Clinical profile and management of craniocerebral Madurella mycetoma

To The Editor: We read with great interest the case report published by Goel et al. (Goel RS, Kataria R, Sinha VD, et al: Craniocephalic maduromycosis. Case report. J Neurosurg Pediatr 10:67–70, July 2012). These authors reported the case of a 17-year-old girl with a craniocerebral mycetoma caused by Madurella mycetomatis (M. mycetomatis). The authors are to be congratulated for the excellent result achieved in managing this case.

We would like to take the opportunity to highlight several key points in the clinicopathology and management of cranial Madurella mycetoma. Cranial involvement in mycetoma is distinctly uncommon and occurs in less than 4% of cases. According to previous reports, the causative organisms of cranial mycetoma are predominantly actinomycetes: Streptomyces somaliensis, Actinomadura madurae, and A. pelletierii. Madurella mycetomatis, the major etiologic agent of human eumycetoma, has rarely been implicated, with only 9 cases reported in the English literature (Table 1).

Early in the clinical course of cranial eumycetoma, the patients typically present with painless scalp swellings discharging black grains, or ear and nasal discharge. Neurological complications of cranial eumycetoma infection include epilepsy, cranial nerve palsies, brain abscess, and meningitis. The incidence of these complications in cranial actinomyces is variable, ranging from 0% to 62%. Interestingly, in the 9 cranial Madurella mycetoma cases reviewed, 7 patients (78%) had clinical evidence of neurological complications. The diagnosis of cranial mycetoma is often based on mycological studies, cytology, histological examination, and, more recently, molecular techniques. Scans using CT and MRI remain the gold standard for assessing the extent and pattern of bone involvement and intracranial extension and planning management; CT is superior to MRI in detection of early bone changes. A general consensus holds that cranial mycetoma infection almost always involves more than one bone and produces mainly osteosclerotic lesions, with loss of the trabecular pattern and dense bone formation.

In contrast, 4 of the 5 cases of cranial Madurella mycetoma for which this information is available were localized to one bone. Moreover, 63% of the patients (5 of 8) with cranial Madurella mycetoma showed predominantly osteolytic changes, such as cortical erosion, cavity formation, or complete bone lysis, a pattern similar to that described in the context of Madurella mycetoma of other sites. It seems, therefore, that the bone tissue response to M. mycetomatis infection is generally the same regardless of the site of involvement.

Treatment of cranial eumycetoma is challenging, and early surgical excision with wide margins offers the only chance of cure. Nevertheless, this is often precluded by the advanced stage of the disease at presentation and the deep anatomical location and multiplicity of the lesions. In the current review, 2 of the cases were considered inoperable, leaving an overall cure rate of 50%. We recommend that a meticulous operative technique be used during exposure and resection of cerebral lesions to prevent spillage and seeding of grains into the adjacent operative field. This should be supported with appropriate antibiotic prophylaxis and intraoperative antibiotic wash, given the high incidence of concomitant bacterial infection, particularly in cases of eumycetoma. Additionally, perioperative chemotherapy with azole-class antifungals is essential, as it helps to stabilize the lesion before and after surgery to reduce the risk of recurrence.

The authors report no conflict of interest.

References

**TABLE 1: Reported cases of craniocerebral *Madurella* mycetoma**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Age (yrs), Sex</th>
<th>Duration (yrs)</th>
<th>Site/Pattern of Bone Involvement</th>
<th>CNS Involvement</th>
<th>Imaging</th>
<th>Medical Treatment</th>
<th>Surgical Treatment</th>
<th>Outcome &amp; Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muyunga-Kasengulu et al., 1971</td>
<td>4.5, M</td>
<td>1</td>
<td>rt maxillary &amp; sphenoid; PL</td>
<td>CN III &amp; VI palsy, meningitis</td>
<td>skull x-ray</td>
<td>parahydroxyphenyl salicylamide</td>
<td>cystic mass excision</td>
<td>died</td>
</tr>
<tr>
<td>Natarajan et al., 1975</td>
<td>25, M</td>
<td>2.5</td>
<td>rt parietal; PL</td>
<td>It hemiparesis &amp; focal Sz</td>
<td>skull x-ray &amp; carotid angiogram</td>
<td>none</td>
<td>abscess drainage followed by craniotomy &amp; excision</td>
<td>persistent sinus, residual weakness, no recurrence; 18 mos</td>
</tr>
<tr>
<td>Gumaa et al., 1986</td>
<td>49, M</td>
<td>15</td>
<td>NR; PS</td>
<td>NR†</td>
<td>skull x-ray</td>
<td>griseofulvin &amp; procaine penicillin</td>
<td>none†</td>
<td>poor response; 1 mos</td>
</tr>
<tr>
<td></td>
<td>26, M</td>
<td>1</td>
<td>NR; PS</td>
<td>NR†</td>
<td>skull x-ray</td>
<td>griseofulvin &amp; procaine penicillin</td>
<td>none†</td>
<td>poor response; 3 mos</td>
</tr>
<tr>
<td>Yagi et al., 1998</td>
<td>22, F</td>
<td>&quot;several years&quot;</td>
<td>It mastoid; PL</td>
<td>CN VII palsy</td>
<td>skull x-ray</td>
<td>griseofulvin &amp; procaine penicillin</td>
<td>radical mastoidectomy</td>
<td>cured; 6 mos</td>
</tr>
<tr>
<td>Arbab et al., 1998</td>
<td>26, M</td>
<td>3</td>
<td>NR; PS</td>
<td>headache</td>
<td>CT</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Beeram et al., 2008</td>
<td>18, M</td>
<td>1.5</td>
<td>lt parietal; PL</td>
<td>generalized Sz</td>
<td>CT (lt parietal cerebral mass)</td>
<td>itraconazole</td>
<td>excision of involved bone &amp; mass</td>
<td>persistent sinus, no recurrence; 5 mos</td>
</tr>
<tr>
<td>Maheshwari et al., 2010</td>
<td>31, M</td>
<td>2</td>
<td>NR</td>
<td>It hemifacial pain &amp; CN VI palsy</td>
<td>MRI (lt paranasal &amp; cavernous sinus mass)</td>
<td>liposomal amphotericin B</td>
<td>craniotomy &amp; subtotal mass excision</td>
<td>recurrence; 18 mos</td>
</tr>
<tr>
<td>Goel et al., 2012</td>
<td>17, F</td>
<td>2</td>
<td>rt parietal; PL</td>
<td>generalized Sz</td>
<td>CT (rt parietal cerebral mass)</td>
<td>voriconazole &amp; terbinafine</td>
<td>excision of involved bone &amp; mass</td>
<td>cured; 6 mos</td>
</tr>
</tbody>
</table>

