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## Brain tuberculoma in Hong Kong

### 香港的腦結核瘤

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We report two cases of brain tuberculoma occurring in patients residing in Hong Kong. Both patients presented with headache and had space-occupying lesions evident on computed tomography scans of the brain. The patients had no history of tuberculosis and no symptoms of concurrent extracranial tuberculosis were evident. The diagnosis of tuberculoma was made at the time of surgical excision. Delayed diagnosis of brain tuberculoma is likely to occur in industrialised countries where tuberculosis is rare. In Hong Kong, however, with a constant influx of foreign domestic workers from endemic regions, a high index of suspicion should be maintained. Imaging studies support, but do not confirm, the diagnosis of brain tuberculoma. We recommend obtaining a definitive histological diagnosis, with computed tomography-guided stereotactic biopsy, before starting antituberculous therapy. Surgical excision is necessary in patients with raised intracranial pressure secondary to the lesion, who are not responding to medical therapy.

我們報告了兩個居於香港的腦結核瘤患者之病例。兩名患者均呈現頭痛，而電腦掃描亦有明顯之病灶。患者並沒有肺結核病史，亦沒有明顯的顱外結核病徵。結核瘤是在外科切除手術時所作的診斷。在肺結核罕見的工業化國家，腦結核瘤的診斷很可能會出現延誤。然而由於外地傭工持續從地方病地區流入本港，我們應對腦結核瘤保持高度警惕。成像檢查只能輔助但不能確認腦結核瘤的診斷。我們建議在開始抗結核治療前，應以電腦掃描立體定位生檢法以確立組織學診斷。倘若患者顱內壓上昇及對藥物治療無效，我們必須施行外科切除手術。

### Introduction

Isolated central nervous system (CNS) tuberculoma is rare. Central nervous system tuberculosis (TB), however, is associated with high morbidity and mortality, despite modern methods of detection and treatment.<sup>1</sup>

As in other developed countries, the incidence of TB in Hong Kong is falling.<sup>2</sup> However, TB remains the most important cause of death among deaths from notifiable infectious diseases (98% of mortality due to such diseases is attributable to TB). Between 1993 and 1995 in Hong Kong, 38 cases of tuberculous meningitis were confirmed bacteriologically in eight regional hospitals and chest clinics, and three were lost to follow-up.<sup>3</sup> Ten of 35 patients died within 2 years. Three of the 35 patients had a brain tuberculoma, one dying within 2 years. Early diagnosis and treatment are crucial for effective treatment of brain tuberculoma.

Two cases of isolated brain tuberculoma seen within 1 month at a regional hospital in Hong Kong are presented.

### Case reports

#### Case 1

A 42-year-old Filipino maid, who had worked in Hong Kong for 16 years, presented with a 1-month history of diffuse headache of gradual onset. The headache was most severe in the morning and had been associated with nausea and vomiting for 1 week. The patient had previously been healthy and had had no seizure episodes. Systemic enquiry and physical examination were unremarkable.

#### Key words:

Diagnosis, differential;  
Hong Kong;  
Magnetic resonance imaging;  
Tomography, X-ray computed;  
Tuberculoma, intracranial

