

# Spinal Intramedullary Tuberculoma Requiring Surgical Treatment

## —Case Report—

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### Abstract

A 71-year-old male presented with multiple central nervous system tuberculomas including spinal intramedullary tuberculoma manifesting as occipitalgia and left hemiparesis. He had received medical treatment for lung and testis tuberculosis. Magnetic resonance imaging revealed an intramedullary lesion at the C-2 level as well as multiple small extramedullary and intracranial lesions. His neurological symptoms gradually worsened despite intensive antituberculous therapy. The C-2 intramedullary lesion responsible for left hemiparesis was surgically extirpated. Postoperatively, his neurological symptoms improved gradually, and no recurrence was evident at the resected site. Surgical intervention is mandatory in patients with intramedullary tuberculoma if neurological symptoms deteriorate or lesions enlarge despite continuous antituberculous therapy.

Key words: tuberculoma, intramedullary lesion, surgical treatment

### Introduction

Tuberculous infections involving the central nervous system (CNS) usually occur secondary to primary infectious foci in the lung or elsewhere in the body. Therefore, the incidence is closely associated with that of tuberculosis. Very recently, the number of patients with tuberculosis has increased, partly because of various immunocompromised conditions and the emergence of drug-resistant tuberculosis.<sup>16)</sup> CNS tuberculosis should be considered in the differential diagnosis of lesions causing neurological signs and symptoms. We report a case of intramedullary tuberculoma which progressed despite medical treatment.

### Case Report

A 71-year-old male presented with occipitalgia, cervical pain, lumbago, and motor weakness on the left 24 weeks after the initiation of medical treatment for systemic tuberculosis. Previously, the patient had undergone removal of left testis tuberculoma. At that time, miliary tuberculosis was identi-

fied in the lung. Antituberculous therapy was instituted using the combination of isonicotinil hydraradin (INH) 300 mg/day, rifanpicin (RFP) 450 mg/day, and streptomycin (SM) 150 mg/day. Magnetic resonance (MR) imaging revealed multiple lesions in the intraspinal and intracranial spaces, and the patient was referred to our department.

On admission, he was clear and alert. The patient could not walk and suffered from vesicorectal disturbance. The muscle power of the upper and lower extremities was fair (grade 3 by the manual muscle test ranging from grade 0 to grade 5). No signs of meningeal irritation were present. Laboratory examination of blood showed no abnormalities. *Mycobacterium tuberculosis* was not detected by sputum or cerebrospinal fluid (CSF) cultures. Chest radiography revealed miliary tuberculosis in the bilateral lungs. Vertebral radiography showed compressed fracture of the vertebral bodies at the T-11, T-12, and L-5 levels. MR imaging revealed a ring-enhanced intramedullary lesion (approximately 3 × 3 × 3 cm) at the C-2 level (Fig. 1) and multiple small extramedullary lesions (approximately 0.1 cm maximum diameter) at the T-10 to L-2 levels. Enhanced lesions (less than 0.5 cm maximum diameter) were also scattered in the vermis and the cerebral

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parenchyma (Fig. 2). Thallium-201 chloride scintigraphy showed no abnormal uptake, suggesting non-tumorous lesions. The weakness of the left upper and lower limbs had deteriorated despite continuation of antituberculous medication for 24 weeks.

The patient underwent removal of the C-2 lesion through a suboccipital craniotomy and laminectomy between the C-1 and C-3 levels. The arachnoid membrane was thickened and gray, and the spinal cord was swollen. Intraoperative echoencephalography was used to delineate the lesion. The lesion was then dissected from the surrounding spinal cord tissue through a midline myelotomy. The lesion was whitish and soft, and the margin was sharply de-



**Fig. 1** Sagittal T<sub>1</sub>-weighted magnetic resonance image with gadolinium revealing a ring-enhanced intramedullary lesion at the C-2 level.

