MRI findings of intramedullary spinal cryptococcoma

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Cryptococcus neoformans (C. neoformans) is a thin-walled, non-mycelial, budding yeast that exists widely throughout nature and causes opportunistic and non-contagious infections in humans. Involvement of the central nervous system (CNS) has been found in 70% of patients at the time of diagnosis, and meningitis and meningoencephalitis are the most common manifestations (1–3). Space-occupying cryptococcoma, on the other hand, is a rare entity characterized by localized, solid, tumor-like masses that are usually found in the cerebral hemispheres or cerebellum, but are extremely rare in the spinal cord (1, 4). To the best of our knowledge, there have been only 5 cases of intramedullary spinal cryptococcoma reported in the literature (1, 3–6) and limited information on imaging features is available. We present another case, review the literature on this entity, and discuss the magnetic resonance imaging (MRI) findings.

Case report
A 47-year-old man was admitted to our hospital with progressive difficulty in walking and bilateral lower limb weakness that had started 3 months earlier. No disorder of the urinary sphincter was noted. A neurological examination revealed grade I paraparesis on the right side and a positive bilateral Babinski sign. Laboratory findings were normal and no history of immunodeficiency, such as AIDS, hematological malignancies, diabetes mellitus, tuberculosis, or sarcoidosis, was observed. There was no data suggesting that there was a fungal infection of the respiratory and digestive systems. Magnetic resonance imaging showed a 1-cm diameter, regularly-shaped intramedullary lesion with a smooth border at the T12 vertebral level. On non-enhanced T1-weighted images, the lesion appeared slightly hyperintense relative to the normal spinal cord (Fig. 1). On T2-weighted images, the lesion was hypointense with hyperintense focus and it had surrounding hyperintense edema (Fig. 2). After administration of gadolinium, an intense enhancement of the lesion was detected (Fig. 3). These findings led to a preoperative diagnosis of intramedullary tumor. The patient underwent surgery and a total resection of the lesion was performed.

Macroscopic examination of the resection specimen consisted of a 10 x 10 x 5 mm gelatinous mass with a yellow cut surface. The histological examination of the hematoxylin-eosin (H&E) stain showed granulomatous inflammation, fibrosis, and numerous refractile yeast forms, which were present in the multinucleated giant cells or in the extracellular areas (Fig. 4). PAS-alcian blue stain demonstrated a mucicarminophilic polysaccharide capsule of yeast forms (Fig. 5). Based on these findings, the diagnosis of a cryptococcoma was made.

Anti-fungal treatment was started after surgery, which included intravenous fluconazole 400 mg for 7 days followed by oral fluconazole 150
mg for 6 weeks. After the treatment, the patient’s clinical condition markedly improved. The six-month postoperative MRI showed atrophic changes at the T11–T12 level and lack of enhancement, confirming the resolution of the infection (Fig. 6).

Discussion

The fungus *C. neoformans* is an encapsulated yeast of which 2 pathogenic varieties are known, *C. neoformans* var. *neoformans* and *C. neoformans* var. *gattii*. *C. neoformans* var. *neoformans* is the variety most commonly seen worldwide. Pigeon feces are believed to be an important source of contamination. *C. neoformans* var. *gattii* is particularly associated with eucalyptus trees and it is found mainly in tropical and subtropical regions. (3, 7). Ergin et al. reported that *C. neoformans* was present in the eucalyptus flora of Turkey, despite the alkaline soil condition (8).

*Figure 1.* a, b. Sagittal (a) and axial (b) T1-weighted MR images show nodular, slightly hyperintense intramedullary lesion (arrow) at the T12 level.

Even though the route of entry of *C. neoformans* into the body is the respiratory tract, CNS infection is the most frequent manifestation of cryptococcosis (2, 6, 7) because soluble anticryptococcal factors present in serum are absent in cerebrospinal fluid (CFS) (2, 7). The majority of affected individuals
present with a clinical picture of meningitis or meningoencephalitis (1–3, 9). Ventriculitis, cerebritis, cerebellitis, and abscess are less frequently observed (1, 3, 9). Spinal involvement is a rare manifestation of cryptococcosis (1–6, 10).

There are 2 types of spinal cryptococcosis: intradural and extradural, depending on localization (2, 3, 10). Intradural involvement has 2 subtypes: extramedullary lesions, essentially arachnoiditis with or without mass lesions, and intramedullary lesions, which are referred to as cryptococcoma, or granuloma and abscess (2, 10).

Cryptococcoma is characterized by localized, solid, tumor-like masses in which the fungus has invaded the parenchyma, producing a chronic granulomatous reaction composed of macrophages, lymphocytes, and foreign body-type giant cells. The incidence of these lesions appears to be the highest in immunocompetent patients infected with *C. neoformans* var. *gattii*. Granuloma formation, however, is uncommon in immunosuppressed patients because of the inability of this patient population to initiate an inflammatory response (2, 10).

