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Clinical Profile of Patients with Intracranial Tuberculosis.

Kenny Thomas[1]

[1]Assistant Professor, Department of Medicine, Mount Zion Medical College, Chayalode, Ezhamkulam, Adoor.

Abstract

Background: In children, tuberculous meningitis is usually a complication of primary infection, with or without miliary spread. In adults it may occur as an isolated form of tuberculosis or in association with another form of the disease, especially pulmonary or miliary. The infection is fatal within 1 to 8 weeks if untreated and carries a high risk of severe sequele if treatment is delayed. **Subjects and Methods:** All patients included in the study had a computed tomography head scan and were evaluated according to the attached protocol. Every patient selected underwent a complete neurological evaluation which consisted of a history and physical examination with special reference to the neurological findings. Fundoscopy, CSF examination, Chest and Skull X-ray, E.E.G etc.., were done whenever needed. **Results:** The most consistent neurological findings were isolated or multiple cranial nerve palsies, motor deficits, papilloedema, sign of meningeal irritation and altered conscious states. **Conclusion:** All the above were more common in patients with tuberculous meningitis.

Keywords: Intracranial Tuberculosis, Tuberculous Meningitis, Neurological Findings.

Corresponding Author: Dr. Kenny Thomas, Assistant Professor, Department of Medicine, Mount Zion Medical College, Chayalode, Ezhamkulam, Adoor.

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Introduction

Tuberculous meningitis continues to be prevalent even though the incidence of intracranial tuberculomas is declining. The incidence of tuberculous meningitis in a given community is directly proportional to the prevalence of tuberculous infections in general, which in turn is dependent upon the socioeconomic and hygienic conditions of the community. The disease can occur at any age, but it is uncommon below 6 months and rare before the age of 3 months. The highest incidence is in the first 5 years of life. The incidence in adults has increased in recent years, probably owing to the later age of acquisition of tuberculous infection. Auerbach found evidence of tuberculous meningitis in 42.2% of a series of 97 fatal cases of tuberculosis in children, but in only 2.9% of 2236 adults. Riggs et al.., reported meningeal involvement in 19.3% of all autopsies on tuberculous patients below 20 years of age and 5.9% of those older than 20 years.

In children, tuberculous meningitis is usually a complication of primary infection, with or without miliary spread. In adults it may occur as an isolated form of tuberculosis or in association with another form of the disease, especially pulmonary or miliary. The infection is fatal within 1 to 8 weeks if untreated and carries a high risk of severe sequele if treatment is delayed.

Multiple clinical studies carried out by Tandon et al; Tandon and Pathak; Tandon and several other workers in India established that tuberculous meningitis has protean manifestations, which are often quite different from that reported in the Western literature. These studies highlighted the frequent occurrence of disease in adults, a bewildering range of clinical syndromes and atypical CSF findings, with consequent difficulties in diagnosis.[1]

Tandon also said that an increasing number of cases of hydrocephalus were being seen by neurosurgeons. Studies by Dastur an Udani; Dastur et al; Dastur Lalitha; and the experimental model by Tandon et al all indicated that the most important factor determining the pathology of tuberculous lesion was the immune or sensitivity status of the host and not so much on the organism itself.

The majority of cases tuberculous meningitis are due to Mycobacterium tuberculosis var hominis. The bovine type of tubercle bacillus is responsible for a small percentage of cases, particularly in developing countries. Meningitis caused by atypical mycobacteria is extremely un usual although there have been reports in which Mycobacterium kansasii and Mycobacterium scrofulaceum were isolated from the cerebrospinal fluid.

Thomas et al analyzed 232 cases of tuberculous meningitis at P.G.I.M.E.R., Chandigarh and found that peak incidence was during the first three decades of life and the main brunt was on children. Males were more prone to tuberculous meningitis than females. In their study 67.6% were male and 32.3% female; about 55% were in the 0-20 years age group, 37% in the 21-50 year age group and 8% above 50 years of age. Singhal et al studying 58 consecutive cases of tuberculous meningitis admitted to the neurological departments at Bombay Hospital made similar observation. Their youngest patient was 9 months of age and the oldest 68 years. 35 out of 58 patients were under 20 years of age

and only 12 were above 30 years. 13 were a male and 25 female.[2]

In the pre chemotherapeutic era, tuberculous meningitis followed a relentlessly progressive classical course that inevitably resulted in death. During the past three decades, however, the clinical presentation of the disease has become increasingly varied, and atypical cases are now more common. The factors responsible for this changing pattern are multiple and probably different in different communities.

