TUBERCULOMA OF THE BRAIN – REPORT OF 2 CASES AND REVIEW OF LITERATURE

W T Seow, T T Yeo, P L Ong

ABSTRACT

Tuberculomas of the brain are relatively uncommon in developed countries nowadays. We report the only two cases that were seen in our Department in the last five years. Both patients presented with seizures and were found to have space occupying lesions on cranial CT scanning. They had no past history of tuberculosis, no evidence of current extracranial tuberculosis and the diagnosis of tuberculoma was made at the time of surgical excision. Underdiagnosis of tuberculoma of the brain is likely to occur in industrialised countries where tuberculosis is rare. The radiological investigation of choice is CT scanning with contrast enhancement and the presence of a target lesion is considered to be pathognomonic of a tuberculoma. Most tuberculomas of the brain can be treated medically with antituberculous chemotherapy. We recommend obtaining a definitive histological diagnosis with CT-guided stereotactic techniques prior to commencing antituberculous therapy. Surgical excision is necessary in patients with raised intracranial pressure secondary to the lesion and not responding to medical therapy.

Keywords : Antituberculous chemotherapy, brain, radiology, stereotactic biopsy, surgery, tuberculoma.

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INTRODUCTION

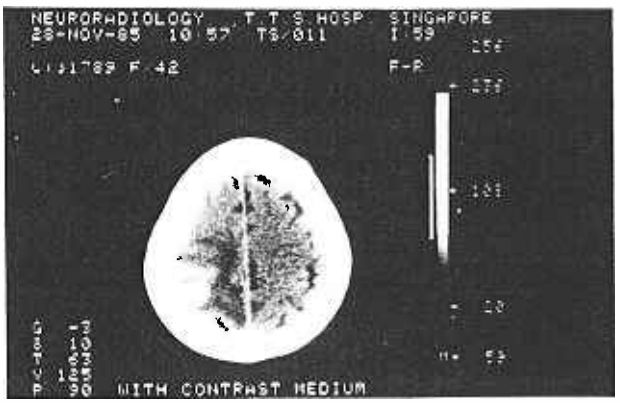
Tuberculomas of the brain are rare in most industrialised countries due to improved socioeconomic conditions and modern anti-tuberculous chemotherapy. In Singapore, slightly over 1600 new cases of tuberculosis were seen in 1989, giving an incidence rate of 60 per 100,000 population which is still high compared with the rate in the industrialised countries. Of the new cases, less than 0.3% were tuberculosis involving the central nervous system[1]. Most of these cases were tuberculous meningitis. We report the only two cases of tuberculoma of the brain seen in our Department during the last five years.

CASE REPORT NO 1

A 32-year-old Chinese lady presented with generalised adult-onset seizures in 1985. She was neurologically intact on examination and CT scan of the cranium showed an area of cerebral oedema in the left parietal region. This was thought to be an area of haemorrhagic infarct and she was treated conservatively. A repeat CT scan of the cranium done six months later did not show any resolution of the oedema and contrast enhanced scans showed a one centimetre diameter contrast enhancing lesion in the region of the oedema (Fig 1).

Cerebral angiography demonstrated an avascular mass. A craniotomy was then performed and at operation, a one centimetre diameter yellowish firm mass was easily resected with a good plane separating the tumour from the surrounding brain. The histology was that of a tuberculoma. Postoperatively, she was immediately commenced on antituberculous medication (SHRZ x 3mths, HRZ x 15mths)*. The patient had no previous history of pulmonary tuberculosis and her chest X-ray was normal. She has not had any more seizures since the operation and a check CT scan in 1988 showed the presence of a left parietal scar but no tumour.

Fig1 - Contrast enhanced CT scan of cranium showing a 1 cm diameter lesion in the left parietal region with surrounding oedema.



CASE REPORT NO 2:

This patient was a 60-year-old Chinese man who had an episode of generalised seizure in January 1990. The neurological examination was normal and he did not have a previous history of tuberculosis. CT scan of the cranium showed patchy enhancement of the gyri on the superior part of the right posterior frontal lobe with surrounding edema (Fig 2). At angiography, no abnormalities were seen on the right internal carotid injection but a selective right external carotid injection revealed a vascular blush corresponding to the lesion seen on CT scan (Fig 3). The lesion was supplied by the right middle meningeal artery and another meningeal branch arising from the right internal maxillary artery, suggesting the radiological diagnosis of a meningioma. A craniotomy was performed and the dura was found to be fairly vascular. On opening the dura, a yellowish firm tumour was found attached to the dura and

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* SHRZ x 3 mths : Streptomycin 0.5 gm/day, Isoniazid 300 mg/day Rifampicin 600 mg/day, Pyrazinamide 1.5 gm/day

* HRZ x 15 mths : Isoniazid 300 mg/day, Rifampicin 600 mg/day, Pyrazinamide 1.5 gm/day

infiltrating the adjacent cortex. The tumour was removed subtotally after frozen section showed it to be a granuloma. Postoperatively, the patient developed weakness and paresthesia of the left upper limb. He was started immediately on antituberculous therapy (SRHZ x 3 months)*. The histology showed fibrous tissue with caseating granuloma composed of epitheloid cells, Langhan type multinuclear giant cells with a chronic inflammatory infiltrate (Fig 4). Acid fast bacilli were also seen on staining. The left upper limb deficits have resolved and he is still on antituberculous therapy (HR)**.

