VOLUME - 11, ISSUE - 12, DECEMBER - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

General Medicine

A CASE REPORT ON INTRACRANIAL TUBERCULOSIS

Dr. Niranjan Kumar R. L	Post Graduate, General Medicine, Rajah Muthiah Medical College and Hospital, Chidambaram, Tamil Nadu
Dr. Paari N	Assistant Professor, General Medicine, Rajah Muthiah Medical College and Hospital, Chidambaram, Tamil Nadu
Dr. Baburaj K	Professor, General Medicine, Rajah Muthiah Medical College and Hospital, Chidambaram, Tamil Nadu

ABSTRACT Tuberculosis of the Central Nervous System includes Intracranial Tuberculosis and Spinal Tuberculosis. The Intracranial Tuberculosis comprises Tuberculous Meningitis, Tuberculous Encephalitis, Tuberculous Vasculitis and Tuberculoma. And the Spinal Tuberculosis consists of Potts Spine, Spinal Meningitis, Spinal Arachnoiditis and Spinal Tuberculoma. Here we discuss a 13 years old female who has the features of the Intracranial Tuberculosis i.e. Tuberculous Meningitis, Tuberculous Encephalitis, Tuberculous Vasculitis and Tuberculoma.

KEYWORDS : Intracranial Tuberculosis, Tuberculous Meningitis, Tuberculous Encephalitis, Tuberculous Vasculitis, Tuberculoma.

1. INTRODUCTION

Intracranial Tuberculosis accounts for approximately 5% of the extra pulmonary manifestations of the Tuberculosis. It is seen most often in young children but also develops in adults, especially those infected with Human Immunodeficiency Virus (HIV). If unrecognized, it is uniformly fatal with high morbidity and mortality. This disease responds to chemotherapy; however, neurological sequelae are documented in 25% of treated cases.

2. CASE DESCRIPTION

2.1. Clinical Presentation

A 13 years old female, presented at our Emergency Department with 2 weeks history of low grade fever associated with headache, vomiting and giddiness. She had 2 episodes of Generalized Tonic Clonic Seizure on the day of admission in her house. She also had history of loss of weight and loss of appetite. The patient took no daily medications, had no surgical history and no significant family history. She received vaccines till date.

On the physical examination, she was conscious, oriented, afebrile (T – 98.2 F), pale with generalized lymphadenopathy largest in the Right Inguinal region and Glasgow Coma Scale (GCS) of 15/15. The pupils were 2.5 mm and equally reacting on both sides. Brudzinski's neck sign and Kernig's sign were positive. Other Central Nervous System and other System Examinations were unremarkable.

2.2 Course in the Hospital

Routine biochemical investigations were done and within normal range during the initial presentation. A brain Computed Tomography (CT) was done which showed no significant abnormality. Ophthalmologist opinion to rule out papilledema and blood sample for blood culture and sensitivity were obtained before Lumbar Puncture (LP). The Lumbar Puncture (LP) revealed a clear Cerebro Spinal Fluid (CSF) with total cell count of 200 with lymphocyte predominance (L – 60%; PMN – 40%); protein - 150 mg/dl; Cerebro Spinal Fluid Sugar/ Blood Sugar – 0.5 and pressure – 250 mmH_2O. Fine Needle Aspiration from the Right Inguinal Lymphadenopathy and the Posterior Cervical Lymphadenopathy were done and smeared and sent to the Pathology Department for the study. She was given a dose of steroid and 30 minutes later started on the empirical treatment consisting of CEFTRIAXONE, VANCOMYCIN and ACYCLOVIR according to her weight. She was planned for Contrast Enhanced Magnetic Resonance Imaging (CE-MRI) with Spectroscopy study of the brain on the next day. The next day, she became drowsy and responding to oral commands ($E_3V_5M_6$ – 14/15). Her mother gave history of reduced responsiveness, deviation of angle of jaw and mouth to the Right side on opening the mouth and regurgitation of foods.

Higher Mental Function (HMF): Slurred speech.