In most patients with tuberculous meningitis there is a history of vague ill health lasting for 2 weeks or longer prior to the onset of meningeal irritation. The symptoms are non specific and misleading, except in cases with known tuberculosis of another organ, known tuberculous contacts, or documented tuberculin conversion.[3]

In children, apathy, lack of interest in play, irritability, restlessness at night, minor headaches, loss of appetite, nausea, vomiting and abdominal pain are the usual presentating symptoms. Intermittent low grade fever may also be present. In adults lassitude, depression, confusion and personality or behavioral changes are the presenting features. Riggs et al observed mental disturbance prior to the development of meningeal irritation in 38 of 185 adult patients, acute onset has been reported in 50 per cent of children but in only 14 per cent of adults.

With the onset meningeal irritation headache and vomiting become the major complaints. In children below the age of 3 years vomiting occurs much more frequently and headache is seldom a complaint. In adults, however, headache is more common. The presence of headache in patients with miliary tuberculosis correlates with meningeal involvement. In one series, 11 out of 12 patients with this complaint had meningitis. Fever of varying degree is usually present although 3-5 per cent of pediatric and 10 per cent of adult patients do not have fever.

Neck stiffness and Kernig's and Brudzinski's signs are present in most patients, expect in the very young, but they are seldom as prominent as in pyogenic meningitis.

Cranial nerve palsies occur in 20-30% of patients with tuberculous meningitis and may be a presenting symptom. The sixth cranial nerve is most commonly involved, followed by the third and then the fourth nerves. Paralysis is unilateral initially but may become bilateral. The facial nerve are rarely affected, although involvement of the optic nerve may produce optic atrophy and blindness.[4]

Convulsions are encountered at all stage of the illness. Focal seizures are more common in adults, whereas generalized seizures are more common in children. They are a presenting or early symptom in 10-15% of children and in fewer adults.

Intracranial hypertension is usually not impressive in the initial stages of illness, but occasionally sign and symptoms of raised intracranial pressure may precede the classical signs of meningeal irritation. It is not common, in areas of high prevalence, to discover that a child with hydrocephalus or an adult with suspected brain tumor is found to have tuberculous meningitis. Gradually the signs and symptoms of increased intracranial pressure become more prominent. Enlargement of the head and a tense fontanelle in infants and papilloedema in adults become manifest in a significant percentage of cases. As the disease progresses, defective CSF circulation and absorption due to a variety of causes may result in hydrocephalus (headache, papilloedema, diplopia and visual blurring) may dominate the clinical picture.[5]

The clinical course may be punctuated by the sudden onset of the focal motor deficits. Although this maybe a postictal phenomenon, it is often due to vascular lesions resulting in ischemia or infraction.

Subjects and Methods

In the following study patients were taken up from among those attending the Department of Medicine, Neuro-surgery and pediatrics at Medical College and Hospital. The study was partly retrospective and partly prospective.

The criteria for selection of patients with a clinically suspected diagnosis of intracranial tuberculous into this study was the presence of one or more of the following:

1. Evidence of extra cranial tuberculosis at the time of admission or in the past or history of tuberculosis contact.
2. Cerebrospinal fluid (CSF) picture suggestive of tuberculous meningitis i.e. raised proteins, low sugars, lymphocytosis, decrased chloroid, CSF sugar/blood sugar ratio more than 0.5.
3. Positive CSF smear/culture for acid fast bacilli on Lowenstein Jensen Media.
4. Computed tomography scan findings suggestive of intracranial tuberculosis e.g: tubercuoma or any of the complications of intracranial tuberculosis.
5. Clinical or computed tomography scan improvement on antituberculous therapy.

All patients included in the study had a computed tomography head scan and were evaluated according to the attached protocol. Every patient selected underwent a complete neurological evaluation which consisted of a history and physical examination with special reference to the neurological findings. Fundoscopy, CSF examination, Chest and Skull X-ray, E.E.G etc.., were done whenever needed.

Age, sex and other associated diseases like hypertension, diabetes, etc.., had no bearing in the selection of patients.

All the selected patients were subjected to similar scanning procedures. Sedation in the form of intravenous diazepam was given to patients who were restless or moving excessively.