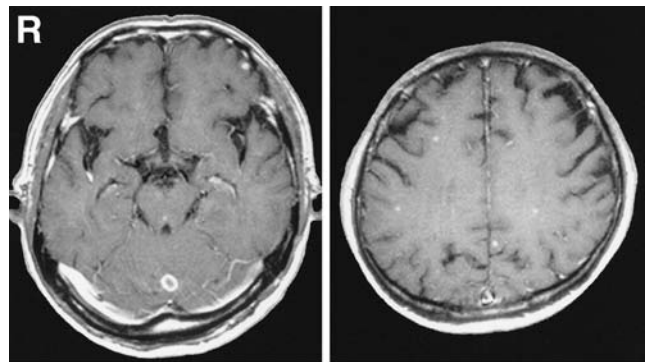
finied (Fig. 3). The center of the granuloma was necrotic and contained a creamy substance. The surrounding rim was rather fibrous. The tumor was extirpated en bloc after internal decompression using an ultrasonic surgical aspirator.

Histological examination of the surgical specimen showed inflammatory and necrotic tissue containing a number of infiltrated lymphocytes. No caseation necrosis or Langhans'-type giant cells were found. Ziehl-Neelsen staining of the resected sample identified *M. tuberculosis* (Fig. 4).

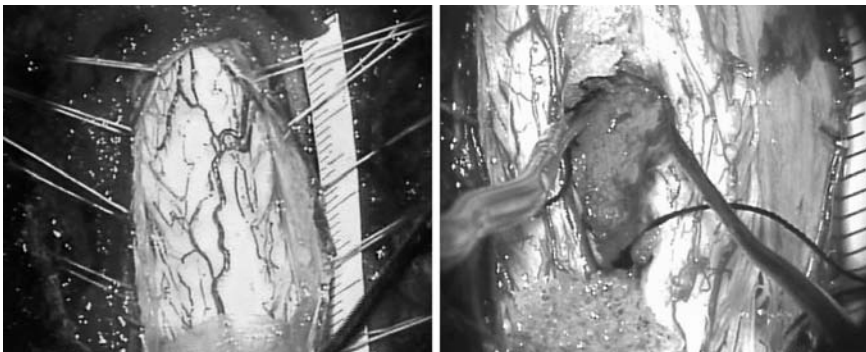
The weakness of the upper and lower limbs improved one month after the surgery, and the patient could walk to some extent with assistance. Antituberculous therapy with INH and RFP was continued for one year. Follow-up MR imaging revealed no evidence of recurrence or regrowth at the resected site. The other extramedullary and intracranial lesions had also disappeared (Fig. 5).

## Discussion

Spinal tuberculosis causes various types of lesions. Pott's disease of the spine is the most common



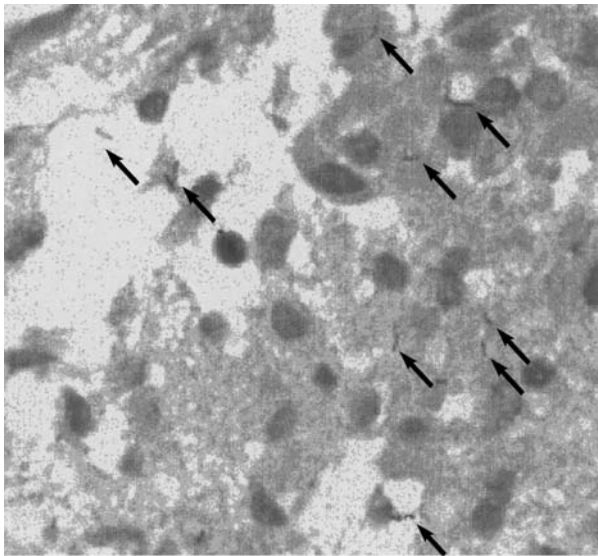
**Fig. 2** T<sub>1</sub>-weighted magnetic resonance images with gadolinium revealing multiple tiny lesions in the vermis (left) and the cerebral hemisphere (right).



**Fig. 3** Intraoperative photographs showing swelling of the spinal cord (left). The lesion consists of gray soft tissue, and contains white discharge (right).

