"Madura Head"—A Rare Case of Craniocerebral Maduromycosis

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Abstract

As maduromycosis is mostly confined to lower extremities. It was rightly named as "Madura foot" by John Gill in 1842, after the name of Madurai district, in Tamil Nadu state of India. Mycetoma is a chronic granulomatous infection mostly caused by a true fungus, *Madurella mycetomatis* (*Eumycotic mycetoma*). Craniocerebral involvement by eumycotic mycetoma is rare in world literature and confined to few case reports only. Here we present an interesting case of craniocerebral maduromycosis presenting with focal seizure, hemiparesis, and multiple discharging sinuses all over the scalp. The patient was diagnosed by histopathologic biopsy and managed conservatively with antifungal medications in view of widespread involvement of the scalp, not amenable to surgery.

Keywords
- craniocerebral maduromycosis
- Madura head
- "dot-in-circle" sign

Introduction

Eumycetoma is a chronic granulomatous infection of fungal origin characterized by extensive subcutaneous nodules, associated with sinuses draining pus, blood, and fungal grains. Although commonly depicted as "Madura foot" because of its affinity for lower extremities, other parts such as the hand, back, perineum, and paranasal sinus are also frequently affected. Craniocerebral involvement by this fungus involving the scalp, skull bone, and brain is very uncommon and restricted to few case reports in medical literature. The story of a small infective focus over scalp, which gradually progressed to cause disastrous effect in the skull bone, dura, and brain, resulting in hemiparesis with intractable seizure, is depicted in this case report with review of literature.

Case Description

A 32-year-old man presented to us with multiple episodes of generalized seizure and left sided weakness for last 1 year. About 2 years back the patient noticed a gradually enlarging nodular mass over the scalp, which subsequently burst out with discharging pus. Since then numerous small nodular scalp lesions have appeared and burst, eventually leading to multiple discharging sinuses with different stages of healing. For the last 1 year he has been having multiple episodes of generalized convulsions with loss of consciousness, which became more frequent in recent months. Simultaneously he noticed weakness of both the upper and lower limbs in left half of the body. Now he could barely walk without support.

Being a wood picker by profession, he showed history of scalp injury several times while carrying wood over his bare head in the past. He was not a known case of tuberculosis, diabetes, and human immunodeficiency virus (HIV).

Local examination of the scalp revealed multiple nodular masses with discharging sinuses and discolored, healed scars (►**Fig. 1A–C**). Multiple cervical lymph nodes were enlarged with overlying discolored skin.

Neurologic examination showed bilateral papilledema with left hemiparesis (grade 4/5). All the remaining cranial

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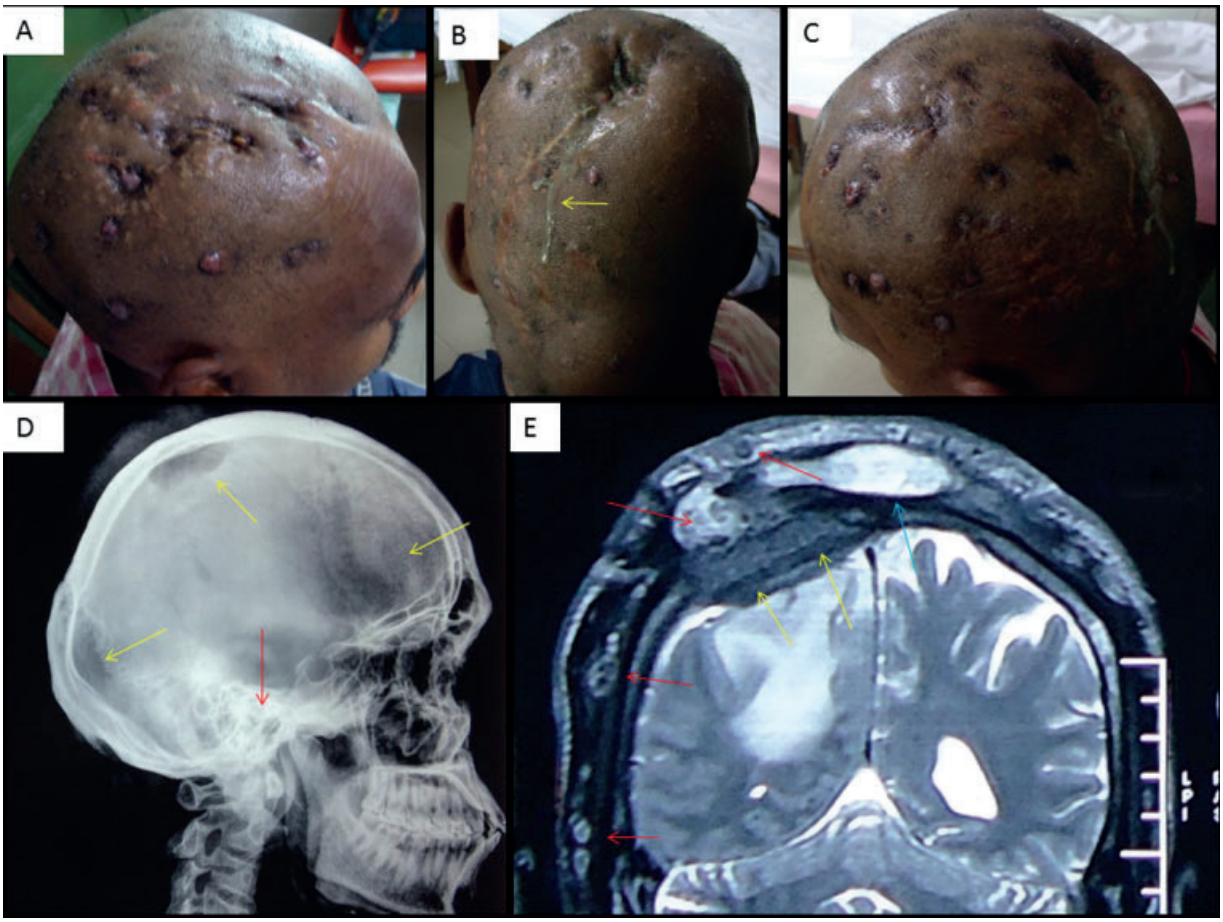