Table provides data from the literature review of intramedullary crypto-

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**Summary of literature for intramedullary cryptococcoma**

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Duration of clinical history (days)</th>
<th>Symptoms</th>
<th>Localization</th>
<th>T1W MRI</th>
<th>T2W MRI</th>
<th>Enhancement on MRI</th>
<th>Treatment</th>
<th>Histology</th>
<th>Evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ramamurthi et al., 1954 (4)</td>
<td>17</td>
<td>F</td>
<td>120</td>
<td>Pyramidal syndrome spasticity</td>
<td>T2</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Operation</td>
<td>Granuloma</td>
</tr>
<tr>
<td>Skultety 1961 (5)</td>
<td>60</td>
<td>M</td>
<td>20</td>
<td>Paraparesis</td>
<td>T6</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Operation, amphotericin B</td>
<td>Granuloma</td>
</tr>
<tr>
<td>Su et al., 1994 (1)</td>
<td>66</td>
<td>M</td>
<td>15</td>
<td>Paraparesis (3/5)</td>
<td>T11-T12</td>
<td>NA</td>
<td>NA</td>
<td>Ring-like</td>
<td>Operation, amphotericin B</td>
<td>Granuloma</td>
</tr>
<tr>
<td>Grosse et al., 2001 (3)</td>
<td>24</td>
<td>F</td>
<td>90</td>
<td>Paraparesis L3-L4 (4/5), distal hypoesthesia and hyporeflexia</td>
<td>L1</td>
<td>Isointense</td>
<td>Moderately hyperintense + surrounding edema</td>
<td>Ring-like</td>
<td>Amphotericin B + 5-fluorocytosine + fluconazole, operation</td>
<td>Granuloma</td>
</tr>
<tr>
<td>Lai et al., 2001 (6)</td>
<td>60</td>
<td>M</td>
<td>90</td>
<td>Paraparesis (3/5)</td>
<td>T12</td>
<td>Slightly hyperintense</td>
<td>Hypointense + surrounding edema</td>
<td>Solid</td>
<td>Operation, fluconazole + amphotericin B</td>
<td>Granuloma</td>
</tr>
<tr>
<td>Gültaşlı et al., 2005 (our case)</td>
<td>47</td>
<td>M</td>
<td>90</td>
<td>Paraparesis, bilateral Babinski’s signs</td>
<td>T12</td>
<td>Slightly hyperintense</td>
<td>Hypointense + surrounding edema</td>
<td>Solid</td>
<td>Operation, fluconazole</td>
<td>Granuloma</td>
</tr>
</tbody>
</table>

T1W: T1-weighted, T2W: T2-weighted, NA: not available
Numbers in parentheses are reference numbers
coccema. In all, 6 cases were reviewed, including ours. The median age of presentation was 45 years (range, 17–66 years), and there were 2 female patients. All patients were immunocompetent. The duration of symptoms ranged from 15 days to 4 months. The most common presentation was paraesthesia (5 cases). Only the case reported by Skultety (5) had a pulmonary cryptococcal infection 6 months before intramedullary localization. The authors did not mention the serotype of C. neoformans, except Grosse et al., who serologically identified the isolate as C. neoformans var. gattii (3). MRI was performed on 4 patients; 1 was isointense and 2 were slightly hyperintense on T1-weighted images. On T2-weighted MR images, 2 were hypointense and 1 was hyperintense. Surrounding edema was seen in 3 cases, including ours. Two lesions showed solid enhancement, while in the remaining 2, enhancement was ring-like. The mean size of lesions was smaller than one vertebral body. All reported cases of intramedullary cryptococcema involved the thoracic (T2, T6, T11–12, and T12) or upper lumbar (L1) region. At the time of diagnosis only 2 cases underwent cranial imaging, and in Grosse et al.’s case cerebral MRI revealed 6 lesions with signal behavior similar to an intramedullary lesion (3). The incidence of combined cerebral and spinal disease has not yet been delineated, but imaging of the brain should be performed in any case of spinal cryptococcosis (3).

Because of its rarity, imaging features of intramedullary cryptococcosis have not been well described. To summarize, lesions are isointense or slightly hyperintense on T1-weighted, hyperintense on T2-weighted MR images with surrounding edema, and show solid or ring-like enhancement after administration of contrast medium. Generally, hyperintensity on T1-weighted MR images may be due to the presence of hemorrhage, melanin, fat, or granulomatous tissue (11). With regard to histological examinations, we believe that in our case and that of Lai et al. the T1-weighted hyperintensity represented fibrosis and inflammatory cellular infiltrates within granulomatous tissue (6). The hyperintensity of the fibrotic tissue may be related to the relatively high protein concentration and low water content compared to adjacent tissue (12). T1-weighted hyperintensity may be suggestive of intramedullary cryptococcema, but is not pathognomonic, as it has been reported in various neoplastic and granulomatous diseases (11). Contrast enhancement probably represents the patient’s ability to mount an immune response (2, 10). Final diagnosis necessitates additional diagnostic confirmation with microscopic identification of the cryptococci or detection of cryptococcal antigen in CSF (1, 2, 6, 7).

As in our case, spinal cord forms of the disease generally improve, due to surgery and antifungal medication, or sometimes due to specific medical treatment alone, but with a sufficient dosage (2, 3, 6, 10).

In conclusion, although extremely rare, cryptococcal infection should be considered in the differential diagnosis of mass lesions of the spinal cord, even in apparently immunocompetent patients, especially when the lesion shows hyperintensity on T1-weighted MR images, enhances solidly or ring-like, involves the thoracic or upper lumbar region, and mean size of the lesion is smaller than one vertebral body.

References