(64%), followed by arachnoiditis (20%) and intramedullary lesion (8%).<sup>12)</sup> Intramedullary lesion is present in approximately two of every 100,000 tuberculous cases and two of every 1,000 cases of CNS tuberculosis.<sup>2)</sup> Intramedullary tuberculoma may be difficult to differentiate from space-occupying lesions such as primary and metastatic spinal tumors and other chronic granulomatous diseases (sarcoidosis, brucellosis, and histiocytosis).<sup>8)</sup>

The present patient had multiple lesions in the cerebellum and the cerebrum as well as in the spine.



**Fig. 4** Photomicrograph showing a number of *Mycobacterium tuberculosis* (arrows). Ziehl-Neelsen stain, × 400.

Intracranial tuberculomas may occur as single lesions, but often multiple with a predilection for the cerebellum. Seventeen intramedullary tuberculomas including the present case have been described recently, eight lesions (47%) located in the cervical cord, eight lesions (47%) in the thoracic cord, and one lesion (6%) in the conus (Table 1).<sup>2,3,5,6,9,10,12,14,15)</sup>



**Fig. 5** Sagittal T<sub>1</sub>-weighted magnetic resonance image with gadolinium revealing no recurrence of the C-2 level lesion or other extramedullary lesions one year after surgery.

**Table 1** Recent cases of intramedullary tuberculoma

Case No.	Author (Year)	Age (yrs)	Sex	Level	Time to surgery (wks)	Period of medication (wks)	Treatment	Result
1	Rhoton et al. (1988) <sup>15)</sup>	65	M	C3-6	8	24	total removal	recurrent*
2	Jena et al. (1991) <sup>5)</sup>	25	F	C2-6	not described	24	medication	improvement
3		23	M	C2-T1	not described	24	medication	improvement
4	Citow and Ammirati (1994) <sup>2)</sup>	31	M	T-11	6	48	total removal	improvement
5	Lin et al. (1994) <sup>9)</sup>	36	M	T6-12	20	72	partial removal	improvement
6	Gupta et al. (1995) <sup>3)</sup>	35	M	T10-11	24	72	total removal	improvement
7		27	M	conus	72	24	not described	improvement
8	Ratliff and Connolly (1999) <sup>14)</sup>	46	F	T10-11	72	not described	biopsy	improvement
9	Kayaoglu et al. (2000) <sup>6)</sup>	65	M	C-4	10	24	total removal	improvement
10	Rao (2000) <sup>12)</sup>	25	F	T11-12	not described	72	medication	improvement
11		16	F	C5-7	not described	32	medication	improvement
12		14	M	C5-6, T-6	not described	32	medication	improvement
13		16	M	C1-6	not described	48	medication	improvement
14	Nomura et al. (2001) <sup>10)</sup>	2	F	T6-10	48	96	partial removal	improvement
15	Present case	71	M	C-2, T10-L2	24	48	total removal	improvement

\*Clinical symptoms improved after reoperation.

Intramedullary tuberculomas mostly develop in the upper spine. This preference may be related to the proximity to the cerebellum. The presence of other CNS lesions should be considered even if the tuberculoma is apparently solitary.

The early diagnosis of intramedullary tuberculoma may be easier if CNS tuberculosis occurs secondary to or during the treatment of primary tuberculosis. In contrast, the diagnosis is very difficult when CNS tuberculosis manifests prior to pulmonary and extra-CNS lesions. CSF examinations are usually helpful to identify CNS tuberculosis, but did not detect *M. tuberculosis* in the present case. CSF findings and culture may be modified or underestimated during medical treatment. CNS tuberculosis is increasingly common in immunocompromised patients. In the present case, human immunodeficiency virus examination was negative. CNS tuberculosis should be suspected in a patient with a history of tuberculosis. The diagnosis of CNS tuberculosis should be established based on multidisciplinary detection of neurological symptoms and signs, laboratory data including CSF examination, and neuroimaging findings.