Parameter		Right	Left
Cranial Nerve	5	Angle of jaw deviation + (Figure 1)	Normal
	6	Lateral Rectus Palsy + (Figure 2)	Lateral Rectus Palsy + (Figure 3)
	7	Angle of mouth deviation +	Normal
	9 & 10	Gag reflex is weak	Gag reflex is weak
Motor	Bulk	Generalized wasting +	Generalized wasting +
	Power	4/5	4/5
	Hand grip	(80 – 90) %	(80 – 90) %
	Plantar	Extensor	Extensor
	Deep Tendon Reflexes	Absent	Absent
Cerebellum	Eye	Normal	Horizontal nystagmus with fast component to right.

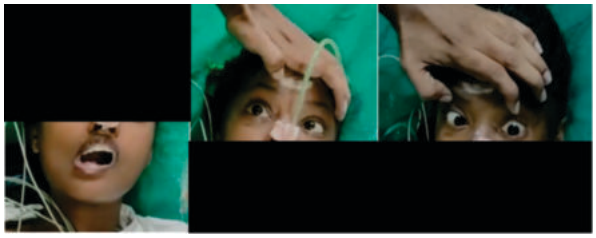

Figure 1 **Figure 2** **Figure 3**

Other examinations were normal.

2.3 Radiological findings

Multiple T2 weighted/ FLAIR (FLuid Attenuated Inversion Recovery) hypo intense **ring enhancing lesions (Figure 4 and 5)** showing no diffusion restriction and no blooming on SW (Susceptibility Weighted) sequences noted in the bilateral

cerebral and cerebellar hemispheres and the right caudate nucleus, the largest is seen in the right cerebellar hemisphere measuring 1.6 * 1.4 cm.

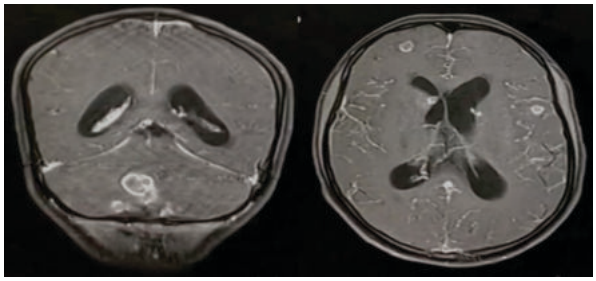

Figure 4 **Figure 5**

There is **leptomeningeal enhancement (Figure 6)** along the brainstem and in the bilateral cerebral sulci with features of obstructive hydrocephalus.

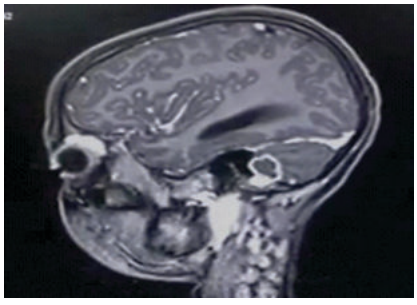

Figure 6

T1 weighted isointense/ T2 weighted and FLAIR (FLuid Attenuated Inversion Recovery) hyper intense foci are noted involving the right caudate nucleus, the left lentiform nucleus, both medial temporal lobes, bilateral cerebral peduncles and left superior cerebellar peduncle showing diffusion restriction and no blooming on SWI (Susceptibility Weighted Images) - possibly acute infarcts **(Figure 7)** due to **vasculitis** (infective etiology).

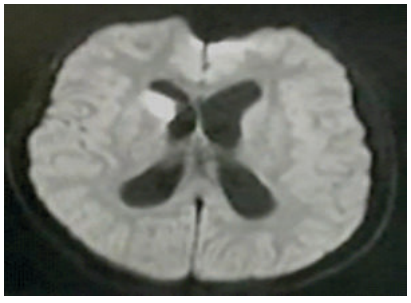

Figure 7

MRS (Magnetic Resonance Spectroscopy) - The lesion in the right cerebellar hemisphere shows elevated choline, reduced NAA (N-Acetyl Aspartic Acid) and a lipid-lactate peak at 1.3 ppm (parts per million) **(Figure 8)**.

