medical literature only 1 other case report exists in which a madura mycetoma involved the cranium and its contents.

Case Report

History and Examination. This 18-year-old man, a farm laborer, presented with a small scalp swelling of 1.5 years’ duration, located in the posterior parietal region on the left side. Swelling had progressively increased and the patient underwent an operation performed by a local surgeon, the details of which could not be obtained. A pus-discharging sinus developed in the upper part of the wound during the early postoperative period. This sinus continued to discharge purulent material for the next 6 months until the patient was admitted to our hospital after an episode of generalized tonic-clonic seizure. Results of his general physical and neurological examination were unremarkable. Local examination of his scalp revealed a pus-discharging sinus in the upper part of the surgical scar with adjacent fibrosis. Routine laboratory investigations were nondiagnostic, and repeated Western blot tests were negative for HIV.

Operation. Subcutaneous pus and necrotic tissue with thick adhesions were noted intraoperatively. A blackish blue, well-defined lesion was noted to infiltrate the bone, dura, and underlying cerebral tissue. The bone was thinned out and fragile and was infiltrated up to its midline in some places (Fig. 2). The dura mater was incised away from the lesion, and nearly 2 cm of the surrounding dura was excised en bloc along with the attached lesion. The lesion was friable and separated from the surrounding brain by a thick gliotic scar. Gross-total excision was performed, and the patient was placed on a 6-week regimen of itraconazole. To the authors’ knowledge, this is the first instance of cerebral mycetoma with CT findings reported in the literature.

Key Words • cranium • fungal granuloma • mycetoma • osteomyelitis

Abbreviation used in this paper: CT = computed tomography.
able and fairly well-delineated from the surrounding brain parenchyma. Reactive gliotic tissue was observed in the adjacent brain parenchyma. Throughout the procedure, lesion spillage was avoided by keeping the surrounding tissues covered; copious irrigation with antibiotic solution was applied after the excision. Duraplasty was performed and the bone flap was replaced after obtaining a clean margin. Skin flap rotation covered the sinus defect. Steroids and antibiotics were administered intraoperatively. The patient made an uneventful recovery and remained neurologically stable throughout the hospital stay. On discharge, the patient was prescribed a regimen of 200-mg itraconazole every 8 hours for the first 3 days, and then every 12 hours for the next 6 weeks.

Histopathological Examination. Histopathological examination revealed multiple abscesses composed of neutrophils and mononuclear cells in the brain parenchyma. Among the abscesses there were 2–4-mm granules, which appeared rust brown on H & E staining and were embedded in a uniform cement-like material (Fig. 3). Some granules showed a central pale color. Staining with Gomori silver methenamine showed hyphal filaments with swollen cells at the periphery of the granules. Foreign body giant cells surrounded these granules. The dura mater and bone showed similar pathological characteristics. Potassium hydroxide testing revealed fungi with black spores. The dura and bone had similar histopathological results. The gross and microscopic findings of the lesion we describe are characteristic features of maduramycosis. Cultures of the granules grew black spore–forming fungi consistent with Madurella mycetomi.

Second Presentation and Follow-Up. The patient presented with a pus-discharging sinus at the surgical site after a 5-month period without symptoms. Wound debridement was performed and tissue was sent for microbiological evaluation. The results of staining and cultures not could identify bacterial or fungal growth at this time, and a CT scan did not reveal recurrence of the granuloma. The patient continues to attend regular follow-up.

Fig. 1. Contrast-enhanced CT scan of the brain showing the lesion with central necrotic area and involvement of cranial vault and soft tissue swelling. There is edema toward the parietal lobe.

Fig. 2. Intraoperative photograph of the lesion. The undersurface of the craniotomy shows erosion and infiltration by the lesion. The brain parenchyma had a thick gliotic response, and the lesion appeared as black friable tissue with interspersed necrotic areas. Dural hitch sutures were applied and the surrounding brain was covered to prevent spillage.