MR imaging is a powerful method for the detection of intramedullary tuberculomas as well as intracranial tuberculomas. MR imaging findings vary among the stages of the tuberculoma formation. In the early phase, tuberculomas are homogeneously enhanced. Later, when the capsule is formed, ring enhancement is common. Caseation results in the "target sign" appearance.<sup>3,7,14</sup> Most of the intracranial and intraspinal lesions in the present case were approximately 0.1 cm in maximum diameter and homogeneously enhanced, whereas the largest lesion at the C-2 level showed a ring enhancement without target sign. Histological examination proved that the C-2 lesion had stayed at the stage of capsular formation with degenerative content. The degenerative content may have been the result of chemotherapy. However, the presence of degenerative content may prevent agents from penetrating into the tuberculoma, whereas agents can easily pass through the lesion due to the abundant vascular network in the initial stages of tuberculoma formation. Persistent cyst and degenerative content during the time of chemotherapy may be an indicator of drug resistance in tuberculomas.

The choice of treatment mode and regimen is an important consideration. Antituberculous agents are widely used and are critical in the treatment of intramedullary tuberculoma. INH and pyrazinamide (PZA) are used frequently as effective chemotherapeutic agents against CNS tuberculosis because of their high blood-brain barrier permeability.<sup>13</sup> A

regimen of antituberculous chemotherapy should continue until clinical and laboratory effectiveness is achieved for 52 weeks (12 months) or more, and consist of at least two agents to overcome drug resistance. Addition of a third agent for the initial 8 to 24 weeks is also recommended.<sup>8,11</sup> Recent guidelines for the treatment of tuberculous meningitis advise initial use of a combination of INH, RFP, and PZA, and, if necessary, addition of SM or ethambutol, although these carry the risk of side effects and have poor penetration through blood-brain barrier.<sup>1</sup>

Progressive neurological deficits indicated surgical intervention in the present case. Drug resistance to chemotherapeutic agents is a major problem in the clinical failure of chemotherapy for tuberculosis. In reported series, progressive neurological deficits or enlarging lesions despite antituberculous treatment were the indicators for surgical intervention.<sup>12</sup> At present, selective application and combination of existing drugs are required to enhance therapeutic effectiveness.

The importance of surgical treatment for intramedullary tuberculoma extends to the diagnostic procedure, curative procedure, and palliation. Advances in the molecular diagnosis of sputum or CSF and neuroimaging have reduced the importance of surgical diagnostic procedures. Curative surgical procedures are less effective for intraspinal and intracranial multiple tuberculomas. Palliative surgical procedures can reduce the volume of tuberculoma causing symptoms, which will promptly ameliorate the symptoms and provide the general condition and sufficient time for ensuring effective chemotherapy. In the present case, the palliative surgical procedure was effective against the lesion responsible for the neurological deficits among multiple tuberculomas. Furthermore, debulking of tuberculoma growing during or after chemotherapy may enhance the effectiveness of chemotherapy by reducing the content of hypoxic, necrotic, or drug-resistant tissue.

Surgical intervention for intracranial tuberculoma is indicated if the medical therapy is ineffective after 8 weeks.<sup>4</sup> In eight surgical cases of intramedullary tuberculomas, the mean time between onset and surgery was  $31.5 \pm 26.1$  weeks. Total removal was performed in five cases, partial removal in two cases, and biopsy in one case. Most patients improved clinically regardless of the extent of resection. Neurological dysfunction attributable to tuberculoma can be improved by prompt and adequate resection if the spinal tissue remains viable or can be restored (Table 1).

Postoperative medical management of in-

tramedullary tuberculoma is necessary, because this disease is usually secondary to pulmonary or extra-CNS infections. Methods to determine the time to discontinue medication have not been established. In most cases, postoperative administration of antituberculous agents was continued for  $51.0 \pm 26.6$  weeks in recent cases. In the present case, postoperative medication for approximately one year has controlled the lesion including the resected site. Practical and clinically useful determinations of sensitivity or resistance to agents is needed to maximize the surgical benefits in patients with intramedullary tuberculoma.

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