

## Tuberculomas of the central nervous system : clinicopathological study of 30 cases.

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*Thirty patients with tuberculoma of the central nervous system were reviewed, the largest series yet reported in Thailand. There were 29 intracranial lesions and 1 intramedullary tuberculoma of the spinal cord. The latter example appears to be the first instance in Thailand in which the tumour was removed surgically. The lesions were most frequent in men in the first decade, but were most common in women in the second to fourth decades by a ratio of 3:1. The peak prevalence was in the first and third decades, the average age was 20.4 years. The patient's age was related to the location; cerebellum was the most common site in children. The length of illness was usually less than one year regardless of the tuberculoma's size. Most patients had clinical symptoms of headache and increased intracranial pressure, while hemiparesis and fever were uncommon. Carotid angiograms often demonstrated an avascular mass. CT appearance was variable showing either enhancing or nonenhancing lesions. There were 4 deaths with neither surgical intervention nor specific therapy, and 3 immediate postoperative deaths in this series.*

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ได้ทำการศึกษาผู้ป่วยด้วยทูเบอร์คิวโลมาของระบบประสาทส่วนกลาง จำนวน 30 ราย ในช่วง 10 ปีแรก มักพบในชายมากกว่าหญิง แต่ในช่วงอายุ 11-40 ปี มักพบในหญิงมากกว่าชาย ด้วยอัตราส่วน 3 : 1 อายุที่พบบ่อย อยู่ในระยะ 1-10 ปี และ 21-30 ปี โดยมีอายุเฉลี่ย 20.4 ปี ก้อนทูเบอร์คิวโลมาเกิดขึ้นที่สมองและสมองเล็กถึง 29 ราย มีเพียง 1 ราย ที่พบบริเวณไขสันหลัง ซึ่งนับเป็นรายแรกของประเทศไทย ตำแหน่งที่เกิดรอยโรคมีความสัมพันธ์กับอายุ กล่าวคือ ในเด็กมักพบก้อนที่สมองเล็ก ระยะเวลาของอาการมักจะสั้นกว่า 1 ปี และ ไม่มีความสัมพันธ์กับขนาดของก้อน ผู้ป่วยมักมีอาการปวดศีรษะ และความดันกะโหลกศีรษะเพิ่มเป็นส่วนใหญ่ และส่วนน้อยที่มีอาการ อัมพาตและ ไข้ การฉีดสีเข้าหลอดเลือดแดงคาโรติคมักพบว่าเป็นก้อนที่มีเส้นเลือดหล่อเลี้ยงน้อย ส่วนลักษณะที่ตรวจพบ โดยเอ็กซเรย์คอมพิวเตอร์ มักมีลักษณะไม่แน่นอน การศึกษานี้พบว่าผู้ป่วยถึงแก่กรรม 4 ราย โดยที่ไม่ได้รับการผ่าตัดหรือรับการรักษาคด้วยยาต้านวัณโรค อีก 3 รายถึงแก่กรรมภายหลังการผ่าตัด

The incidence of tuberculomas of the central nervous system (CNS) ranges from 0.15% amongst the 2200 intracranial tumours in Britain<sup>(1)</sup> to 30% of 373 brain tumours in India.<sup>(2)</sup> According to Shuangshoti and Hongsaprabhas the lesion represents about 1% of 1028 intracranial tumours which is as low as some western countries, although tuberculosis remains a significant problem in Thailand.<sup>(3,4)</sup> We here analyze the clinical and pathological findings in 29 intracranial tuberculomas and a case of intramedullary tuberculoma of the spinal cord. The latter example appears to be the first reported case in this country.

