Acta Neurochir (2003) 145: 513–517
DOI 10.1007/s00701-003-0019-0

Acta Neurochirurgica
Printed in Austria

Case Report

Intracranial tuberculomas mimicking a malignant disease in an immunocompetent patient

A. Giese[1,5], **T. Kucinski**[2], **C. Hagel**[3], and **F. Lohmann**[4,5]

[1] Department of Neurosurgery, University Hospital Luebeck, Luebeck, Germany
[2] Department of Neuroradiology, University Hospital Eppendorf, Hamburg, Germany
[3] Department of Neuropathology, University Hospital Eppendorf, Hamburg, Germany
[4] Department of Neurosurgery, Saarbruecken Hospital, Saarbruecken, Germany
[5] Department of Neurosurgery, University Hospital Eppendorf, Hamburg, Germany

Published online 24 June, 2003

Summary

We present the unusual occurrence of multiple systemic and two central nervous system tuberculomas in an immunecompetent young patient. A large left frontal epidural tuberculoma with transcalvarian extension was removed surgically and chemotherapy was initiated. The patient remained on a chemotherapy with INH, RMP, and EMB and was followed clinically and with MRI scans for 24 months.

Findings. The clinical presentation and neuroimaging studies initially suggested malignant disease. Surgical resection of the left frontal lesion was required to relive the mass effect. The histological evaluation showed a granulomatous inflammation with epitheloid and Langhans giant cells, but no acid-fast bacilli. Cultures of the specimens yielded a mixed infection with Corynebacterium species and Staphylococcus epidermidis. Based on the histological findings, chemotherapy for tuberculosis was initiated. Subsequently, Mycobacterium tuberculosis was cultured from the surgical specimen and sputum.

Interpretation. Parenchymal CNS tuberculosis with or without extracerebral manifestations may present as a space-occupying lesion. Because a tuberculoma is rarely suspected especially if there is atypical morphology, biopsy is required to establish the diagnosis and expedite specific treatment.

Keywords: Intracranial tuberculoma.

Introduction

Tuberculosis of the central nervous system, with brain and spinal cord meningitis or meningo-encephalitis, becomes symptomatic in 10–20% of patients with extra pulmonary tuberculosis. Only 1% of tuberculosis patients develop an intracranial tuberculoma, usually as part of with miliary tuberculosis [10]. In developing countries, tuberculomas still constitute 30% of intracranial space-occupying lesions [9] whereas, in the industrial nations, intracranial tuberculomas have become rare and may represent as little as 0.1–0.2% of space-occupying lesions [2]. A tuberculoma is typically a solitary lesion, but 15–34% may be multiple, arising from hematogenous spread from extra cerebral foci [16] and 10% may be associated with tuberculous meningitis. Mycobacterium tuberculosis is the dominant agent cultured from intracranial tuberculomas [8, 14, 18]; other Mycobacterium species are rarely found [4]. Most intracranial tuberculomas manifest as an intracerebral lesion and a dural-based mass is rare [14, 18]. Here we present an unusual young immunocompetent patient, diagnosed with multiple soft tissue and bone lesions who had two epidural masses with penetration of the calvarium and growth in the subcutaneous tissues.

Case report

Patient history and initial presentation

A 17-year-old woman born in the Philippines, mother of two children, came to Germany in 1990. She returned to the Philippines to give birth to her second child where she was in contact with a cousin who later was diagnosed to have tuberculosis. After returning to Germany, a Tine-test and a chest x-ray were done with no pathological findings. Two years later she first noticed a protrusion on her left forehead, which slowly increased in size over a few weeks and was subsequently biopsied on an outpatient basis, four months prior to admission. Histologically a non-specific inflammatory reaction was found and no specific therapy was suggested. Over the course of the following months, increasing weakness, memory disturbance, and back pain occurred. A visual

disturbance lead to admission in the department of ophthalmology where papilledema was diagnosed and further diagnostic imaging was initiated.

