Original Article

Tuberculoma Brain: Diagnostic Criteria and Conservative Management

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ABSTRACT

Background: There is evidence that medically treated Tuberculoma patients have a significantly better functional recovery than those having surgical excision. This would not be possible theoretically unless strict diagnostic criteria are applied and if there is still doubt, resort to surgical excision or biopsy so that patient' health is not jeopardized .

Objectives : To evaluate the Effectiveness of Conservative management of Tuberculoma of Brain based on strict Diagnostic Criteria.

Study Design: Prospective Study

Place and Duration of Study: This study was conducted at Assir Central Hospital Abha KSA from March 2001 to August 2003.

Materials and Methods: Out of total thirteen patients, Eight Patients presented with signs of raised intracranial tension (Headache, Vomiting), Two with localizing symptoms or signs (Hemiparesis and Diplopia), Two with history of Fever, Night sweats, Cough, and had been receiving immunosuppressive agents. One pregnant patient presented with history of convulsions on term. Three patients had Solitary and Ten patients Multiple Lesions. Maximum number of Lesions in our cases were Eleven and minimum was one.

Results: Patients were diagnosed based on Strict Criteria like Blood Smears, ESR , CRP , Acid-fast Bacillus in Sputum smears, CSF serology X-ray Chest, Contrast- enhanced CT and MRI.

Failure of medical treatment occurred in two patient. One pregnant patient was operated due to intractable Epilepsy following caesarian section on term. The patients were followed for six months to Two years without recurrence.

Conclusion: Diagnostic Criteria helped us to filter out TB Positive cases as against Bacterial, fungal and Actinomycotic infections of brain. Conservative management alone was successful in the Treatment of Tuberculoma of Brain.

Key Words: Tuberculoma, Brain, Anti-tubercular Treatment, Chemotherapy, Diagnostic Criteria, Non-surgical.

INTRODUCTION

Tuberculosis is a major public health problem in Pakistan with an estimated prevalence of 355/100000 and a mortality rate of 33/100000[1]. Multi-drug resistant tuberculosis (MDR-TB), defined as mycobacterium tuberculosis (MTB) resistant to both Isoniazid and Rifampicin , is a worldwide problem with an estimated 14 million cases in 2009[1]. The rate of MDR-TB in Pakistan is reported to be between 1.8% of the new TB cases[2] . WHO estimated that the prevalence of MDR tuberculosis among patients never previously treated for tuberculosis was 1·7—18·0%, and among previously treated patients was 6·7—46·0%(25).

The non-specific symptoms and signs of tuberculomas of the brain based on their characteristic CT or MRI patterns on contrast enhancement needs final diagnosis with CT scan evidence. A therapeutic challenge with triple drug anti-tuberculous proves it finally. Our aim of this study was to Investigate the effects of conservative management on the course of Tuberculoma Brain based on established diagnostic criteria.

MATERIAL AND METHOD

A clinical-radiographic syndrome was recognized, consisting of an avascular enhancing mass lesion surrounded by marked edema. Based on Specific diagnostic criteria, this prospective study was conducted at Assir Central Hospital Abha KSA between March 2001 to August 2003.

Potential participants were chosen as consecutive patients when after admission, their diagnostic status as Tuberculoma Brain was confirmed by Clinical and Neuro-radiological features.

A series of thirteen patients with single or multiple tuberculomas were treated Between March 2001-August 2003 with anti-tuberculous drugs.

The Age range was 4 yrs to 72 yrs with a Mean age of 38. Eight Patients presented with signs of raised intracranial tension (Headache , Vomiting).

Two Patients presented with localizing symptoms or signs (Hemiparesis and Diplopia).

One pregnant patient with history of convulsions presented with tuberculoma. CT scan of Brain clinched the diagnosis of tuberculoma..The patient was delivered by caesarean section to avoid any straining during Labour. Excision of tuberculoma was planned and a left fronto-temporoparietal craniotomy with excision of tuberculoma in temporoparietal region was done five days following caesarean section. The diagnosis of tuberculoma was confirmed later on histopathology.

Two Patients presented with history of Fever, Night sweats, Cough, who had been receiving immunosuppressive medications.

RESULTS

Patients were diagnosed based on strict Criteria like Sputum and Blood Smears, ESR , CRP , Acid-fast Bacillus in Sputum smears, PCR based Serology of Blood and CSF, Xray Chest, Contrast enhanced CT and MRI.