Fig. 1 (**A–C**) Multiple nodular scalp lesions over frontal/ parietal/temporal/occipital region with discharging pus from sinus (yellow arrow). (**D**) X-ray of skull bone showing petrous bone sclerosis (red arrow) along with punched out lytic lesions (yellow arrows). (**E**) T2W MRI coronal section showing multiple "dot-in-circle" signs (red arrows) all over scalp with a hyperintense area over scalp (blue arrows) suggesting an abscess with bony changes (yellow arrows).

nerves were intact with no sensory deficit. There were no cerebellar or meningeal signs.

Routine laboratory investigations were normal except high erythrocyte sedimentation rate (ESR) and C-reactive protein. X-ray of the skull bone revealed multiple radiolucent areas suggestive of bone erosion along with petrous bone sclerosis (►**Fig. 1D**). Magnetic resonance imaging (MRI) of the brain revealed an extra-axial lesion over right frontoparietal region abutting superior sagittal sinus, featuring T1 hyperintensity, T2 hypointensity with irregular contrast enhancement and perilesional edema (►**Fig. 1D,** ►**Fig. 2A–C**). Multiple contrast-enhancing lesions were found all over the scalp (►**Fig. 2B**). Multiple fungal grains surrounded by granuloma and fibrous septa were typically seen as "dot-in-circle" sign in T2W/FLAIR (fluid-attenuated inversion recovery) sequence of MRI (►**Fig. 1E**). Restriction in diffusion-weighted image (DWI) suggests microabscess (►**Fig. 2C**).

In view of extensive infected scalp lesions, the plan for complete excision of the lesion was not a viable option at that time. An excisional biopsy of the scalp nodule was performed under local anesthesia to plan further course of management. A grayish-black colored mass with pus-filled cavity was excised and sent for histopathologic biopsy.

Histopathology revealed presence of multiple abscess composed of neutrophils and mononuclear cells surrounding fungal grains (tangled masses of fungal hyphae up to 1–2 mm in size held together by cement-like material) in the dermis (►**Fig. 2D**). Masses of fungal hyphae/filaments with peripheral widened chlamydospores enclosed by a rim of eosinophilic Splendore-Hoeppli material (in vivo antigen antibody precipitation around clumps of hyphae) are characteristic of *Madurella mycetomi*, from subgroup *Monosporium epispermosum* (►**Fig. 2E**).

After being diagnosed as a case of craniocerebral mycetoma, the patient was treated with a regimen of injection amphotericin B (1 mg/kg/d) for 1 week and discharged with oral itraconazole (200 mg twice daily) along with oral antiepileptics for 6 weeks. Unfortunately the patient was lost to the next follow-up.