Baseline evaluations on admission

Apart from a local protrusion and ulceration on the left forehead and a right-sided facial nerve weakness, clinical examination was normal. Laboratory findings demonstrated an elevation of CRP (152 mg/1) and fibrinogen (6.54 g/1), a decrease of T-lymphocytes and T-helper cells with normal T-suppressor cells and B-cells. Granulocyte function was normal and bone marrow cytology showed a normal differentiatial pattern. A Tine-test was now strongly positive. HIV-I and HIV-II were negative.

Diagnostic imaging

An MRI of the head demonstrated a lesion of the skull protruding into the intracranial space with a severe space occupying effect. It had central hypo- to isointensity (T1) and peripheral massive enhancement (Fig. 1a). Perifocal oedema contributed substantially to the mass effect in the left frontal region, where the cerebral cortex was poorly delineated. There was also an extracranial part, involving the subcutaneous tissues. On transcranial B-scan sonography, the lesion appeared as an epidural tumour with no delineation of a dural barrier and no defined cortical interface, suggesting invasion of the brain surface (Fig. 1a). A spinal MRI showed primary osseous lesions with imaging characteristics similar to those of the cerebral lesion. Initially, there was minor epidural bulging into the spinal canal, which resolved completely after therapy. A chest X-ray showed no pulmonary lesions, but an osteolytic destruction of the proximal parts of the left 7 and 9 ribs. CT scanning showed multiple mediastinal, and paravertebral soft tissue masses with accompanying bone infiltration and destruction (Fig. 1b).

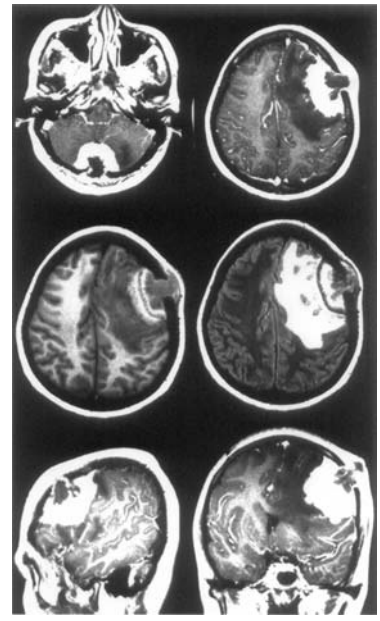
Surgical treatment

Raised intracranial pressure and a significant mass effect required resection of the left frontal lesion. The eroded skin above the protrusion was excised and a left frontal craniotomy was performed. Necrotic tissue underneath the skin and within the bone defect was removed. The tumor presented as a solid, yellowish tumour with little vascularization. No dural tissue was found delineating the mass from the brain surface. The mass was decompressed using a monopolar wire loop. However, arachnoidal infiltration and perivascular extensions of the lesion did not allow the definition of a cortical cleavage plain. The dura was closed with a Gore-Tex patch and the bone defect was reconstructed with a polymer implant (Palacos™).

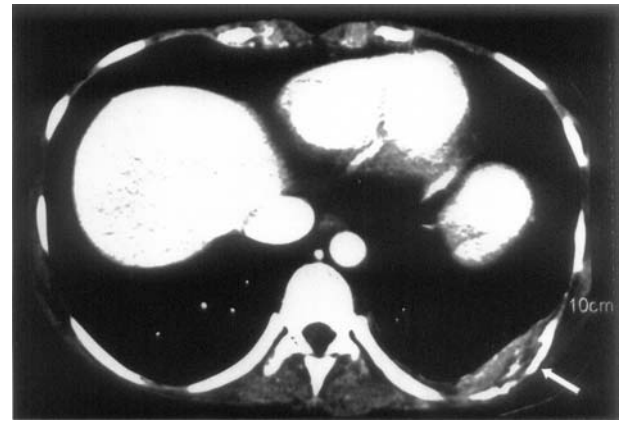
Histology and microbiology

Histological evaluation of the left frontal tumour demonstrated a granulomatous inflammation within connective tissue and skeletal muscle, which consisted of lymphocytes, plasma cells and numerous epitheloid and Langhans giant cells (Fig. 2) As in a tuberculoma, large areas of necrosis were found, but the typical pattern of central caseation, surrounded by lymphocytes, epitheloid cells and Langhans giant cells was not observed and using Fite's staining, no acid-fast bacilli could be demonstrated in any of the specimens. Furthermore, no other infections agents like fungi or gram-positive bacilli could be detected.