Blood Smears showed prominent Lymphocytosis, ESR was uniformly raised within the range of 12-78 and was found to be important marker of effective Anti-tuberculous therapy. Other Morphometric Markers like Pus smears ,positive paraffin tissue staining. Capsule thickness, Angio -genesis and Inflammatory zone thickness were not available due to Non-surgical Approach.

Chest X-rays were requested for all patients. Only five patients have Pulmonary Lesions on Chest x-rays.

PCR based CSF serology for Mycobacterium Tuberculosis was positive in 10 patients and negative in 3 patients.

Mean initial levels of CRP in tuberculoma group was 19.2 micrograms/ml while in the normal control group it was 2.11 micrograms/ml.

Contrast Enhanced CT or MRI scans were obtained which showed increased attenuation, isodense ring or a disc lesion with perilesional oedema which persisted for few weeks in the follow-up MRI Brain . MRI finding were consistent with those of previously reported cases of intracranial tuberculomas.

All patients treated with initial intensive phase of four drugs - Isoniazid (300mg/d), Rifampicin (600mg/d), Pyrazinamide (1g/d) and Ethambutol (800mg/d) , followed by Isoniazid and Rifampicin daily for at least one 12-18 months.

Patients showed good response to medical treatment, especially a Pyrazinamide containing regimen. There was no need of surgery for Ten (78 %) of these cases. The patients were followed intensively for 2 years from the start of treatment.

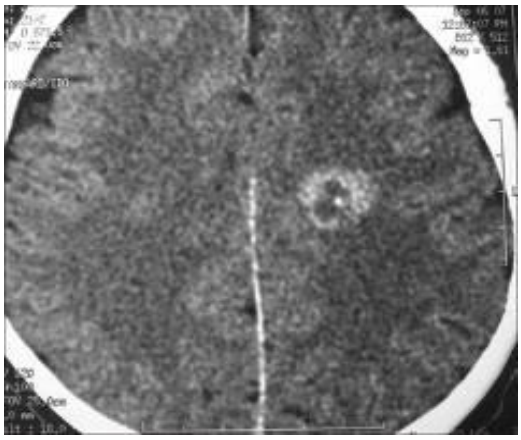

Figure No.1: Contrast-enhanced CT Brain showing Solitary Tuberculoma in the Left Parietal lobe

A failure of medical treatment occurred in three patient, one due to non-compliance and in another patient, the residual cerebral lesion after the tuberculoma had healed, needed surgery to control epilepsy. One pregnant patient was operated due to intractable Epilepsy following caesarian section on term.

For the patients on ATT, ESR fell within the range of 12 -20 mm from 57-75 before the treatment.

Table No. 1: Morphometric Criteria fundamental to the differential diagnosis of Tuberculer infection.

Category	Pus Smear Positive	Positive paraffin tissue staining	Morphometry			
			Capsule thickness	Angio-genesis (No./HPF)	Inflamm-atory zone (um)	Predominant inflammatory cells (%)
Bacterial	88% (Grams)	30%	223.72 ± 61.25	7.4 ± 2.3	125.01 ± 31.78	Lymphocytes 58 ± 10.4
Tubercular	100% (AFB)	75%	180.85 ± 59.03	8.2 ± 1.9	224.87 ± 49.81	Lymphocytes 76 ± 12.4
Fungal	100% (GMS)	100%	216.46 ± 73.38	6.4 ± 2.3	268.47 ± 48.41	Neutrophils 55 ± 9.3
Actino-mycosis	100%	100%	191.25	6.9	219.48	Neutrophils 61

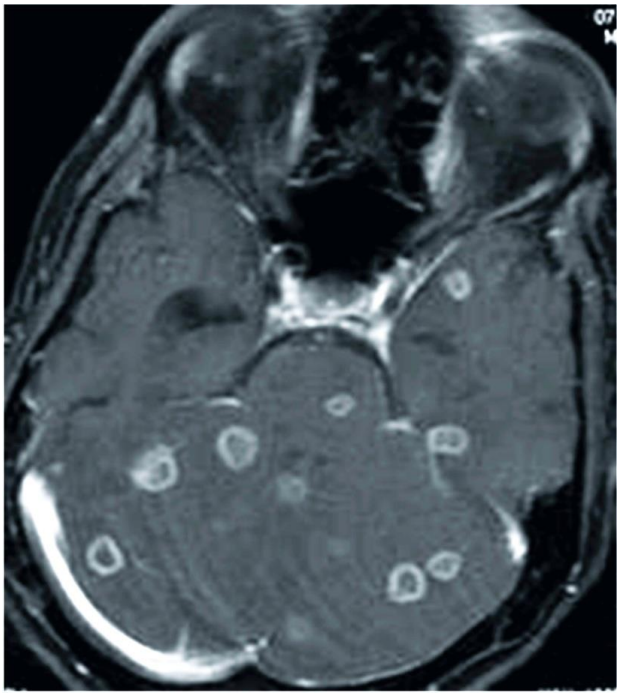

Figure No. 2. Contrast enhanced Sagittal MRI brain showing Multiple Tuberculoma predominantly in posterior fossa.