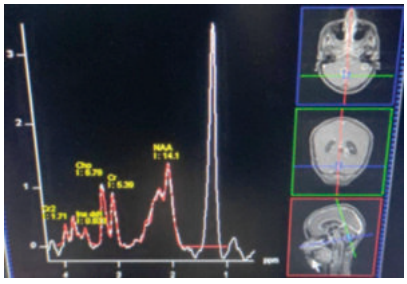

Figure 8

Overall features suggestive of CNS (Central Nervous System) Tuberculosis with intracranial and involvement.

2.4 Pathological findings

On peripheral smear, RBC (Red Blood Cells) are microcytic hypochromic with anisocytosis. WBC (White Blood Cells) and Platelets are adequate in number. Reticulocyte count - 0.5 %.

On FNAC (Fine Needle Aspiration Cytology) of the Left Posterior Cervical and the Right Inguinal Lymph Nodes: Few degenerated epithelioid granuloma against the background of cells of lymphoid series, amorphous granular eosinophilic material resembling caseous necrosis and debris suggestive of Granulomatous lymphadenitis of tubercular etiology. (Figure 9)

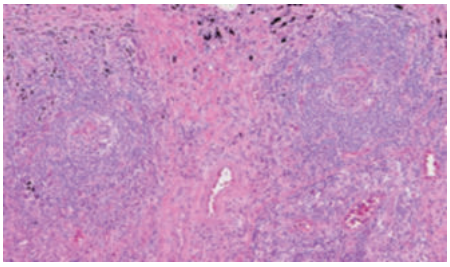

Figure 9

2.5 Outcome

The patient was diagnosed with CNS (Central Nervous System) tuberculosis and started on ATT (Anti-Tuberculous Therapy) under NTEP (National Tuberculosis Elimination Program). Neurosurgery opinion obtained and VP (Ventriculo Peritoneal) shunt was placed under GA (General Anesthesia). She is symptomatically better and so being discharged at stable vitals.

3. CLINICAL DISCUSSION

Although the morbidity and the mortality risk of tuberculosis has declined significantly after the discovery of ATT (Anti-Tuberculous Therapy), CNS (Central Nervous System) involvement still carries the burden of mortality and neurological morbidity[1]. The patient in this report is a female child, coming from a rural area with high number of tuberculosis cases reported in the country. We report an interesting case of CNS (Central Nervous System) tuberculosis with intracranial involvement in an immuno competent patient.

As the brain is highly oxygenated, it is targeted by Mycobacterium Tuberculosis[1]. Once the organism is acquired, it is deposited as sub ependymal tubercles. These tubercles go for rupture into the sub arachnoid space resulting in the inflammatory changes at the base of the brain producing proliferative basal arachnoiditis. The exudates form fibrous mass and 1. Encasing cranial nerves producing cranial nerve palsies 2. Blocks CSF (Cerebro Spinal Fluid) outflow producing obstructive hydrocephalus and 3. Encasing penetrating vessels producing necrotizing arteritis and ischemic infarcts. The dynamic contrast-enhanced MR (Magnetic Resonance) perfusion is used to assess the BBB (Blood Brain Barrier) permeability by measuring K^{Trans} which is high in patients with intracranial tuberculoma[2]. The Matrix Metallo Proteinases (MMPs) are responsible for surrounding tissue destruction in intracranial tuberculoma[3]. Inflammatory cytokines like IL-1β and TNF-α secreted by monocytes have been described to play a significant role in the up regulation of MMP-9[4]. MMP-9 is also responsible for the extracellular matrix destruction adjacent to the BBB (Blood Brain Barrier) and type IV collagen destruction present in the basal lamina[5]. The high K^{Trans} and diffusion tensor imaging indices correspond to the expression of MMP-9[2,6]. The formation of tuberculous foci in the brain parenchyma or meninges is the initial step in the CNS (Central Nervous System) tuberculosis and tuberculous meningitis tends to be the primary presentation of the CNS (Central Nervous System) tuberculosis[1]. The primary targeted cells in the CNS (Central Nervous System) tuberculosis are microglial cells[1].