Results

Table 1: Age Group

Age Group in Years	No. of Patients	Percentage
0 – 9 Yrs.	13	22
10 – 19 yrs.	14	23
20 – 29 yrs.	12	20

30 yrs and above	21	35
Total	60	100

There were 35 males and 25 females in the study. The male to female ratio was 1.4: 1.

Table 2: Sex distribution

Age Group	0 - 9 Yrs	10 - 19 Yrs	20 - 29 Yrs	30 Yrs & above
Males	8	10	6	11
Females	5	4	6	10
Total	13	14	12	21

The mean age of the 29 cases with tuberculoma was 19.37 years. Nine were in the 0 – 9 age group, 7 were in the 10 – 19 age group, 6 in the 20 – 20 age group and in the age group of 30 years and above.

The mean age of the 31 cases with tuberculous meningitis was 30.6 years. Four were in the 0 – 9 age group, 7 in the 10 – 19 age group, 6 in the 20 – 29 age group and 14 cases were above 30 years of age.

Table 3: TB and Age

Age Group	Tuberculomas	Tuberculous Meningitis
0 – 9 Yrs.	9	4
10 – 19 Yrs	7	7
20 – 29 Yrs	6	6
30 Yrs & above	7	14
Total	29	31

In the 0 – 9 age group 5 were males and 4 females; in the 10- 19 age group males and 3 females; in the 20 – 29 age group there were 2 males and 4 females and above 30 years there were 5 males and 2 females.

Of the cases of tuberculous meningitis studied; there were 3 males and 2 females in the 0 – 9 age group, 6 males and 1 females in the 10 – 19 age group, 4 were males and 2 females in the 20 – 29 age group 6 males and 8 females above 30 years of age.

Table 4: TB and Gender

Age Group	Tuberculomas		Tuberculous Meningitis	
	Male	Female	Male	Female
0-9 Yrs	5	4	3	1
10 – 19 Yrs	4	3	6	1
20 – 29 Yrs	2	4	4	2

The youngest patient with tuberculoma was 1 ¾ years of age and the oldest was 49 years whereas the youngest patient of tuberculous meningitis was 7 months and the oldest 72 years of age.

Table 5 : Presentation of TB

	Minimum age	Maximum age
Tuberculomas	21 Months	49 Years
Ruberculous Maningitis	7 Months	72 Years

Clinical Features

The duration of symptoms prior to admission ranged from 4 ½ hours to 60 months in case of patients with tuberculomas and from 24 hours to 12 months in those with tuberculous meningitis.

In analyzing the clinical features the patients are divided into 2 group viz:

GROUP 1: With intracranial tuberculoma and

GROUP 2: With tuberculous meningitis.

The presenting complaints were protean and included headache, vomiting, neck stiffness, seizures ,motor or sensory deficits, alteration of sensorium, fever, visual distribution , tinnitus, unsteadiness of gait and some nonspecific complaints like cough, anorexia, weight loss, lethargy and giddy-ness.

The most frequent chief presenting complaints were seizures or headache in the tuberuloma group whereas it was fever and alteration of sensorium in case of tuberculous meningitis.

Table 6: Symptoms

		Number Of Patients	
Sysptoms		Group 1	Group 2
Headache		12	20
Vomiting		7	12
Seizures		24	10
Altered sensorium		5	22
Fever		7	23
Visual disturbance		1	5
Neck Stiffness		1	4
	Cr. Nerve palsies	2	2
Motor Deficits	Hemiparesis	5	3
	Monoparesis	-	1
Sensory deficits		1	-
Anorexia, Wt.loss, Lethargy		1	3
Giddiness		2	2
Cough		1	2
Unsteady Gait		-	1
Tinnitus		1	-

Neurological deficits were found in 14 of the 29 cases with tuberculoma (48.28%) in contrast to 26 out of 31 cases (83.87%) with tuberculous meningitis. Among the 15 cases of tuberculoma without neurological deficits, 9 were children and 6 were adults. Of the 5 patients in group 2 (TBM) without focal deficits, 3 were children who were fully conscious and 2 were adults with altered sensorium.

The most consistent neurological findings were isolated or multiple cranial nerve palsies, motor deficits, papilloedema, sign of meningeal irritation and altered conscious states. All the above were more common in patients with tuberculous meningitis.