Cultures of the neurosurgical specimens yielded a predominant growth of Corynebacterium species and less abundant Staphylococcus epidermidis. Radiometrically material of the Mycobacterium complex could be demonstrated, which was further differentiated by gene analysis as Mycobacterium tuberculosis. Subsequently this agent was cultured



a



b

Fig. 1. (a) T1 weighted, contrast-enhanced images (top and bottom row) showing peripheral enhancement within a thick, apparently cell rich layer surrounding a centre of lower signal intensity possibly representing necrosis. Note the primary high signal of the intracranial portion (middle, left) and the massive, space occupying oedema (fluid attenuated inversion recovery) (middle, right). The bone is penetrated and the dura appears as a thin convex layer within the intracranial part of the lesion, which represents infiltration. (b) Contrast enhanced abdominal CT scan: Contrast enhancing, centrally hypodense lesions were found originating from the dorsal part of left ribs. Additional lesions were identified in the dorsal soft tissues of the spine and within the foramen ischiadicum (not shown)

from the surgical specimen and sputum and a resistance analysis showed sensitivity to Isoniazid (INH), Rifampicin (RMP), Pyranzinamid (PZA), Myambutol (EMB), and Streptomycin (SM).

Clinical course and outcome

Postoperatively the patient was started on an i.v. combination of Unacid and Elzogram for 10 days. Anti-tuberculosis therapy was

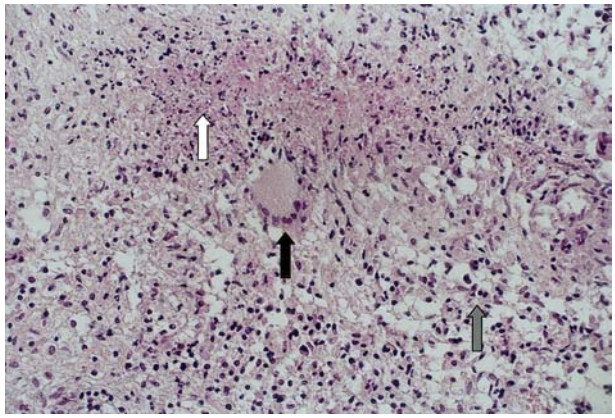


Fig. 2. H&E stained section of the left frontal lesion showing a granulomatous inflammation with epitheloid and Langhans giant cells (black arrow), plasma cells and lymphocytes (grey arrow), and abundant areas of necrosis (white arrow)

initiated with INH, RMP, PZA, and alternating EMB and SM. SM was discontinued after a cumulative dose of 30 g. The patient was maintained on INH, RMP, and EMB over a period of 24 month. Episodes of fever and elevation of CRP occurred for several weeks. All symptoms resolved after two months. At six months, the residual left frontal lesion had significantly decreased in size with resolution of the perifocal oedema. The infratentorial lesion showed a decrease of approximately 50%. Eighteen months after diagnosis all contrast enhancement of both intracranial lesions (Fig. 3) and the spinal manifestations had resolved (Fig. 4).

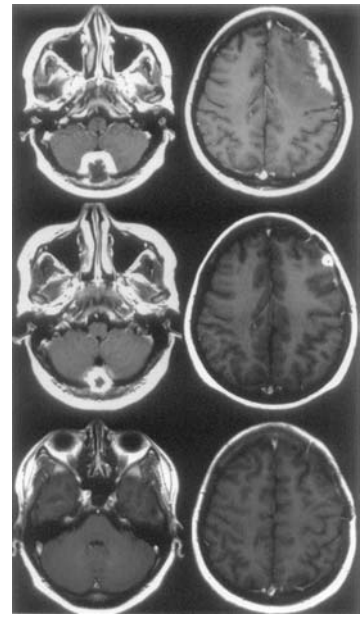


Fig. 3. Follow-up MRI scan after resection of the left frontal lesion: T1 gadolinium enhanced images, 24 hours after surgical decompression (top row), 4 months (middle row) and 18 months (bottom row) follow-up showing resolution of the tuberculomas under an INH, RMP, and EMB regimen. Interestingly, despite the invasive growth and dural and bone destruction no complications due to erosion of the sinus such as haemorrhage or thrombosis had occurred