The elevated CRP levels (19.22 micrograms/ml) fell significantly to 5.93 micrograms/ml in the Tuberculoma Group after one month of treatment and by 3 to 6 months of treatment had fallen to normal values while in the normal control group it was 2.11 micrograms/ml (p less than 0.001). It was concluded that CRP can serve as a sensitive indicator of activity of the disease and the return to normal values of initially elevated CRP levels may indicate a good therapeutic response.

It is concluded that medical treatment with anti-tuberculous drugs is the treatment of choice for tuberculomas of the brain provided the diagnosis is well established.

DISCUSSION

Mycobacterial infections of Brain, always prevalent in developing countries, are now re-emerging in the United States and Europe, especially in immunodeficient persons. Intra-cranial Tuberculosis constitutes approximately 15% of extra-pulmonary cases or about 0.7% of all clinical tuberculosis.

Tuberculomas of the brain constitute 5% to 8% of intracranial space-occupying lesions in developing countries[9]. In clinical studies brain tuberculomas are commonly single, but as many as 100 lesions have been found in one patient[7]. These have in the past been treated with antituberculous drugs and with excision of large masses when the intracranial tension was high. Brain stem and cerebellar tuberculomas are rare[3,6]. The incidence of neurotubeculosis in the United States is less than 0.5 per cent[11]. The incidence of neurotuberculosis in a community is directly related to the incidence of tuberculosis in general, and to the socioeconomic conditions of that community[12]

Computed tomography (CT) and MRI has modified this approach. These modalities have resulted in earlier diagnosis and has been of help in monitoring the results of medical treatment of tuberculomas in children. Neuro imaging shows basal exudates, hydrocephalus, infarcts, tuberculoma, brain edema.

With such monitoring there has been less need for surgical excision. At the same time, down side of this approach is that image morphology of a tuberculoma could simulate other lesions like a glioma, and surgical excision needs to be carried out when in doubt[16] or when there is failure of medical treatment as evidenced by no appreciable improvement in CT appearances. To avoid such occasions, Strict Diagnostic Criteria must be defined as in our study.

Before effective chemotherapy was available for tuberculosis, tuberculoma made up 20 per cent of intracranial lesions in one large series[10]. These tuberculous lesions can occur anywhere in the brain, mainly in the cerebral or cerebellar hemispheres but rarely in the brain stem and basal ganglia[11]. The increasing prevalence of atypical mycobacterial infections in patients with AIDS and other immunocompromised patient, will lead to a higher incidence of tuberculous meningitis and tuberculomas.

Epithelioid cell granulomas with Langhans giant cells, lymphocytic infiltrates, and caseous necrosis are the hallmark of tuberculosis. The bacteria are transmitted through inhalation. Usually an early haematogenous spread occurs. Cerebral location of TB is related to the pattern of blood flow and usually involves the corticomedullary junction and periventricular regions. Hematogenous spread of tubercle bacilli is further supported by the vascular distribution of the lesions in the region of middle cerebral artery[5].

During hematogenous dissemination of tuberculosis, small caseating lesions (tubercles) develop in the meninges and in brain tissue. Mycobacteria can survive in these lesions for a long time. When tubercles rupture, mycobacteria are discharged into the CSF causing tuberculous meningitis

Tuberculoma is second only to neoplastic lesions as a cause of raised intracranial pressure. It may occur in both, the supratentorial and infratentorial compartments[4]. Presentation is with increased intracranial pressure or with focal neurologic deficits over month to years[9,10,13,14]. Up to two thirds of patients have no evidence of systemic tuberculosis and 50 per cent of patients will have normal chest radiograph[9].

Blood Smears are important in showing prominent Lymphocytosis. ESR is significantly raised in most cases and is found to be important marker of effective Anti-tuberculous therapy. Other Morphometric Markers like Pus smears, positive paraffin tissue staining,

Capsule thickness, Angio-genesis and Inflammatory zone thickness cannot be used due to Nonsurgical Approach.