The initial clinical features of the intracranial tuberculosis varies depending on the location, size and number of the lesions. Intracranial tuberculous lesions tend to be multiple and located in areas with high blood supply[7]. The patients usually present with sub-acute symptoms and signs of raised intracranial pressure with focal neurological deficits[1]. Raised intracranial pressure presenting as headache and papilledema are the most common presentation found in more than two-thirds of the patients[8]. Other common presentations include vomiting, visual disturbance, seizures, drowsiness, confusion, hemiparesis, paraparesis, and ataxia[9].

The radiological investigations are used to consolidate the clinical presentation. A brain Computed Tomography (CT) scan has relatively low specificity for the diagnosis of tuberculoma, and false positives have been reported if used alone in the 80% of the cases[8]. On the Computed Tomography (CT) scan, tuberculoma appear as isodense or hyper dense calcified lesions with ring enhancement[10]. The target sign, the presence of calcification with ring enhancement, is specific for tuberculoma[11]. The presence of multi lobulated or aggregated ring appearance might help in distinguishing the tuberculoma from the brain tumors[9]. The appearance of the tuberculoma on the Magnetic Resonance Imaging (MRI) depends on the stage of maturation. The stages are noncaseating, caseating with a solid center and caseating tuberculoma with a liquefied center[12]. Noncaseating tuberculoma usually appears as hypo intense on the T1-Weighted Images (T1WI) with homogeneous nodular enhancement when contrasted and hyper intense on the T2 Weighted Images (T2WI) and Fluid Attenuated Inversion Recovery (FLAIR) images[13]. Caseating tuberculoma with a solid center exhibits an isointense/ hypo intense enhancement on both T1WI and T2WI, an isointense/ hyper intense rim on the T2WI, and a ring-enhancing appearance when contrasted[13]. Caseating tuberculoma with liquefied center appears as hypo intense on the T1WI, hyper intense with a hypo intense rim on the T2WI, and with ring-enhancing appearance when contrasted[13]. Because of the reciprocal causation relationship between tuberculous meningitis and tuberculoma, radiological evidence of meningitis may also be observed[13].

The definitive diagnosis is established through brain biopsy. Open brain biopsy is more invasive method than stereotactic biopsy; however, it has higher chance of obtaining diagnostic tissue[14]. Many surgeons consider stereotactic biopsy as a selected diagnostic method because it has lower chances of obtaining the diagnostic sample rendering the need for the open biopsy[15, 16]. Microscopically, the typical epithelioid and giant cell granuloma with central caseous necrosis are diagnostic[8]. An Acid Fast Bacilli (AFB) culture and Tuberculosis (TB) Polymerase Chain Reaction (PCR) are positive for Mycobacterium tuberculosis[17].

The treatment of the intracranial tuberculosis includes symptomatic treatment, medical treatment with Anti-Tuberculosis Therapy (ATT), and surgical procedures like resection of the lesion, Ventriculo Peritoneal (VP) shunt if needed. Steroids, dexamethasone, are clinically recommended to alleviate the risk of inflammation, decrease cerebral edema, and reduce the intracranial pressure[18]. The initial regimen of Anti-Tuberculosis Therapy (ATT) includes Isoniazid (H), Rifampicin (R), Pyrazinamide (Z) and Ethambutol (E) for 2 months. Followed by Isoniazid (H), Rifampicin (R) and Ethambutol (E) for 7 – 9 months. Surgical resection is considered in cases of mass effect or visual disturbance[19].

4. CONCLUSION

Intracranial tuberculosis are rare but serious form of the extra pulmonary tuberculosis. They have high rate of morbidity and mortality. It is critical to consider intracranial tuberculosis in the differential diagnosis of intracranial lesions with such clinico-radiological features, especially in the developing countries.