Table 7: Neurological Findings

	No. of patients		Total	%
Signs	GP.1	GP.2		
Cranial Nerve palsies	8	23	31	51.66
Hemiplegia	5	11	16	26.66
Motor Deficits				
Monoplegia	1	2	3	5.0

Pallor, evidence of weight loss or protein energy malnutrition (in children), hepatosplenomegaly, pleural effusion, galactorrhea, hypotension and hyperpigmentation presenting with Addisonian crisis,etc.

Table 8: Signs.

Signs	Tuberculoma	Tuberculos Meningitis
Pallor	1	5

Evidence of wt.loss/PEM	2	8
Hepatosplenomegaly	1	2
Pleural effusion	-	2
Galactorrhoea	-	1
Hypotension & hyperpigmentation	1	-

Facial nerve was most commonly involved (45.8%) followed by the abducent (18.7%) multiple cranial nerve involvement was seen in 11 patients, 5 of whom had bilateral involvement.

7 out of the 60 patients (11.7%) in this study had a past history of tuberculosis. 8 patients (13.3%) had appositive history of TB contact in the family.

A total of 45 patients (75%) had direct or indirect evidence of extra cranial tuberculosis out of whom 31 had evidence of pulmonary tuberculosis on the basis of chest X-ray or on examination of the respiratory system. 14 out of 31 patients (54.84%) with tuberculous meningitis had evidence of concomitant pulmonary tuberculosis.

Twenty patients (33.3%) had an elevated erythrocyte sedimentation rate (more than 20 mm in the first hour).

Thirteen patients (21.7%) had a positive mantoux intradermal skin test.

Six patients (10%) had microbiologically demonstrable mycobacteria infection in the form of either positive AFB smear or culture.

Sixteen patients had an abnormal electroencephalogram (26.7%). A total of 5 patients (8.3%) had abnormal skull X-ray. Sixteen patients with tuberculoma had skull X-ray and 4 showed abnormally in the form of calcifications in 3 and silver beaten appearance in one patient. Only one child out of 6 patients with tuberculous meningitis showed abnormally in the form of sutural diastasis. All 13 patients with tuberculomas who had E E G showed an abnormal focus with asymmetry whereas 3 out of 4 patients with tuberculous meningitis had an abnormal record which showed only diff use slow wave pattern.

Discussion

In the present study, there were 35 males and 25 females' giving rise to a male female ratio of 1.4.4. Twenty nine of these patients had intracranial tuberculoma and thirty-one had tuberculous meningitis. Two patients of tuberculoma developed tuberculous meningitis during the course and thus on the whole thirty-three patients had tuberculous meningitis.

The subjects were studied under four age groups viz: 1) 0-9 years (2) 10-19 years (3) 20-29 years and (4) 30 years and above. Thirteen patients (22%) were in the 0-9 group, 14 (23%) in the 10-19 age group, 12 (20%) in the 20-29 age group and 21 (35%) were in the age group above 30 years. This distribution suggests that neurotuberculosis is becoming more common in the older age groups. Lalitha and Dastur (1980) had also indicated a rising incidence in adults and a decline in children. The mean age of patients' with tuberculoma was 19.37 years and of those with tuberculouse meningitis was 30.6 years.

The minimum age of patients with tuberculous meningitis was 7 months and the maximum 72 years.

The incidence of tuberculoma was more in the younger age groups, maximum being in the 0-9 age group. This coincides with the incidence quoted by Dastur (1972). In our study 55.17% were below 20 years of age. Bhargava and Tandon (198) in their series had nearly 50% patients below 20 years of age. Mathal (1979) reviewed case records of 200 intracranial tuberculomas and found that 58.5% were below the age of 20 years. A relative increase in the incidence of tuberculomas was seen in adults above 30 years by us. Cerebral tuberculomas are rare in developed world (Bishburg et al., 1986) and are seen mostly in the middle aged. Damergis et al (1978) reported 4 cases of cerebral tuberculoma, all of whom were males I the 5th and 6th decades.

We found that the majority of patients with tuberculous meningitis were older, the maximum number being in the age group above 30 years.

In the present study males outnumbered females among both patients with brain tuberculoma and tuberculous meningitis. Females are at special risk for developing neurotuberculosis in the child bearing age groups (Kalyanaraman, 1983).