Discussion

Dr. John Gill is credited for his first description of "Madura foot" in 1842, though the term was introduced by Colebrook as a distinct disease entity of Madurai region in 1846.[1–4] This fungal disease is prevalent in Africa, India, Mexico, Argentina, and many other tropical countries.[2] In his series

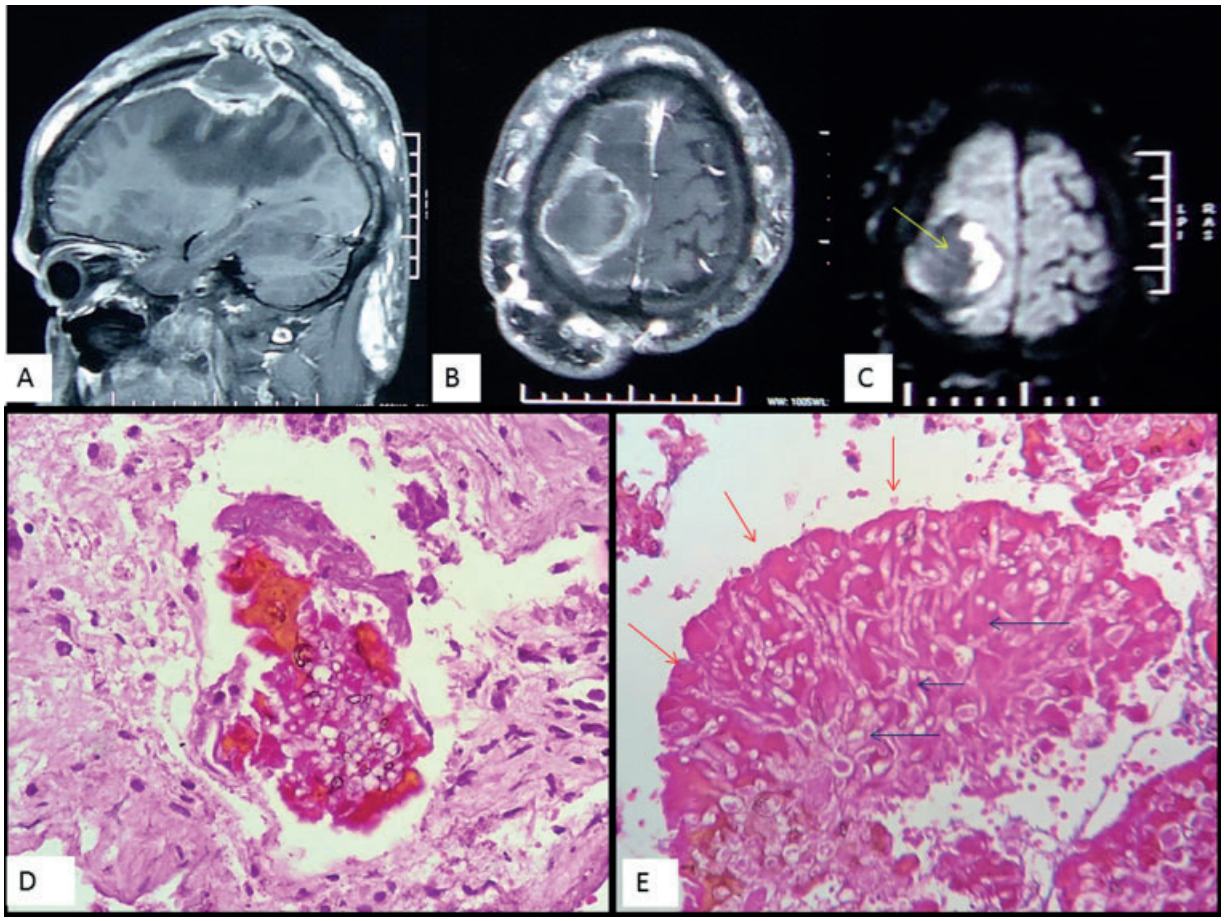

Fig. 2 (**A**) T1 contrast sagittal MRI showing rim-enhancing dural-based lesion with perilesional edema. (**B**) T1 contrast MRI axial view showing rim-enhancing lesion over right motor cortex along with multiple enhancing scalp lesions. (**C**) Diffusion restriction in DWI sequence of MRI (yellow arrow). (**D**) Multiple fungal hyphae with peripheral cement-like eosinophilic material. (**E**) Multiple fungal hyphae with chlamydospores (blue arrows) enclosed within Splendore-Hoeppli material (red arrows) and variable inflammatory cells.

of 184 cases of maduromycosis, Grantham Hill in 1931 recorded only one case of cranial maduromycosis in Khartoum.[5] In 1950, Hickey reported on three patients of cranial eumycetoma without penetration of the dura.[5]

Mycetoma is a chronic granulomatous destructive lesion involving the skin, subcutaneous tissue, and bone, which can be caused by fungi (eumycetoma) or actinomycetes (actinomycotic mycetoma).[1,3,6] Traumatic subcutaneous inoculation of this microorganism is manifested by painless nodules, which swell up and rupture to form sinus tract with discharging fungal grains (aggregates of fungal hyphae embedded in a cement-like material), pus, and blood.[2] This infection spreads through fascial planes to destroy the skin, subcutaneous tissue, bone, and underlying structures.[2] *Madurella mycetomatis* is known to produce black colored grains, which was an indirect evidence of this fungal infection in our case.[1,2]