### Materials and Methods

Twenty cases of tuberculomas of the CNS with tissue confirmation were obtained from the Department of Pathology, Chulalongkorn Hospital during the 17-year period from January 1973 through February 1990. Two examples (case 11,12) have been reported elsewhere.<sup>(3)</sup> Cases were identified by a search of the neuropathology records. The clinical data and pathological findings of these patients were studied in detailed. As far as can be ascertained 10 additional cases have been described in Thailand thus bringing the total to 30 in this review (Table 1).<sup>(5-10)</sup> The cases of Sangcham et al (case 2), and Viriyavejakul et al (case 3) have not been included because of lack of tissue diagnosis.<sup>(9,10)</sup>

### Results

The 30 patients were distributed in the following age decades: 9 cases in the first, 5 cases in the second, 8 cases in the third, 4 cases in the fourth, 2 cases in the fifth, 1 case in the sixth and 1 case in the eighth decades. The youngest patient was a 1-year-old boy and the oldest patient was a 74-year-old man. The average age was 20.4 year. There were 13 men and 17 women. The male preponderance was noted in the first decade by a ratio of 3.5:1 while the lesions were found more frequently in

the second, third and fourth decades by the same ratio. Two women were pregnant (case 17 and 21) at the time of diagnosis.

We met 2 cases of multiple tuberculomas, the remainders were solitary. There were 17 infratentorial lesions and 14 supratentorial masses. The most frequent recorded sites in decreasing order of frequency were cerebellum in 14 cases, temporal in 4 cases, frontal in 3 cases, parietal in 2 cases, brainstem in 2 cases, frontoparietal in 1 case, temporoparietooccipital in 1 case, thalamus in 1 case, basal ganglia in 1 case, base of skull in 1 case, region of cerebellopontine angle in 1 case, and spinal cord in 1 case. The patients' age was related to the location. In patients under 10 years, the lesion was found mostly in infratentorial region by a ratio of 4:1 After the age of 20; it occurred more often in the supratentorial region by a ratio of 3:2.

The size of tuberculoma ranged from 0.9 cm to 7 cm in greatest dimension. Eleven cases were small (2 cm or less in diameter); twelve were medium (between 2.1 to 4 cm); and four were larger than 4 cm. Analysis of size of tuberculoma in relation to duration of symptoms revealed that most lesions regardless of size were associated with a short time of illness often less than 1 year. The shortest duration was 2 days in a patient with a 2 cm tuberculoma; the longest was 4 years, related to a 7 cm lesion.

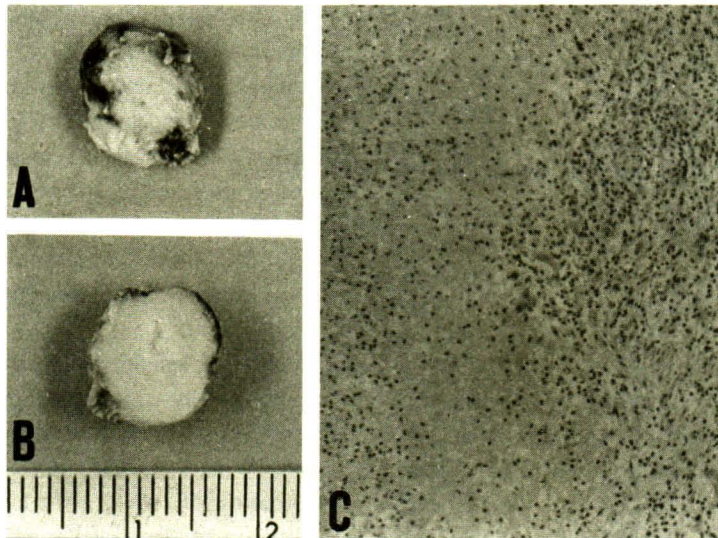
The lesions were grossly well circumscribed, firm with gray-white cut surface (Fig 1) which often showed central areas of caseation (Fig 2,3). Microscopically, the mass was essentially similar to the tubercles in tuberculosis elsewhere. The lesion was characterized by infiltration of lymphocytes, epithelioid and giant cells, accompanied by variable central caseation necrosis with sparse reticulin and collagen fibers on the periphery (Fig 3C,4). Acid-fast bacilli were found in 9 surgical specimens and 3 necropsy cases (Fig 4).