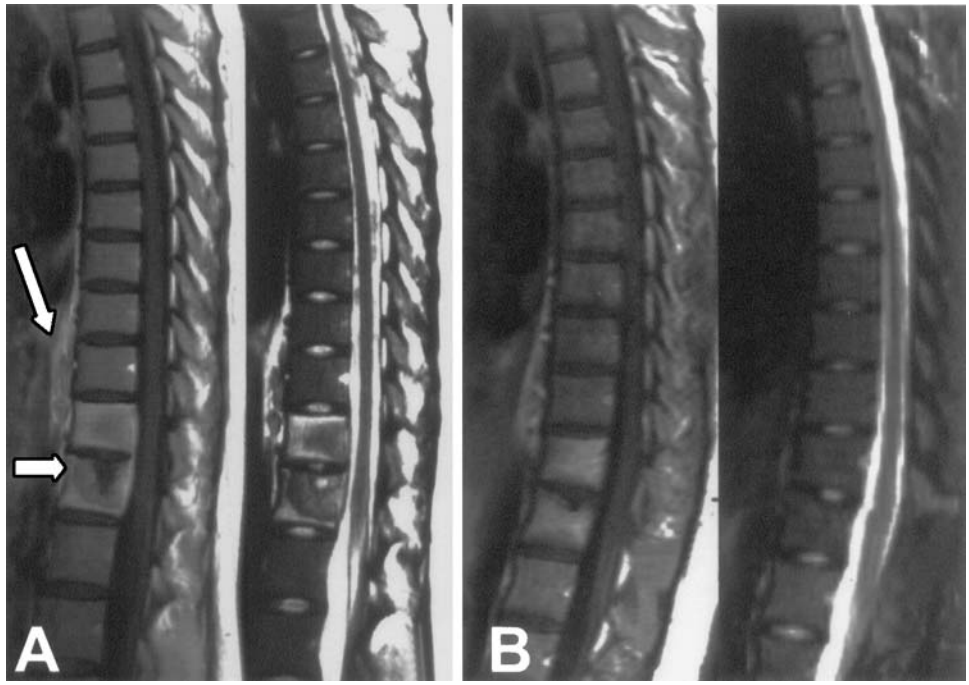


Fig. 4. Image series (T1 weighted, gadolinium enhanced, and T2 weighted sagittal scans of the lower thoracic spine) demonstrating resolution of the lesions within the vertebrae (short arrows) and the dorsal spine including the surrounding soft tissue (long arrows). The morphology of the tuberculomas resembled those of the cranial manifestations. (A) Initial presentation, (B) 18 months follow-up under tuberculostatic therapy

Discussion

Tuberculomas with a dural-based growth pattern are rare and those described have had radiological features of a slow growing meningeoma, some with transcalvarian extension [8, 14, 18]. The patient presented here is unusual because of a relatively short history in an immunocompetent young person who presented with signs of raised intracranial pressure. The MRI demonstrated intracranial tumour-like lesions with marked contrast enhancement, perifocal oedema, bone destruction, dural spread and brain invasion. These imaging characteristics were suggestive of a malignant tumor, supported by the presence of multiple extracerebral soft tissue and osteolytic lesions.