Fig. 3. Photomicrogram showing multiple abscesses composed of neutrophil and lymphomononuclear cells in the brain parenchyma. There were black granules composed of club-shaped filamentous structures in the center of the abscess. Foreign body giant cells surrounded these granules. H & E, original magnification × 10.
Cerebral mycetoma

Discussion

Mycetoma is a chronic granulomatous infection caused by true fungi (eumycetoma) or bacterial actinomyces (actinomycetoma). Madurella mycetomatis is 1 of 23 fungal species that cause mycetoma, and it belongs to the Monosporium epipermosum subgroup. Traumatic injury to local tissue is considered its route into the subcutaneous tissue, where these saprophytic fungi cause chronic granulomatous inflammation. 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 narrow. The appearance of various granules on pathological examination is characteristic and allows a specific diagnosis of the causative organism. These grains, also known as sclerotia, are aggregates of fungal hyphae or bacterial filaments, sometimes embedded in a tough, cement-like material. The morphological characteristics and color of the grains provide clues about the species of the agents.

Mycetoma is clinically manifested by the appearance of painless papules or nodules that swell up and rupture, leading to sinus tract formation. As the infection spreads, similar lesions appear in adjacent skin and soft tissues. The tissue undergoes a recurring cycle of swelling, suppuration, and scarring. Ultimately the infected site becomes a swollen, deformed mass of destroyed tissue with many fistulas through which grains are discharged.

In 1950 Hickey reported on 3 instances of cranial maduromycetoma without penetration of the dura. One case involved the cranial vault quite extensively in a 20-year-old shepherd, and only a biopsy was done (not surgical excision). The other 2 cases, 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. There was no chemotherapy. In 1975, the first reported case of mycetoma involving the cerebral cortex in the English literature was reported by Natarajan et al. Their patient had a pyogenic brain abscess at the site of the cranial mycetoma. Both their case and the one in the present study occurred in the parietal region of young men with a long history of swelling and discharging sinus. Ours is the first case in which a cerebral mycetoma/granuloma was identified without secondary infection.

Susceptibility data for a large number of clinical isolates were obtained for the antifungal agents amphotericin B and itraconazole. Most isolates were more susceptible to itraconazole, which might be the most obvious current choice for therapy of mycetoma. Currently, itraconazole and ketoconazole are the best treatment options. Itraconazole at 400 mg/day is the usual prescribed dosage in adults. The duration of treatment varies with the severity of the infection and the general health status of individual patients. Treatment may need to continue for years, and the liver function of such patients requires regular monitoring. Clinical follow-up at the Mycetoma Research Center in Khartoum, Sudan has shown that itraconazole treatment has high success and low recurrence rates. After treatment with itraconazole, these lesions remain well-encapsulated, localized, and easily excisable. The disadvantage of the azole drugs is their cost, which limits immediate availability to some patients. It may be noted at this point that neither streptomycin with penicillin (advocated by Natarajan et al.) nor the itraconazole could eliminate the fungus completely, and both patients continued to have discharging sinuses at follow-up. In his time, Hickey had no medical treatment available at all.

There are some conflicting reports about the role of the immune status of the susceptible population. Some investigators reported partial impairment of the cell-mediated immune response in severely infected patients or in those who do not respond to medical treatment. In patients with HIV infection, pulmonary mycetoma is associated with Pneumocystis carinii pneumonia, and HIV-infected individuals show a tendency toward accelerated mycetoma progression. The small number of case studies available on HIV-positive patients who present with various forms of mycetoma does not yet allow definite conclusions to be drawn concerning the relationship between immune status and mycetoma susceptibility and progression. The host in the present study was immunocompetent.

Conclusions

Madaura mycetoma involving the cerebrum is extremely rare. We report on the second case of craniocebral maduromycetoma. Early diagnosis followed by antifungal treatment in combination with surgical excision appears to be a reasonable treatment. However, the disease has been ignored by public health authorities and neglected by the scientific community. Consequently, the infection remains difficult to treat and diagnose properly. Although M. mycetomatis is the major cause of eumycetoma, little is known about its ecology, the most susceptible hosts, and the host–pathogen interactions. Many questions remain to be answered, but this entity must be considered in view of the spread of acquired immunosuppression and the globalization of trade.

References


Address correspondence to: Prasad Vannemreddy, M.D., Department of Neurosurgery, Nizam’s Institute of Medical Sciences, Hyderabad, 500 082, India. email: prasad4458@hotmail.com.