Common sites of maduromycosis include dorsum of the feet (70%) followed by the hands (12%).[2] Craniocerebral involvement is very uncommon and confined to only six case reports in medical literature till date, excluding the index case (►**Table 1**).[1,3,4,6–8] Common presentations in craniocerebral maduromycosis are due to mass effect, which may present as seizure, focal neurologic deficit, discharging scalp lesions, or ear/nasal discharge.[1,3,7,9]

None of the blood investigations are specific for maduromycosis, although a polymerase chain reaction (PCR) assay has evolved recently to detect the microorganism in patient as well as from the environment.[2] Conventional X-ray of the skull bone features sclerotic changes with punched-out rarefaction, which are characteristically small in number and large in size with clear margin.[1,2] Similar X-ray findings are seen in the index case. Hypointense dots within hyperintense granuloma separated by hypointense septa, giving rise to the characteristic "dot-in-circle" sign in T2W magnetic resonance images, correlate histologically with central fungal grains surrounded by dense granulomatous inflammation partitioned by fibrocollagenous tissue.[6,8] Similar findings were evident in the index case. Although culture of the fungus is gold standard for diagnosis of eumycetoma, it takes long time with false-positive results due to contamination of sample.[10]

Craniocerebral maduromycosis should be treated with adequate antifungal therapy complemented by complete surgical excision of the small, localized mass lesion, as either surgery or antifungal therapy alone has high recurrence rates.[2] Complete surgical excision must be attempted to address the mass effect and focal neurologic deficit caused by the lesion.[2,6] Surgical excision also helps in reducing the

Table 1 Previous cases of craniocerebral maduramycosis

Sl. no	Case reports	Age/sex	Chief complaints	History	Imaging features	Organism	Treatment
1	Natarajan et al, 1975	25/M	Focal seizure, left hemiplegia, discharging scalp sinus.	Carrying overhead material	X-ray—right parietal bone defect with loculated air. Carotid angio—left side shift of right ACA.	*Madurella mycetomatis*	Surgery-twice. Chloromycetin, streptomycin penicillin.
2	Sai Kiran et al, 2007	21/F	Left ear discharge with hearing loss, right hemiparesis	Nothing suggestive	CT—left CPA solid-cystic lesion with erosion of petrous. MRI-T1 hypointense with contrast enhancement.	*Pseudallescheria boydii*	Surgery, amphotericin-B, ketoconazole.
3	Beeram V et al, 2008	18/M	Discharging scalp sinus, generalized seizure	Farm labor, no history of trauma	CECT—parietal punched-out bony lesion with enhancing intra- and extradural mass.	*M. mycetomatis*	Surgery, itraconazole.
4	Ahmed et al, 2011	31/M	Scalp mass, seizure,right hemiparesis	History of trauma to scalp	CECT—dural-based enhancing lesion with osteomyelitis of skull bone. MRI—left parasagittal enhancing dural-based mass. Dot-in-circle sign in T2W.	*Madurella grisea*	Surgery, itraconazole.
5	Goel et al, 2012	17/F	Scalp mass, seizure, discharging sinus	Carrying wooden sticks overhead	X-ray—right parietal lytic skull lesions. CECT—hyperdense, enhancing extra-axial mass with scalloping and erosion of overlying bone.	*M. mycetomatis*	Surgery, voriconazole, terbinafine
6	Rao et al, 2015	26/M	Generalized seizure, blurring of vision, no scalp lesion	No history of trauma	CECT—left parieto-occipital enhancing dural-based lesion with bone hyperostosis along with punched-out lesion.	*P. boydii*	Surgery, itraconazole.

Abbreviations: ACA, anterior cerebral artery; CECT, contrast-enhanced computed tomography; CPA, cerebellopontine angle; CT, computed tomography; F, female; M, male; MRI, magnetic resonance imaging.

recurrence rate and limiting the long term use of antifungal therapy.[2] Both itraconazole (400 mg/d) or ketoconazole (400–800 mg/d) are equally effective first-line medical management with a duration that may continue for years, depending on the severity of the disease and health status of the individual,[2] as no strict recommendations citing the duration of medical therapy are found in the existing literature. Though newer drugs such as caspofungin and posaconazole are available in market, their high cost and no specific advantage over itraconazole have questioned their long-term use.[2]

Long-term follow-up revealed discordant results among the existing literatures as far as the sinus healing and radiologic changes are concerned.

In our report, we must acknowledge few limitations such as (1) biopsy was taken from scalp lesions only, (2) culture of the organism was not done, and (3) lack of long-term follow-up.

Conclusion

Craniocerebral maduromycosis is a rare entity. Only six cases have been reported in the literature. In view of this rare cranial involvement of maduromycosis, we propose a word "Madura head" for description of similar lesions in future. Early diagnosis followed by antifungal therapy combined with surgical debridement may be a reasonable treatment, though long-term follow-up is necessary.

Conflict of Interest
None.

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