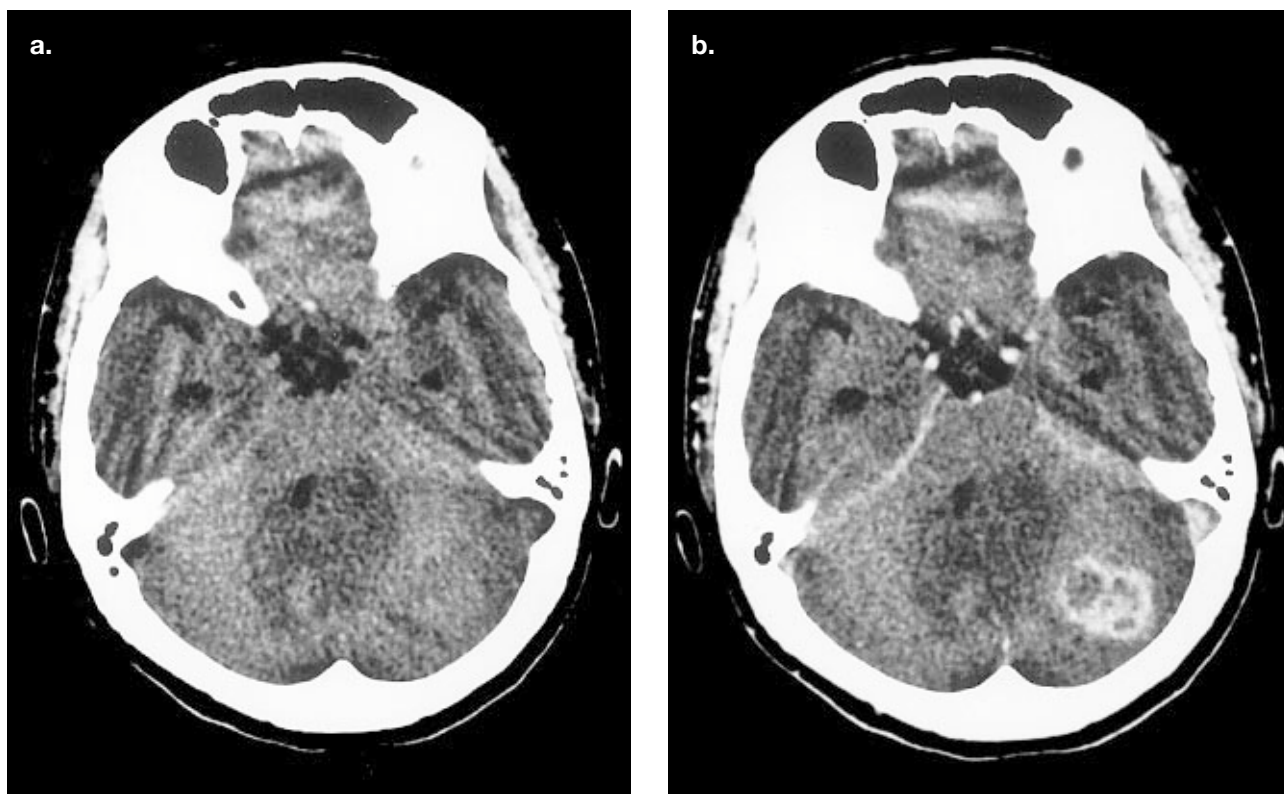
#### 關鍵詞：

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**Fig 1. Computed tomography scans of the brain**

(a) Plain computed tomography; and (b) contrast-enhanced computed tomography scans of the brain show displacement of the fourth ventricle, suggesting a space-occupying lesion in the left cerebellum

Routine blood tests were normal, apart from the erythrocyte sedimentation rate (ESR) of 35 mm/h (normal range, 0-30 mm/h). The chest X-ray was normal. A plain computed tomography (CT) scan of the brain showed a displaced fourth ventricle with moderate hydrocephalus, suggesting a space-occupying lesion in the posterior fossa. An urgent contrast CT scan of the brain was performed (Fig 1). An irregular, rim-enhancing, hypodense lesion with a probable solid component was noted in the left cerebellum. Significant vasogenic oedema with mass effect was present. A further 0.5 cm enhancing isodense lesion in the left centrum semiovale was noted.

The differential diagnoses considered were brain abscess or brain metastasis, in view of the multiple enhancing lesions with perifocal cerebral oedema. Urgent suboccipital craniotomy was performed to remove the posterior fossa mass and obtain a histological specimen. Pathology confirmed the lesion as a tuberculoma, due to the presence of florid granulomatous inflammation, extensive caseous necrosis, Langhans giant cells, lymphocytic infiltration, and acid-fast bacilli (AFB) on Ziehl-Neelsen stain.

The patient made an uneventful recovery. Headache, nausea, and vomiting subsided. Cerebrospinal fluid (CSF), sputum, and early morning urine were negative for TB on assessment postoperatively. Antituberculous chemotherapy was started and the patient was referred to the chest clinic for follow-up. A CT scan 1 year postsurgery showed normal appearance of the fourth ventricle (Fig 2).