There were 17 males and 12 females with intra cranial tuberculoma i.e. male female ratio of 1.4.1. Bhargava and Tandon (1980) had a male female ratio of 30:25 i.e. 1.2:1 while Mathai (1979) had found a ratio of 1:1.2).

Females outnumber males if all tuberculomas are considered (Ganaoathy and Kalmanaraman 1985).

This may be explained by the male preponderance seen among all patients brought to this hospital for various illnesses. But as in this study, Matai (1979) and Ganapathy and Kalyanaraman (1985) had observed that male children were more frequently affected below the age of 10 years.6

Tuberculomas are known to get exaggerated during pregnancy and puerperium (Kalyanaraman, 1983). Two of our patients belonged to this category. Bhargava and Tandon (1980) found that in the young adult group, females predominate though in the under 10 and over 30 years, males predominate. This was also observed by earlier authors (Dastur, H.M. et al., 1965 and 1972), (Sinh et al., 1958) and is consistent with our observation.[7]

Tuberculomas are usually found is patients who are batter nourished (Ramamurthi and Tandon, 1980). In the present series, 8 patients with tuberculous meningitis had evidence of weight loss or protein energy malnutrition in contrast to only 2 patients with intracranial tuberculoma.[8]

75% of the total patients had evidence to extra-cranial tuberculosis. Lungs were the most common organ affected 51.66%), next being the lymph nodes (11.66%). Other organs that were affected were bones in 3 patients, the terminal 11eum, adrenals, pituitary and the uterus is one patient each.

54.84% patients with tuberculous meningitis had X-ray evidence of active or dormant pulmonary tuberculosis similar to 60% seen by Reed and Ferguson (1978). In contrast, Shah (1973) found an incidence of concomitant pulmonary tuberculosis in only 22.68% of 97 children with

tuberculous meningitis.

48.27% patients with tuberculoma had evidence of concomitant pulmonary tuberculosis while Harder et al (1983) had an incidence of 30%. In Mathai's series (1979), 51% with intracranial tuberculoma had positive X-ray evidence of pulmonary tuberculosis in contrast to 12.5% with other intracranial space occupying lesions. Lack of clinical evidence of extracranial tuberculosis of intracranial tuberculoma (Harder et al., 1983): (Whelan and stern, 1981).[9,10]

A significant finding in this study was the history of family contact in 13.3% cases. It was 15.46% in the study by shah (1973).

11.7% had past history of cranial or extracranial tuberculosis which was treated. Kalyanaraman (1983) studying 69 cases had found a similar incidence of 11.59%.

The tuberculin skin test was positive in 21.7% of our cases as opposed to 17.24% in Kalyanaraman's series. Today, the limitations of this test are well recognised (Mayers et al., 1978: Kalyanaraman, 1983: Harder et al., 1983).[7]

The erythrocyte sedimentation rate was elevated in 33.3% of the present series. Mathai (1979) had found significant elevation of ESR in tuberculoma in comparison with other ICSOL's but pointed out that one had to consider the possibility of malignant metastatic lesion in the brain. Kalyanaraman (1983) had found ESR above 30 in only 10 out of 50 adults (20%).

A high degree of asymmetry on EEG was seen in patients with tuberculoma who presented with tuberculoma who presented with focal seizures though it showed only diffuse abnormality in 3 out of 4 patients with tuberculous meningitis. Kalyanaraman (1983) found that EEG was suggestive of a space occupying lesion in only five out of 17 cases (29.4%).

Skull X-ray abnormality in the form of calcification or evidence of raised intracranial pressure, was seen in 5 out of 22 patient (22.72%). 10.3% of our patients with tuberculoma showed intracranial calcification. Mathai (1979) had found calcified intracranial lesions in only 3 out of 200 tuberculomas, while Beleparameswara rao and Dinakar (1972) and Ramamurthi and Vardarajan (1962) noticed an incidence of 5% and 6% respectively.

Conclusion

- The male female ratio was 1.4:1
- The mean age of patients with tuberculoma (19.37 years) was less than in those with tuberculous meningitis (30.6 years).
- A significant number (75%) had evidence of extracranial tuberculosis. Positive history of tuberculous contact or tuberculosis in the past was obtained in 25% cases.
- A higher incidence of neurological deficits and mortality (32.25%) was seen in patients with tuberculous meningitis. This was because 83.87% presented in the advanced stages II and III of the disease.

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