CNS tuberculomas occur in the cerebrum, cerebellum, the subarachnoid, the subdural space, or epidural space. In children, infratentorial lesions dominate, whereas in adults supratentorial lesions are more frequent and tend to be located at the grey to white matter junction and the periventricular regions. Only half of the patients reported have a previous history of tuberculosis. The clinical course is subacute or chronic and presenting signs typically are those of intracranial hypertension, headache, and seizures (reviewed in 10). The tuberculin skin test is positive in 85% of patients [3] but reported-rates of diagnoses of pulmonary tuberculosis on chest radiographs vary from 30–80% [17]. On MRI, a tuberculoma appears isointense to grey matter on T1 images with a nodular or rim enhancement. Caseating lesions may show a central hypointense signal on T2 weighted images [19, 21]. In our patient, a brisk contrast enhancement of the mass was present with a hypointense zone adjacent to the osteolytic defect possibly indicating early transition into an abscess or as the consequence of a mixed infection with Corynebacterium and Staphylococcus epidermidis. Transformation of the caseous core may lead to the formation of a tuberculous abscess, which are less frequent and tend to have greater mass effect and perifocal oedema as well as an accelerated clinical course with fever and focal neurological deficits [22]. These lesions contain abundant bacilli, appear thin walled, uniform with peripheral rim enhancement and a central area of hyperintensity on T2 weighted images [21]. In vivo proton MR spectroscopy and magnetization transfer MR imaging have recently been demonstrated to differentiate tuberculous from other pyogenic brain abscesses [12]. Less frequently, enhancement of adjacent brain indicates an area of cerebritis [20]. Generally, parenchymal CNS tuberculosis is more common in immunocompromised patients and has been reported in 15–40% of AIDS patients with CNS tuberculosis [5].

Medical therapy with a regimen of isoniazid, ethambutol, pyrazinamide, rifampicin, and steroids usually results in a decrease in size and complete resolution of a tuberculoma within 3 months [15]; nevertheless, much longer times, up to years, may be required [7]. Second line drugs include streptomycin, kanamycin, capreomycin, ciprofloxacin, ofloxacin, ethionamide, and cycloserine (reviewed in 11). When a tuberculoma is suspected, medical therapy alone is indicated in the majority of cases but because of the difficulties in differentiation of these lesions from other disorders on neuroimaging alone, a biopsy may be required to expedite treatment [6]. Histology is often fails to demonstrate acid-fast bacilli [8] and, a caseating granulomatous lesion, with typical Langerhans'-type cells in combination with a positive tuberculin skin test may provide an adequate basis, on which to start chemotherapy. Growth of Mycobacterium tuberculosis from CSF, if successful, may take up to six weeks. The patient presented here was made more complex by having a mixed infection, with cultures demonstrating two other agents, before the diagnosis of Mycobacterium tuberculosis could be established.

Surgical resection is indicated for lesions that cause increased intracranial pressure and severe neurological deficits. It may be required also when there is a failure to respond to drugs or even a paradoxical response despite a response of the systemic disease [1, 13].

Conclusion

Parenchymal CNS tuberculosis, with or without extracerebral manifestations, may present as a space-occupying lesion with complex neuroimaging morphology suggesting a benign or malignant neoplasm. Because a tuberculoma is suspected rarely, surgical biopsy is required to establish the diagnosis, especially in those with an atypical morphology. Demonstration of acid-fast bacilli in a tuberculomas is often not possible and treatment has to be initiated based on histological criteria. In a mixed infection, cultures may demonstrate other infections agents whereas bacilli of the Mycobacterium complex may take a long time to be confirmed.

Acknowledgment

We thank Sker Freist for his help in the preparation of the illustrations.