### Case 2

A 21-year-old, previously healthy, Indonesian maid, who had worked in Hong Kong for 2 years, presented with a 4-month history of headache and progressive right-sided

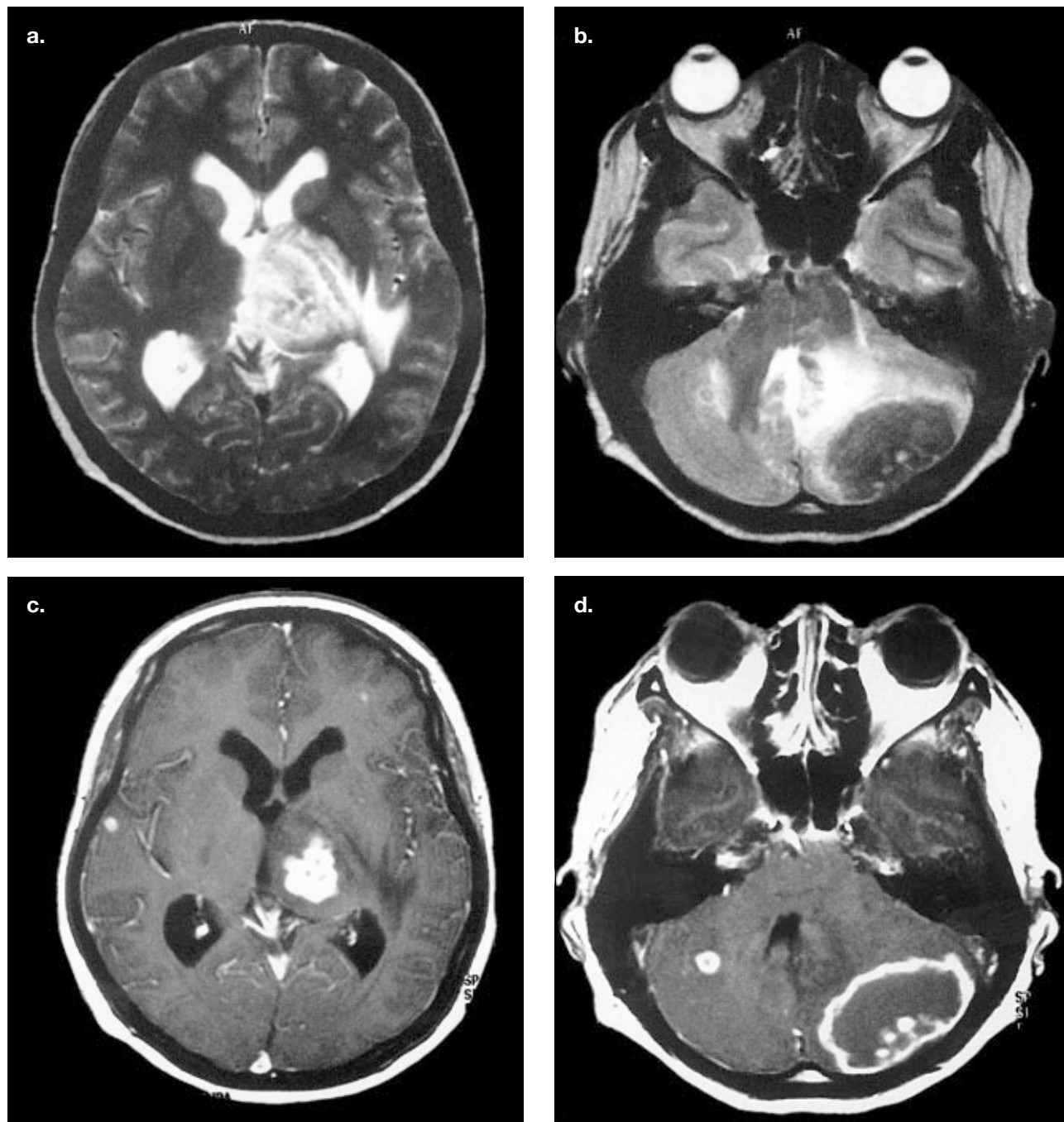


**Fig 2. Computed tomography (plain) scan completed 1 year postsurgery shows the normal appearance of the fourth ventricle**

weakness. There was no other significant history of note. The patient had had no seizure episodes. Neurological examination showed that the patient was fully conscious with a right hemiparesis (power grade 3/5). Reflexes on the right side were brisk, and the plantar reflex was equivocal. The patient was afebrile and had no neck rigidity. There were no other findings of note on physical examination.