* CN = cranial nerve; NR = not reported; PL = predominantly osteolytic; PS = predominantly osteosclerotic; Sz = seizure.
† One patient had epilepsy and right-sided hemiparesis.
‡ These patients had advanced lesions, and no definitive surgery was attempted.
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**Response:** We thank Hytham K. S. Hamid and colleagues for showing interest in our article on craniocerebral maduromycosis. It is interesting to know that cranial mycetoma infection almost always involves more than one bone. Our patient is doing fine, with a follow-up period of more than a year.

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Neonatal intraventricular hemorrhage

To the Editor: We found the article by Alan et al.1 very interesting (Alan N, Manjila S, Minich N, et al: Reduced ventricular shunt rate in very preterm infants with severe intraventricular hemorrhage: an institutional experience. Clinical article. J Neurosurg Pediatr 10:357–364, November 2012). This study reported a decline in the need for surgery in very preterm infants with intraventricular hemorrhage and hydrocephalus, with suggestions about the probable reasons for this decrease. These authors have treated symptomatic hydrocephalus with serial lumbar punctures (LPs). Surgical intervention was limited to ventriculostubagaleal shunt insertion as a temporary intervention whenever serial LPs failed, and in case of active hydrocephalus this shunt was changed to a standard ventriculoperitoneal shunt at a later age.

Prolonged symptomatic hydrocephalus is a potentially destructive pathology that impairs normal development of the CNS. The literature is full of studies related to conservative management for neonates with prematurity and posthemorrhagic hydrocephalus. This treatment included LP, diuretic therapy, and also acetazolamide. Serial LPs have been accepted in most studies as a mainstay of conservative treatment, but there is no agreement about acetazolamide and diuretics. Some reviews and original articles found acetazolamide useful, and others reported it to be useless and even harmful for management of hydrocephalus. The prescribed dosage for acetazolamide with or without furosemide was 100 mg/kg/day in most previous studies. Nephrocalcinosis has been reported in neonates who received acetazolamide as a conservative treatment.2–5

Some studies have claimed that they could decrease the risk of shunt surgery with conservative treatment and some have rejected it. What we can conclude from the published series is that conservative treatment helps protect the premature neonates from high intracranial hypertension consequences and to postpone shunt surgery to a later time at which the child can tolerate physiologically the anesthesia and surgical intervention with fewer complications.

With this philosophy in mind, the proposed protocol for management of hydrocephalus in premature neonates with posthemorrhagic hydrocephalus in our department is acetazolamide and serial LPs, with daily measurement of head circumference and fontanel in addition to serial brain ultrasonography studies.2 To decrease the metabolic complications of acetazolamide we use it at a dosage of 20 mg/kg/day, which is lower than the dose that causes nephrocalcinosis. To decrease metabolic acidosis the child is checked clinically for tachypnea and by laboratory tests for venous blood gas. In case of acidosis the medication is stopped. If conservative treatment fails, ventriculostubagaleal shunt insertion is a good alternative to control hydrocephalus until the child can successfully tolerate a ventriculoperitoneal shunt surgery.

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Disclosure

The authors report no conflict of interest.