Chest X-rays must be requested for all patients. Cerebrospinal fluid analysis is often not helpful, with slightly elevated protein levels and normal glucose concentrations[15]. PCR based CSF serology for mycobacterium tuberculosis is a very reliable marker and comes into a must use category unless Lumbar Puncture is contraindicated because of papilloedema. Mean initial levels of CRP in tuberculoma is consistently raised when compared with the normal values.

Differentiation of tuberculomas from other neoplastic and non-neoplastic lesions is essential as tuberculomas can be managed conservatively with anti-tuberculous drugs and unnecessary surgical intervention can be avoided.

Tuberculoma have been reported to mimic glioma, CPA lesions, pinealoma and meningioma[1,17,18,19]. Modern imaging is helpful in differentiating tuberculoma from glioma or metastatic lesions[9,20]. Because the different therapeutic plan in immunocompromised patients, the diagnosis of brain lesion is very important. For this reason many authors perform surgical biopsy(open or stereotactic brain biopsy) for surgically accessible lesions[21]. To provide histological diagnosis of brain lesions, CT-guided stereotactic brain biopsy has been widely used, because its less invasive technique compared with open brain biopsy[22]. Paradoxically CT-SBB is not always diagnostic and early open brain biopsy may be considered[23,24].

The diagnosis is more difficult during pregnancy where eclampsia becomes the presumptive diagnosis in patients with convulsions unless Tuberculoma is suspected in the differential diagnosis[2] .

On a CT scan, an increased attenuation, an isodense ring or a disc lesion with perilesional oedema which persists for few weeks and is not a post ictal phenomenon strongly suggests the diagnosis of a tuberculoma[1].

Application of MR imaging and spectroscopy in tissue characterization of intracranial tuberculomas is extremely important. The diagnosis of intracranial tuberculomas can be made more objectively with MR imaging. MRI is considered superior to CT for better localization and characterization of intracranial tuberculomas.

Contrast Enhanced MRI scans show increased attenuation, isodense ring or a disc lesion with perilesional oedema which persists for few weeks and is not a postictal phenomenon, strongly suggesting the diagnosis of a tuberculoma.

Magnetic resonance spectroscopy (MRS) is a non-invasive, powerful technique that can give biochemical information of the patho-physiological process of the tissue in question. The technique has been used in differentiation of neoplastic from inflammatory intracranial masses[3]. Hence application of MRI and MRS in tissue characterization of intracranial tuberculomas is extremely important.

In our Series MR Spectroscopy was not available as a Diagnostic tool but our application of the Diagnostic Criteria mentioned above significantly reduced the Drug Failure rate which was our objective tobegin with.

Neuro-tuberculosis is the most serious form of tuberculosis. It needsmore intensive and prolonged therapy. Even with prompt and adequate treatment, the mortality rate can go up to 27%. Drug resistance is strongly associated with previous treatment. The key principle of managing drug-resistant TB is never to add a sing le drug to a failing regimen.

In our Series , all patients were treated in the initial intensive phase , with four drugs - Isoniazid (300mg/d), Rifampin(600mg/d), Ppyrazinamide(1g/d) and Ethambutol (800mg/d) , followed by Isoniazid and Rifampicin daily for at least one 12-18 months.

It is concluded that medical treatment with anti-tuberculous drugs is the treatment of choice for tuberculomas of the brain.

Only 34 cases of intracranial tuberculomas with negative response to anti -tuberculous chemotherapy have been documented worldwide,

It is Recommended that Patients who are suspected to have a CNS-tuberculosis & Respond Paradoxically should receive a prolonged (12-30 months) course of effective antituberculous therapy. In such cases systemic dexamethasone as adjuvant therapy for 4 to 8 weeks is worthwhile and effective.

Surgical intervention may be necessary in situations with acute complications of CNS tuberculosis such as shunting procedures for the treatment of hydrocephalus. When the diagnosis is in doubt and there is no response to therapy within 8 weeks, a stereotactic biopsy of a suspected tuberculoma should be performed. If the largest lesion is not located in high risk deep regions of the brain, it should be totally removed surgically.

The evidence of new intracranial tuberculomas or the expansion of older existing lesions does not indicate the need to change the antituberculous drug program.

A minimum of 10 months treatment is needed, due to influences of disease severity, CNS drug penetration, undetected drug resistance and patient compliance.

The rate of hepato-toxicity in adults receiving Isoniazid is 1% . Medically treated patients had a significantly better functional recovery than those from whom the tuberculoma was excised.

CONCLUSION

Diagnostic Criteria helped us to filter out TB Positive cases as against Bacterial, fungal and Actinomycotic infections of brain. Conservative management alone was successful in the Treatment of Tuberculoma of Brain.

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