Routine blood tests indicated a hypochromic microcytic anaemia (haemoglobin level, 104 g/L; normal range, 120-150 g/L) and a raised ESR of 57 mm/h. Chest X-ray showed

apical calcified lesions. An urgent CT scan of the brain showed moderate hydrocephalus with left thalamic and left cerebellar hypodense lesions. Magnetic resonance imaging (MRI) of the brain identified multiple, rim-enhanced, oval lesions (0.5-5.0 cm) in the supratentorial and infratentorial compartments (Fig 3). Most lesions were not periventricular, and some showed target configuration. The lesions demonstrated iso-intense or hypo-intense signals on T1-weighted images (T1WI), iso-intense or hyperintense signals on proton-density and T2-weighted images (T2WI), and rim gadolinium enhancement, with moderate to marked



**Fig 3. Magnetic resonance imaging of the brain** (a, b) T2-weighted images; and (c, d) post-gadolinium T1-weighted images showing three layers of brain tuberculoma: the central, isodense, caseous, necrotic core (iso-intense and hypo-intense signals in T1-weighted image and T2-weighted images, respectively); the middle Langhans giant cells (enhancing and hyperintense signals in T1-weighted images and T2-weighted images, respectively); and the outer capsule (iso-intense and hypo-intense signals in T1-weighted image and T2-weighted images, respectively)

perifocal, vasogenic oedema. The largest lesion (5.0 x 3.5 x 4.4 cm) was located in the left posterior cerebellum, with an intralésional, enhanced nodule simulating a target lesion. The second largest lesion (2.5 x 2.5 x 3.0 cm) was slightly lobulated and located in the left thalamus; oedema extended to the left cerebral peduncle.

An urgent ventriculoatrial shunt was inserted, followed by suboccipital craniotomy and excision of the cerebellar mass. A ventriculoatrial rather than ventriculoperitoneal shunt was inserted to relieve the hydrocephalus due to extensive peritoneal adhesions encountered intraoperatively. Peritoneal biopsy showed granulomatous inflammation but no AFB were demonstrated. The CSF yielded no growth, and cytology and biochemistry were normal. The differential diagnosis was pulmonary TB with brain tuberculoma and peritoneal TB, or intra-abdominal malignancy with brain, chest, and peritoneal metastases. Empirical antituberculous therapy was started.

Finally, the cerebellar mass was excised because of mass effect, and tuberculoma was confirmed by the presence of florid granulomatous inflammation, extensive caseous necrosis, Langhans giant cells, lymphocytic infiltration, and AFB on Ziehl-Neelsen stain. The patient had an uneventful recovery and continued antituberculous therapy on return to Indonesia.

## Discussion

### Pathogenesis

Tuberculosis is an airborne disease caused by the bacterium *Mycobacterium tuberculosis*. The two primary pathogenic processes of CNS TB are meningoencephalitis and granuloma (tubercle) formation.<sup>4</sup> Both patients presented with left-sided lesions, which supports the theory that haematogenous spread is to the dominant left brain.<sup>5</sup> The pathological process begins with the formation of bacilli-containing caseous tubercles (Rich's foci) in the brain parenchyma.<sup>5</sup> The tubercles may enlarge to form sizeable tuberculomas, especially if the site of Rich's foci is deep, and has greater tensile strength than the surrounding tissue. Alternatively, the Rich's foci may rupture, leading to the development of meningoencephalitis.