References


Response: We read with interest the thoughtful letter to the editor submitted by Nejat and colleagues regarding our article in the Journal of Neurosurgery: Pediatrics on the declining need for surgical intervention for extremely preterm infants with symptomatic hydrocephalus from intraventricular hemorrhage. We agree that nonoperative strategies such as serial LPs can sometimes delay or avoid the need for surgical intervention, and that older and larger preterm infants suffer fewer perioperative complications than younger and smaller infants. Nejat et al. suggest a combination of serial LPs and acetazolamide (20 mg/kg/day) as a temporizing measure for symptomatic hydrocephalus prior to surgical intervention, with daily head circumference measurements and serial head ultrasonography studies to assess efficacy. They recommend screening for metabolic acidosis by checking for tachypnea and serial venous blood gas measurements.

As recently discussed in 2 reviews of the management of neonatal posthemorrhagic hydrocephalus from...
prematurity,\(^3\)\(^4\) a large randomized controlled trial of acetazolamide (100 mg/kg/day) and furosemide (1 mg/kg/day) across 55 centers demonstrated no improvement with the addition of these agents to standard therapy, which included CSF removal with LPs.\(^2\) At 1 year, infants treated with acetazolamide and furosemide did not require fewer shunt insertions and had poorer neurological outcomes than those infants who received only standard therapy. Adverse effects were attributed to the drug intervention in 43% of the treatment group and resulted in treatment cessation in 26%. The acetazolamide dose suggested by Nejat and colleagues is much lower than the dose used in the controlled trial. Given that the high dose was ineffective in lowering the need for surgical intervention, it seems unlikely that a lower dose would be effective in altering the need for surgical intervention. Both acetazolamide and furosemide probably have unanticipated side effects on neurological development, which may have contributed to the inferior neurological outcomes observed in infants treated with the regimen. For example, furosemide is a nonspecific inhibitor of the potassium chloride cotransporter (KCC2) found primarily on neurons, and KCC2 regulates key components of neuronal development.\(^1\)

In summary, although we agree with Nejat that aggressive treatment of symptomatic hydrocephalus in this population is essential, and that a trial of nonoperative intervention is warranted given the relatively high complication rate associated with early surgical procedures, we cannot at this time endorse the use of acetazolamide in these infants without further support from high-quality preclinical studies.

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References

Occipitocervical fusion


The article elegantly demonstrates the utility of this technique in children, and highlights some of the major contributions to our understanding of the biomechanics of occipitocervical fusion, and the surgical techniques that have made fusion across the craniovertebral junction safe and effective.

Despite the wealth of references, the authors have missed some of the most important contributions in terms of technique as well as biomechanical insight gained over 4 decades, mainly resulting from work performed at the Barrow Neurological Institute. We will briefly highlight some of these contributions, and put in perspective the importance of techniques not mentioned by the authors for fixation across the craniovertebral junction.

The technique of using a threaded Steinmann pin for fusion of the craniovertebral junction was first reported by Dr. Volker Sonntag and colleagues in 1996.\(^1\) This report was followed by the publication of a technical paper on the use of the BendMeister rod bender (Medtronic, Inc.) for contouring rods up to 5.5 mm in diameter for occipitocervical fusion.\(^2\) This technique made it possible to contour rods to fit across the craniovertebral junction, especially that of children, and allowed for internal fixation and early mobilization in these patients. The group from the Barrow Neurological Institute further reported a novel technique for atlantooccipital fixation in which a novel transarticular screw method was used, and validated the biomechanical properties of this construct.\(^3\)\(^4\)\(^5\)

More recently, our group has reported a novel occipitoatlantal fusion construct for treatment of avulsion fractures of the foramen magnum, as well as a novel dual transarticular screw fixation technique for simultaneous fixation of occipitoatlantal and atlantoaxial dislocations.\(^5\)\(^9\) In 2007 we reviewed our experience with treating 33 survivors of occipitoatlantal dislocations, including 17 pediatric patients.\(^7\) This review highlighted the clinical correlates that the patients presented with, and presented techniques for the treatment of these rare but devastating injuries.

Again, we congratulate the authors on excellent results with the use of the contoured rod technique and remind other practitioners of other useful adjuncts available for fusion across the craniovertebral junction.

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Disclosure
The authors report no conflict of interest.

References
1. Apostolidis PJ, Dickman CA, Golfinos JG, Papadopoulos SM,
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Response: We thank Drs. Theodore, Kalani, and Sonntag for their interest and comments regarding our paper. We acknowledge the prior work done at Barrow Neurological Institute on the topic of craniocervical fixation. Our paper did not allow an in-depth analysis of all relevant publications on this large topic. The 75 publications we referenced is, in our opinion, a substantial number. Reference 1 in their list appears to be a variation of the original Hartshill-Ransford contoured-loop technique, which predated their paper by 10 years. References 3–6 and 9 detail screw fixation techniques (performed primarily in older adolescents and adults), which was not the focus of our paper as a whole, nor of the Discussion section in particular. Reference 7 would have been appropriate if the focus of our paper had been on a particular disease (that is, atlantooccipital dislocation) rather than the operation and its application in children with various pathologies. This leaves us with Reference 2, a brief, 2-page technical note that we would have referenced if we had known about it. However, it has been cited only 5 times in the literature since its publication in 1998 (determined using Google Scholar and the Neurosurgery website), and 2 of these instances were self-citations.

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Reference

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