DISCUSSION

Tuberculoma of the brain used to be a commonplace lesion in the early part of this century. They constituted 34% of all intracranial space-occupying lesions seen at necropsy in a study reported in 1933 from Leeds, England[2]. In 1972, they comprised only 0.15% of 2200 intracranial tumours reported by Maurice-Williams[3]. The decline in frequency of these lesions in Britain and in the industrialised countries of Europe was due to the improved socioeconomic conditions and to improved anti-tuberculous chemotherapy. However tuberculomas of the brain are still significant in countries where tuberculosis is

Fig 2 - Contrast enhanced CT scan of cranium showing patchy enhancement of gyri on superior part of the right posterior frontal lobe with surrounding oedema.

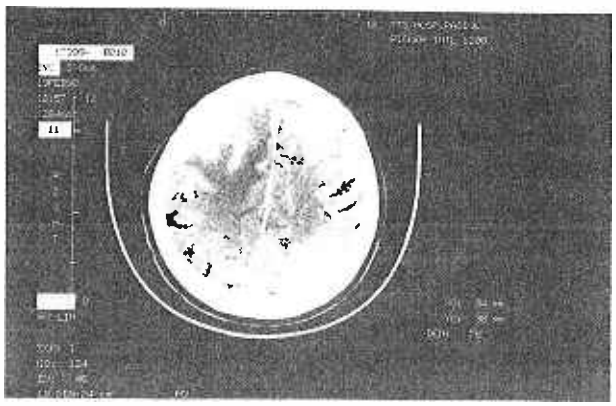
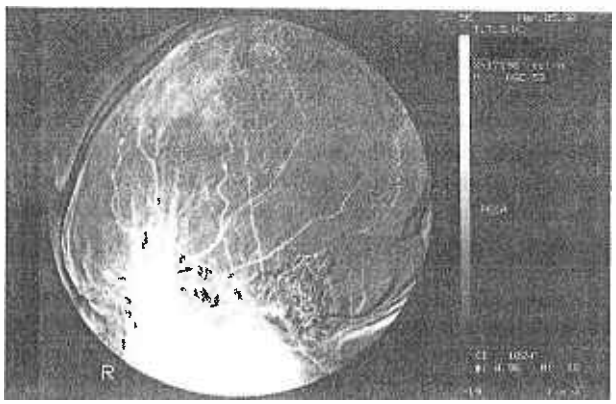


Fig 3 - Selective right external carotid angiogram showing the lesion (vascular blush) supplied by the right middle meningeal artery and meningeal branch of the right right maxillary artery.



* SHRZ x 3 mths : Streptomycin 0.5 gm/day, Isoniazid 300 mg/day, Rifampicin 600 mg/day, Pyrazinamide 1.5 mg/day

** HR : Isoniazid 300 mg/day, Rifampicin 600 mg/day.

Fig 4 - Dura showing multiple caseating granulomas with gliotic brain at one corner (H + E x 100).

endemic, such as India (12.3 to 20%), South America and Africa[4-8]. With the influx of immigrants and the increasing prevalence of the human immunodeficiency (AIDS) virus, there has been an increase in the number of cases of tuberculosis reported in many industrialised countries where a decade ago, it was almost nonexistent[9]. The incidence of tuberculomas of the brain is likely to increase pari passu. In Singapore, whilst tuberculosis is not endemic, it is still prevalent. Hence we are likely to see more cases of intracranial tuberculomas.

The clinical presentation of intracranial tuberculoma is usually that of increased intracranial pressure with papilledema and focal neurological deficits related to the site of the lesion[4,6,7,10-13]. Epilepsy is not commonly mentioned although this was the presenting symptom in both our patients. In a recent paediatric series, the majority presented with focal seizures[14]. Our patients also did not present with any neurological deficits. More than half the reported cases had an extracranial site of tuberculosis, either in the past or as a current infection[4,7,10,11,13,15]. Both our patients did not have any history of tuberculosis. The Mantoux test was negative in both patients and this test may not be reliable with intracranial tuberculomas[10,11]. The CSF of patients with intracranial tuberculomas was not examined in most studies, although in one study the most common abnormality was isolated protein elevation[12].

The radiological investigation of choice in patients suspected of having intracranial tuberculoma is CT scanning with contrast enhancement[10,15-18]. Whelan and Stern described two patterns of contrast enhancement on CT scanning; the "micro-ring" which is a small ring of enhancement surrounding a central punctate lucent area representing the caseating tuberculous granuloma and the less definitive "nodular enhancement" type of lesion[18]. Welchman described the "target sign" which is a central nidus of calcification with peripheral ring of contrast enhancement and suggested that this is specific and pathognomonic of an intracranial tuberculoma[19]. Van Dyk reported 12 out of 58 intracranial tuberculomas having this target sign[20]. Choudhury reported that the central portion of a tuberculous ring is isodense or hyperdense compared to the

hypodense centre of a pyogenic abscess or a cystic glioma[17]. In the solid form of tuberculoma, he suggested that the lucent core, indicating caseation, is pathognomonic of a tuberculous lesion. There is usually surrounding cerebral oedema and in some cases, the area of oedema far surpasses the size of the lesion[20]. Patient 1 had a ring lesion whilst patient 2 had a solid lesion but both did not have a target sign lesion.