### Endemic regions

Domestic workers in Hong Kong may be at high risk for CNS TB because these workers come from countries where TB is endemic. Indonesia, The Philippines, and Thailand are three endemic regions that are on the World Health Organization's observational list for TB<sup>6</sup> and where TB is a major cause of mortality.<sup>7,8</sup> Pre-employment medical assessments, including chest radiographs and skin tests for TB, along with medical examinations, at least annually, are important for such migrants.<sup>9</sup>

### Diagnostic dilemma

A well-described correlation exists between MRI and histological findings of brain tuberculoma.<sup>10</sup> Magnetic

resonance imaging reveals three concentric layers within the tumour (Fig 3). The central core with caseous necrosis shows iso-intense and hypo-intense signals in T1WI and T2WI, respectively. The middle layer contains Langhans giant cells and epithelioid cells with substantial oedema. It shows hypo-intense and hyperintense signals in T1WI and T2WI, respectively. The outer collagenous capsule shows iso-intense and hypo-intense signals in T1WI and T2WI, respectively. Only the middle layer is enhanced by gadolinium.

A tuberculoma with mass effect on the brain, as with other space-occupying lesions, is a surgical emergency because of the need to control intracranial pressure. For a small brain tuberculoma, however, controversy exists concerning appropriate treatment following diagnostic radiology assessment. Some authors recommend empirical medical therapy, without the need for histological confirmation,<sup>11</sup> while others consider that such therapy should be withheld until a definitive diagnosis is made.<sup>12-16</sup>

Although the sensitivity of CT in diagnosing intracranial tuberculoma is 100% and its specificity is 86%, the positive predictive value has been reported to be as low as 33% even in a high-incidence population in India.<sup>17</sup> Magnetic resonance imaging is slightly superior to CT in demonstrating the extent of lesions, especially in brainstem tuberculoma.<sup>18</sup> Nevertheless, intracranial metastatic tumours,<sup>19,20</sup> malignant gliomas,<sup>21,22</sup> meningiomas,<sup>23</sup> and neurocysticercosis,<sup>24,25</sup> may appear similar on CT and MRI.

Furthermore, in a patient with tuberculoma without meningitis, samples of CSF taken for AFB smear or TB culture are usually not informative.<sup>26</sup> An *M tuberculosis* complex-specific polymerase chain reaction assay of CSF can be used to diagnose tuberculoma,<sup>27</sup> but is not generally available as an emergency test.

When diagnosis is uncertain, histology is mandatory to differentiate tuberculoma from other infectious or neoplastic disease. Tissue culture is also of particular value in non-compliant patients or multidrug-resistant cases.<sup>28</sup> Computed tomography-guided stereotactic biopsy, which is minimally invasive, is particularly helpful in the management of small, deep-seated intracranial tuberculomas, which can be treated medically once a diagnosis is established.<sup>29-31</sup> Such use of CT-guided biopsy excludes neoplasms and avoids the empirical treatment of brain masses.

Patients with CNS TB should receive a prolonged (12-30 months) course of effective antituberculous therapy. Evidence of a new intracranial tuberculoma, or of expanding existing lesions, does not necessitate a change to the antituberculous regimen.<sup>32</sup> Such an immune-mediated, paradoxical response to antituberculous therapy has been documented worldwide.<sup>32</sup> In such cases, systemic dexamethasone as adjuvant therapy for 4 to 8 weeks is effective.<sup>32</sup> With appropriate and timely treatment of brain

tuberculoma, only approximately 10% of patients die, while 50% of patients recover completely.<sup>16,32</sup>

## Conclusion

Delayed diagnosis of brain tuberculoma is likely to occur in industrialised countries where TB is rare. In Hong Kong, however, as there is a constant influx of foreign domestic workers from endemic regions, a high index of suspicion should be maintained. Pre-employment and periodic (at least annual) medical assessments are important. Headache, with symptoms of raised intracranial pressure, should prompt consideration of brain tuberculoma in high-risk groups.

Imaging studies support, but do not confirm, the diagnosis of brain tuberculoma, and prognosis and treatment differ between brain tuberculoma and other brain lesions such as metastatic brain tumour, malignant glioma, or neurocysticercosis. Thus, the authors recommend obtaining a definitive histological diagnosis by CT-guided stereotactic biopsy before starting antituberculous therapy. Histological diagnosis also serves to alleviate any doubt of original misdiagnosis in patients where follow-up imaging studies show progressive lesions, as seen with a paradoxical response to antituberculous drug therapy, multidrug-resistant TB, or a non-compliant patient. Surgical excision is necessary when intracranial pressure is raised, secondary to the lesion, and medical therapy has failed.<sup>17</sup>

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