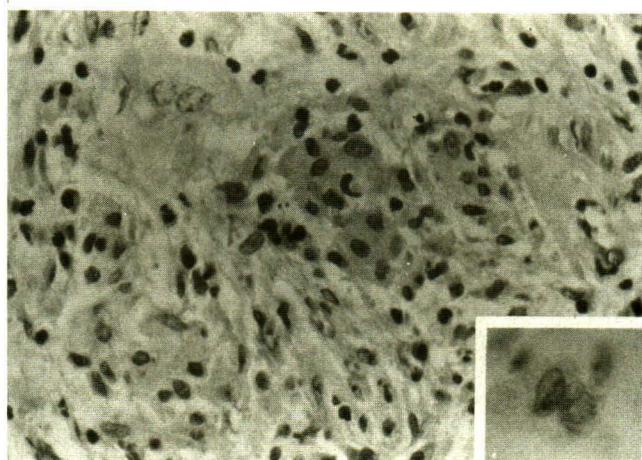
Figure 1. Tuberculoma confined to the left cerebellar hemisphere.



**Figure 2.** Section through a tuberculoma which was removed from the right frontal lobe showing areas of caseous necrosis.



**Figure 3.** (A) Tuberculoma extirpated from the spinal cord.  
 (B) The cut surface showing necrosis which is visible in the central area.  
 (C) Fibro caseous granuloma of the intramedullary spinal lesion. H & E  $\times$  100.



**Figure 4.** Granuloma containing epithelioid cells, lymphocytes and Langhans' giant cells. H & E  $\times$  400. Inset : High power view of the macrophage showing acid-fast bacilli. Kinyoun's acid-fast stain  $\times$  1000.

Table Summary of 30 cases with tuberculomas of the CNS.

Case No	Author(s) year	Age Sex	Length of illness	Clinical Features	Site	Size (cm)	Roentgenographic Investigations			Outcome	
							Chest	Skull	Angriogram		CT findings
1	Chitanondh et al, 1966	26 F	4 yr	Headache, hydrocephalus, bilat. optic atrophy	R. Frontal	Multiple 5x7	Neg	+	NA	ND	Recovery
2	Promkupt, 1988	33 F	10 d.	Headache, R.hemiplegia, bilat. papilledema	L. Basal ganglia	2	Neg	NA	SOL	ND	Recovery
3		26 F	5 mo.	Headache, L. facial palsy	R. temporal	4	+	+	SOL	ND	Recovery
4		12 F	1 mo.	Headache, ataxia, bilat. papilledema	R. cerebellum	3	Neg	+	NA	ND	Recovery
5	Poungvarin et al, 1982	18 F	2 yr.	Headache, fever, ataxia, bilat. ptosis & 6 <sup>th</sup> CN palsy	R. cerebellum	0.9	+	NA	NA	Neg	Death (autopsy)
6	Viriyavejakul et al, 1983	2 F	3 mo.	Ataxia, Leg weakness, bilat. cerebellar signs	R. thalamus Cerebellum	Multiple 0.8	+	+	NA	Multiple enhanceable masses	Recovery
7		22 F	7.5 mo.	R.hemiparesis, headache, R. facial palsy, bilat. papilledema	L. parietal	NA	NA	NA	Avascular mass	ND	Recovery
8	Sangcham et al, 1986	1 M	3 mo.	Scalp mass, increased intracranial pressure	Brainstem	1	+	+	NA	ND	Post op. death (immediate) Recovery
9		3 M	NA	Headache, fever, ataxia, bilat. papilledema	L. cerebellum	3	+	NA	NA	ring-enhancement	Recovery
10	Phuenpathom et al, 1988	49 F	6 mo.	Headache, L. cerebellar sign, bilat. papilledema	Vermis	3	+	NA	NA	ring-enhancement	Recovery
11*	Present study	16 F	8 mo	Headache, bilat. optic atrophy L.hemiparesis	R. fronto-parietal	5	-	+	SOL	ND	Postop. death (immediate) Recovery
12*		22 F	1 mo	Headache, bilat. papilledema and ICP	R. cerebellum	3	+	-	SOL	ND	Recovery
13		34 F	3 yr.	Headache, seizures bilat. papilledema and ICP	R. cerebellum	3	-	+	avascular mass	ND	Postop. death (immediate) Death (autopsy)
14		8 M	1 mo	Fever, cough, dyspnea	L. cerebellum	2.5	+	ND	ND	ND	Death (autopsy)
15		40 F	NA	NA	R. cerebellum	2	NA	NA	NA	NA	Death (autopsy)
16		22 F	3 mo	Fever, 6 <sup>th</sup> CN palsy, nystagnus	Pons	1	-	-	-	-	Death (autopsy)
17		18 F	2 d.	Headache, 3 <sup>rd</sup> CN palsy	L. cerebellum	2	-	NA	NA	Solid enhancement	NA