References

1. Afghani B, Lieberman JM (1994) Paradoxical enlargement or development of intracranial tuberculomas during therapy: case report and review. Clin Infect Dis 19: 1092–1099
2. Artico M, De Caro GM, Carloia S, Salvati M, D'Ambrosio M, Delfini R (1999) Advances in diagnosis, treatment and prognosis of intracerebral tuberculomas in the last 50 years. Report of 21 cases. Neurochirurgie 45: 129–133
3. Bagga A, Kalra V, Ghai OP (1988) Intracranial tuberculoma. Evaluation and treatment. Clin Pediatr (Phila) 27: 487–490
4. Baksh FK, Handler MS (1996) Central nervous system Mycobacterium avium complex infection. Arch Pathol Lab Med 120: 614–615
5. Dube MP, Holtom PD, Larsen RA (1992) Tuberculous meningitis in patients with and without human immunodeficiency virus infection. Am J Med 93: 520–524
6. Bouchama A, al-Kawi MZ, Kanaan I, Coates R, Jallu A, Rahm B, Siqueira EB (1991) Brain biopsy in tuberculoma: the risks and benefits. Neurosurgery 28: 405–409
7. DeAngelis LM (1981) Intracranial tuberculoma: case report and review of the literature. Neurology 31: 1133–1136
8. Di Patre PL, Radziszewski W, Martin NA, Brooks A, Vinters HV (2000) A meningioma-mimicking tumor caused by Mycobacterium avium complex in an immunocompromised patient. Am J Surg Pathol 24: 136–139
9. Dolin PJ, Raviglione MC, Kochi A (1994) Global tuberculosis incidence and mortality during 1990–2000. Bull World Health Organ 72: 213–220
10. Garcia-Monco JC (1999) Central nervous system tuberculosis. Neurol Clin 17: 737–759
11. Gropper MR, Schulder M, Sharan AD, Cho ES (1995) Central nervous system tuberculosis: medical management and surgical indications. Surg Neurol 44: 378–384
12. Gupta RK, Vatsal DK, Husain N, Chawla S, Prasad KN, Roy R, Kumar R, Jha D, Husain M (2001) Differentiation of tuberculous from pyogenic brain abscesses with in vivo proton MR spectroscopy and magnetization transfer MR imaging. AJNR Am J Neuroradiol 22: 1503–1509
13. Hejazi N, Hassler W (1997) Multiple intracranial tuberculomas with atypical response to tuberculostatic chemotherapy: literature review and a case report. Acta Neurochir (Wien) 139: 194–202
14. Isenmann S, Zimmermann DR, Wichmann W, Moll C (1996) Tuberculoma mimicking meningioma of the falx cerebri. PCR diagnosis of mycobacterial DNA from formalin-fixed tissue. Clin Neuropathol 15: 155–158
15. Jacobs RF, Sunakorn P, Chotpitayasunonah T, Pope S, Kelleher K (1992) Intensive short course chemotherapy for tuberculous meningitis. Pediatr Infect Dis J 11: 194–198
16. Jinkins JR (1991) Computed tomography of intracranial tuberculosis. Neuroradiology 33: 126–135
17. Loizou LA, Anderson M (1982) Intracranial tuberculomas: correlation of computerized tomography with clinico-pathological findings. Q J Med 51: 104–114
18. Lindner A, Schneider C, Hofmann E, Soerensen N, Toyka KV (1995) Isolated meningeal tuberculoma mimicking meningioma: case report. Surg Neurol 43: 81–83
19. Shah GV (2000) Central nervous system tuberculosis: imaging manifestations. Neuroimaging Clin N Am 10: 355–374
20. Villoria MF, de la Torre J, Fortea F, Munoz L, Hernandez T, Alarcon JJ (1992) Intracranial tuberculosis in AIDS: CT and MRI findings. Neuroradiology 34: 11–14
21. Whiteman ML (1997) Neuroimaging of central nervous system tuberculosis in HIV-infected patients. Neuroimaging Clin N Am 7: 199–214
22. Whitener DR (1978) Tuberculous brain abscess. Report of a case and review of the literature. Arch Neurol 35: 148–155

Comment

Intracranial tuberculoma is rare today in the developed countries, but tuberculosis is still a very common infectious disease worldwide. Therefore, it must be kept in mind to diagnose and treat properly.

The tuberculoma reported in this paper demonstrated unique morphological findings in the frontal lobe and cerebellum, destroyed the cranial bone and showed growth in the subcutaneous tissue. The pictures of the MRI and CT scans are very fine and show the detailed morphology in this case.

K. Takakura
Toyko

Correspondence: Alf Giese, M.D., Department of Neurosurgery, University Hospital Lübeck, Ratzeburger Allee 160, 23538 Lübeck, Germany. e-mail: alf.giese@neurochirurgie.mu-luebeck.de