REFERENCES

1. R.B. Rock, M. Olin, C.A. Baker, T.W. Molitor, P.K. Peterson Central nervous system tuberculosis: pathogenesis and clinical aspects Clin. Microbiol. Rev., 21 (2) (2008), pp. 243-261.
2. M. Haris, N. Husain, A. Singh, et al. Dynamic contrast-enhanced (DCE) derived transfer coefficient (ktrans) is a surrogate marker of matrix metalloproteinase 9 (MMP-9) expression in brain tuberculomas J. Magn. Reson. Imaging, 28 (3) (2008), pp. 588-597.
3. X.W. Zhu, N.M. Price, R.H. Gilman, S. Recarvarren, J.S. Friedland Multinucleate giant cells release functionally unopposed matrix metalloproteinase-9 in vitro and in vivo J. Infect. Dis., 196 (7) (2007), pp. 10761079.
4. P. Saren, H.G. Welgus, P.T. Kovanen TNF-alpha and IL-1beta selectively induce expression of 92-kDa gelatinase by human macrophages J. Immunol., 157 (9) (1996), pp. 4159-4165.
5. S.L. Leib, D. Leppert, J. Clements, M.G. Täuber Matrix metalloproteinases contribute to brain damage in experimental pneumococcal meningitis Infect. Immun., 68 (2) (2000), pp. 615-620.
6. R.K. Gupta, M. Haris, N. Husain, S. Saksena, M. Husain, R.K.S. Rathore DTI derived indices correlate with immunohistochemistry obtained matrix metalloproteinase (MMP-9) expression in cellular fraction of brain tuberculoma J. Neurol. Sci., 275 (1–2) (2008), pp. 78-85.
7. E. Mayasari Multiple intracranial tuberculomas: diagnosis difficulties in a clinical case Procedia Chem., 18 (2016), pp. 199-204.
8. A. Bouchama, M.Z. Al-Kawi, I. Kanaan, et al.Brain biopsy in tuberculoma: the risks and benefits Neurosurgery, 28 (3) (1991), pp. 405-409.
9. J.H. Chin Neurotuberculosis: a clinical review Seminars in Neurology, Vol 39, Thieme Medical Publishers (2019), pp. 456-461.
10. A.E. White, K.G. Davies, S. Anwar, J.W. Neal, J.A. Vafidis Cerebral tuberculoma Br. J. Clin. Pract., 48 (4) (1994), pp. 222-223.
11. J. Bargalló, J. Berenguer, J. García-Barrionuevo, et al. The "target sign": is it a specific sign of CNS tuberculoma? Neuroradiology, 38 (6) (1996), pp. 547-550.
12. A.R. DeLance, M. Safaee, M.C. Oh, et al. Tuberculoma of the central nervous system J. Clin. Neurosci., 20 (10) (2013), pp. 1333-1341.
13. H. Ma, Y. Liu, C. Zhuang, Y. Shen, R. Wu Clinical features and MRI findings of intracranial tuberculomas Radiol. Infect. Dis., 5 (4) (2018), pp. 154-159.
14. K. Haddadian, O. Rezaei, M. Samadian Multiple brain tuberculomas and role of open brain biopsy: a case report and review Int. J. Infect. Dis., 4 (1) (2005).
15. R. Sakuma, K. Jin, M. Nagai, et al. A case of multiple intracranial tuberculoma diagnosed by open brain biopsy Rinsho Shinkeigaku, 37 (10) (1997), pp. 895899.
16. H. Nakamura, H. Tanaka, S. Ibayashi, M. Fujishima A case of intracranial tuberculoma early diagnosed by open brain biopsy No To Shinkei, 53 (4) (2001), pp. 387-390.
17. W. Chen, L. Huang, Q. Tang, S. Wang, C. Hu, X. Zhang Central nervous system tuberculosis: challenge and perspective Radiol. Infect. Dis., 7 (4) (2020), pp. 160-169.
18. K. Prasad, M.B. Singh, H. Ryan Corticosteroids for managing tuberculous meningitis Cochrane Database Syst. Rev. (4) (2016).
19. N. Hejazi, W. Hassler Multiple intracranial tuberculomas with atypical response to tuberculostatic chemotherapy: literature review and a case report Infection, 25 (4) (1997), pp. 233-239.