Angiographically, these lesions are avascular with evidence of space occupation[4,10,13-15,20,21]. Ramamurthi and Varadarajan reported a subgroup which is superficial and shows mild vascularity[4]. Both these angiographic types were seen in our patients.

At operation, tuberculomas usually appear as well circumscribed yellowish or grayish-white masses. An area of often gritty, central caseating necrosis may be seen[15,16]. On histological examination, the picture is that of a typical granulomatous lesion with a necrotic core surrounded by epitheloid cells, lymphocytes and Langhans giant cells. Acid-fast bacilli may be seen, as in case 2 but not in all reported series[3,4,10,12,13,22]. Cultures of the organism is thought to be even harder with a recovery rate of about 50%[3,10,12,13,16]. Cultures for M tuberculosis were positive in case 2.

Treatment

Most studies suggest that tuberculomas of the brain can be treated non-surgically with anti-tuberculous chemotherapy[10,14,17,23,24]. They suggest that chemotherapy should be started in patients who have evidence of extracranial tuberculosis and who have a typical lesion seen on the CT scan. This should be for a period of 18 months and should include drugs such as isoniazid, rifampicin, pyrazinamide and ethambutol which are bactericidal and can cross the blood brain barrier. Triple anti-tuberculous therapy consisting of isoniazid (300mg/daily), rifampicin (10mg/kg body wt/daily or 600 mg/day) and ethambutol (25 mg/kg body wt/daily for two months and 15 mg/kg subsequently) has been recommended with discontinuation of ethambutol after 3 to 5 months. Streptomycin (750 mg/daily) and pyrazinamide (30 to 50 mg/kg body wt/daily) may also be added to the regime[10,14,15]. Both our patients were treated with a combination of isoniazid, rifampicin and pyrazinamide (30 mg/kg, to avoid liver toxicity) with streptomycin added on as a fourth drug in the initial period. The combination of isoniazid, rifampicin and pyrazinamide is preferred as it is more potent than that of isoniazid, rifampicin and ethambutol[25,26]. Our patients were referred to the chest physicians in our hospital for supervision of their anti-tuberculous chemotherapy because of their familarity with the drugs used. Corticosteriods such as dexamethasone have also been used as an adjunct in the treatment of tuberculomas of the brain. They are especially useful in treating the associated raised intracranial pressure. With anti-tuberculous drug coverage, exacerbation of the disease is not common[17,27].

When patients are treated on such a presumptive diagnosis of tuberculoma of the brain, they should be examined regularly and have regular follow-up CT scans to monitor the progress of the disease. A repeat CT scan after 12 weeks of chemotherapy is recommended by Choudhury and if the lesion has not regressed, biopsy of the lesion is mandatory to establish the pathology[17]. However, we feel that definitive histological diagnosis of tuberculosis should be obtained whenever possible prior to commencement of chemotherapy. This is especially so in patients with no extracranial tuberculosis and in places where tuberculoma is uncommon. Definitive histological diagnosis can be effectively and safely taken care of with CT-guided stereotactic techniques[28,29]. This will avoid delay in the diagnosis of other cerebral mass lesions and unnecessary anti-tuberculosis therapy which is not without side-effects. Certainly in centres where this surgical technique is available, histological diagnosis should be obtained prior to starting anti-tuberculosis therapy.

CT-guided stereotactic biopsy is specifically recommended for deep-seated lesions such as those in the basal ganglia, thalamus or even brainstem and for atypical lesions in which the diagnosis is in doubt[16]. Stereotactic aspiration is particularly useful in decompressing tuberculomas with liquified centres.

Surgical excision of tuberculomas is necessary in patients who have raised intracranial pressure secondary to the lesion and not responding to medical treatment[10,15,16,23,24]. This is especially so in patients who have superficial lesions easily accessible to excision. At surgery, it may not be possible to remove the lesion completely and debulking of the lesion is all that is needed unless it proves to be easily resectable[16]. In these patients, anti-tuberculous chemotherapy should be continued to prevent the complication of tuberculous meningitis, which in the past has been responsible for the high mortality associated with excision of these lesions[11,12].

A subgroup of patients undergoing surgery are those who are thought pre-operatively to have a tumour and in whom the differential diagnosis of a tuberculoma had not been entertained. This was the situation seen in both our patients, and is likely to occur more frequently in the industrialised countries where tuberculosis is rare but which has a large immigrant population. Frozen sections will reveal the diagnosis and in such a setting, the lesion should be totally excised only if this can be easily done. Immediately post-operatively, these patients should be started on anti-tuberculous therapy and should continue the therapy for the recommended 18 months, preferably under the care of a physician familiar with the treatment of tuberculosis.

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