Table (cont'd)

Case No	Author(s) year	Age Sex	Length of illness	Clinical Features	Site	Size (cm)	Chest	Skull	Angiogram	Investigations	CT findings	Outcome
18		5 M	2 mo	Fever, L. hemiparesis, ataxia	L. cerebellum	NA	-	+	avascular mass	ND	ND	NA
19		11 M	1 yr.	Headache, seizure, L. hemiparesis, Bilat. optic atrophy	R. temporoparietocci pital	4	-	+	avascular mass	ND	ND	Recovery
20		48 M	2 yr.	5th CN palsy, L. facial pain, dysphagia	Base of skull	2	-	+	avascular mass	ND	ND	Death 3 yr. later due to metastatic carcinoma
21		22 F	7 mo	Headache, bilat. papilledema	R. temporal	5	NA	NA	NA	NA	NA	Recovery
22		5 M	2 mo	Headache, seizures. ICP	L. cerebellum	2.5	NA	NA	NA	Solid enhancement	Solid enhancement	Recovery
23		5 F	NA	NA	cerebellum	NA	NA	NA	NA	NA	NA	Recovery NA (refugee)
24		3 M	3 mo	Headache, ataxia, ICP, bilat. optic atrophy	R. cerebellum	4	-	+	NA	non-enhancement	non-enhancement	NA
25		55 F	2 mo	Fever, seizures, R. facial palsy, R. hemiparesis	L. frontal	4	-	+	ND	Solid enhancement	Solid enhancement	NA
26		32 M	2 mo	Seizures, headaches	R. frontal	2	+	NA	ND	Isodense	Isodense	Recovery
27		23 M	3 mo	Headache, fever, R. facial palsy	R. CPA	NA	-	+	ND	ring-enhancement	ring-enhancement	Recovery
28		25 M	1 yr	Headache	L. temporal	3	-	+	ND	non-enhancement	non-enhancement	Recovery
29		6 M	3 d	Fever, headache, R. facial palsy, R. hemiparesis	R. parietal	1.5	-	-	ND	solid-enhancement	solid-enhancement	Recovery
30		74	1 mo	Weakness of Legs	C7-T1	1	-	ND	ND	enhancement	enhancement	Recovery

M = Male, F = Female, L = Left, R = Right, d = day, mo = month, yr = year, NA = not available, ND = not done, + = positive, - = negative, SOL = space occupying lesion; ICP = increased intracranial pressure

\* Case No 11 and 12 have been reported by Siuangshoti et al.<sup>(3)</sup>

Clinically, nineteen patients had progressive headaches, twelve had evidence of increased intracranial pressure such as papilledema, eleven showed palsies of the cranial nerves, eight had fever, seven presented with hemiparesis, seven developed ataxia, and five had seizures. A scalp mass was noted in one instance. One patient with cerebellar lesion had no neurological deficits.

Chest roentgenograms revealed evidence of pulmonary tuberculosis in eight patients, negative findings in twelve cases. Skull films showed evidence of increased intracranial pressure in eleven instances. Carotid angiograms performed in eight patients disclosed avascular mass in these cases. Computerized axial tomography (CT) showed a variety of changes including five solid-enhancing lesions, three ring-enhancing masses, two non-enhancing tumors, one isodense lesion, and one patient with negative finding.<sup>(7)</sup>

Twenty six patients underwent craniotomy. Of these, 25 individuals had additional antituberculous drugs. There were 8 deaths, 17 were known to be alive, and 5 could not be followed. Among the deaths, only 3 died shortly after craniotomies. Four patients died without either surgery or specific therapy. One patient died from metastatic carcinoma of the colon 3 years after craniotomy for the tuberculoma.

## Discussion

Tuberculomas of the CNS occur most frequently in children and young adults in developing countries where tuberculosis is widespread.<sup>(11)</sup> By contrast most patients with intracranial tuberculomas in western countries were adults.<sup>(12)</sup> In this study the peak prevalence was in the first and third decades. Our findings thus differ from reports from developing and industrialized countries. The results also suggest that tuberculomas may occur at any age and remain a problem of either children or adults in Thailand.

According to Dastur et al, intracranial tuberculomas affected women more than men particularly in patients who either recently delivered a child or were pregnant.<sup>(2)</sup> Our findings showed that women of child-bearing age had more frequent lesions than men by a ratio of 3:1 Furthermore, two patients were pregnant. Such high incidence of intracranial tuberculoma in women could be attributed to a reactivation of tuberculosis by pregnancy.<sup>(2)</sup>

Infratentorial lesions are considered to occur more frequently in children and supratentorial tuberculomas more often in adults.<sup>(1,11,12)</sup> This observation was confirmed in our study. Although the lesion can appear anywhere in the CNS, cerebellum is the most common location in patients under 10 years. It should be noted that

intramedullary spinal tuberculoma is extremely rare. The paucity of case is shown by Lins' 1960 review who collected only 105 cases since the early reports in 1930 and only 16 were removed surgically.<sup>(13)</sup> The proportion of intracranial to intramedullary spinal lesion ranges between 20:1 and 48:1.<sup>(13,14)</sup> Our single report of such intramedullary tuberculoma appears to be the first one in Thailand.

Although multiple tuberculomas were reported in more than half the cases in a review from India, we found only 2 cases with multiple lesions.<sup>(15)</sup> The reason is not known. Two-third of masses were of small and medium size. However, most patients had symptoms for less than 1 year, regardless of tumour size. Some tuberculomas were asymptomatic or produced symptoms for many years. Hence the duration of illness was not proportional to the size of the lesions.

Most patients present with symptoms and signs of space occupying lesions. The incidence of papilledema varies from 42% to 93%, headaches in 60 to 75%, and seizures in 50 to 85%.<sup>(2,11,16-18)</sup> In our series, about two-thirds had progressive headaches and one-third showed evidence of increased intracranial pressure and palsies of cranial nerves. The large series, do not report the latter clinical manifestation.<sup>(2,17)</sup> Additionally seizures were seen in fewer patient in our experience. Hemiparesis and fever are uncommon in most series including the present study.<sup>(1,2,17)</sup>

The incidence of abnormal chest roentgenograms compatible with pulmonary tuberculosis ranges from 25% to 50% in patients with tuberculomas of CNS in industrialized countries, while in Chile, 83% of patients had abnormal chest films, many with active disease.<sup>(4,12,16,18)</sup> About 27% of patients in our series showed evidence of pulmonary infiltration. The skull roentgenograms often demonstrate evidence of increased intracranial pressure but offer no specific diagnostic features.<sup>(4,12,16,19)</sup> Calcification in an intracranial tuberculoma is rare occurring in 1.3% to 2.5% of reported cases.<sup>(2,16,17)</sup> None of our patients showed roentgen evidence of calcification. The carotid angiograms usually depict an avascular mass as noted in our patients.<sup>(16,17)</sup> The CT appearance is variable and may be classified as non-enhancing and enhancing lesions.<sup>(20)</sup> It should be noted that CT alone can not differentiate tuberculoma from abscess or neoplasm. Moreover CT may show a negative finding.<sup>(7)</sup> It is thus reasonable to conclude that CT finding is not absolutely diagnostic of an intracranial tuberculoma. However CT is still helpful for detecting small lesions that may not be suspected clinically. It is also useful for monitoring therapeutic response especially when treating by medical means.

Previously, surgery was the only therapy. The mortality for excision was 84.5% and 34% for decompression.<sup>(7)</sup> Attempted excision of the posterior fossa tuberculoma seemed to be uniformly fatal.<sup>(4,14)</sup> The primary postoperative complication was tuberculous meningitis. However after the discovery of antituberculous drugs, Arseni reported only a 6.3% operative mortality and a 6% late mortality.<sup>(7)</sup> Similar results were reported by others.<sup>(19)</sup> There were 3 immediate deaths after the

craniotomy in this series and there were no postoperative deaths after 1976. The greatly improved mortality is undoubtedly the result of improved surgical technique and antituberculous drugs.

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