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Ayurveda

AN *AYURVEDIC* OUTLOOK ON STROKE SYNDROME AS NEUROLOGIC SEQUELAE OF TUBERCULOUS MENINGITIS (TBM)

Dr Mini V.G* Associate Professor, Department of Kayachikitsa, Government Ayurveda College, Thiruvananthapuram. *Corresponding Author

Dr Aswathy S Associate Professor, Department of Kayachikitsa, Government Ayurveda College, Kannur.

Dr. Soumya R Post Graduate Scholar, Department of Kayachikitsa, Government Ayurveda College, Thiruvananthapuram.

ABSTRACT Tuberculous meningitis (TBM), a potential extra-pulmonary manifestation of tuberculosis (TB) affecting the central nervous system (CNS) is an infectious bacterial disease caused by *Mycobacterium tuberculosis*. TB follows air borne transmission and mostly affects the lungs but can also involve the gastrointestinal, genitourinary and skeletal systems, brain, lymph nodes and pleura. Among CNS TB, TBM is the most threatening with increased mortality and associated neurological sequelae. It can occur with or without a pulmonary onset with occasional evidences of old pulmonary lesions. The symptoms include low-grade fever, malaise, anorexia and irritability for over weeks followed by headache and slight mental derangement. Unrecognized, symptoms may progress to severe headache, confusion, lethargy, altered sensorium and neck rigidity. The disease can evolve to coma, with hydrocephalus and intracranial hypertension. Culture of cerebrospinal fluid (CSF) remains the gold standard in diagnosis with the Gene-Xpert as the widely accepted initial diagnostic tool. Imaging techniques (MRI and CT) are also widely done to detect tuberculoma, infarcts or hydrocephalus. Anti-tubercular treatment (ATT) is the baseline therapy initiated on diagnosis of TB. Among the complications, stroke syndrome that usually manifests as hemiparesis is highly common. The tubercular zone of the basal ganglia comprising of the caudate nucleus, anterior thalamus, anterior limb and genu of the internal capsule is the predominant site involved. According to *Ayurveda*, the clinical features of acute TBM can be simulated with *lakshana* of *sannipata jwara, majjagata jwara* and *kantakubja.* The major inflammatory processes involved in the aetiopathogenesis of TBM can be considered as *dhatupaka* eventuating in *balahani* that manifest as *pakshaghata* in TBM survivors. Treatment which is predominantly *vata-pittahara, balya* and *rasayana* can be effective in reversing the condition.

KEYWORDS : Tuberculous meningitis, tuberculoma, pakshaghata, stroke syndrome, *rasayana*

INTRODUCTION:

Tuberculous meningitis (TBM), an airborne infectious disease caused by *Mycobacterium tuberculosis* is one among the extra-pulmonary manifestation of TB that has been on top in morbidity and mortality since years. TB remains an absolute public health threat, being the second leading infectious disease to cause death, only next to Covid-19[1]. Although pulmonary tuberculosis is the predominant type, extra-pulmonary manifestations represent approximately 15% of all TB infections including TB of lymph node, pleura, gastrointestinal, genitourinary, skeletal and central nervous system (CNS) [2]. Among these, CNS TB accounts for an estimated 1% of all cases of TB of which tuberculous meningitis (TBM) is the most severe form[3].

Pathogenesis:

TBM results from the hematogenous meningeal seeding or contiguous spread from a tuberculoma or parameningeal granuloma, with subsequent rupture into the subarachnoid space. Local foci of infection along the meninges, brain or spinal cord also release the bacilli to this space, evoking intense inflammatory reaction initially at the brain base resulting in occlusive arteritis, small vessel thrombosis and brain infarction[4].

Clinical Features:

TBM often presents subtly as headache and slight mental changes after a prodrome of weeks of low-grade fever, malaise, anorexia and irritability. It typically evolves over 1-2 weeks with rapid progression involving headache, fever, vomiting, confusion, meningismus and cranial nerve deficits, particularly sixth nerve palsy[5]. Evidence of old pulmonary lesions or a miliary pattern on chest radiography is found in majority of the cases. The disease can evolve to coma, with hydrocephalus and intracranial hypertension.

Staging: [6]

The disease severity in TBM is classified as per the British Medical Research Council (MRC) staging into three:

Stage 1: Mild cases, for those without altered consciousness or focal neurological signs
Stage 2: Moderate cases, for those with altered consciousness who are not comatose and those with moderate neurological signs, e.g. single cranial nerve palsies, paraparesis, and hemiparesis
Stage 3: Severe cases, for comatose patients and those with multiple cranial nerve palsies, hemiplegia or paraplegia, or both.

Diagnosis:

Lumbar puncture is the cornerstone of diagnosis of TBM with a minimum of 6 mL of CSF collected from adults and 2-3 mL from children. CSF glucose level less than two-thirds that of the serum glucose level; CSF protein level greater than 50 mg/dL and increased WBC count with lymphocyte predominance are classical of TBM[7]. Microbiologic diagnostic tools include PCR analysis and culture, with the Gene-Xpert- a CBNAAT (cartridge based nucleic acid amplification test) as the initial diagnostic option. HIV screening is strictly done to rule out TBM associated with HIV infections. Image findings (MRI or CT) specific for TBM includes leptomeningeal and basal cisternal enhancement, tuberculoma, hydrocephalus and periventricular infarcts. High-viscosity and high-protein exudates are commonly found throughout the basal cisterns[8]. Tuberculoma, which present as contrast-enhanced ring lesions on imaging, manifest as one or more space occupying lesion (SOL) that cause seizures and focal signs, whereas, hydrocephalus results from inflammatory exudates obstructing CSF flow in the subarachnoid space. Parenchymal TB infarctions usually involve the bilateral basal ganglia, thalami, and internal capsule. When hemorrhage occurs, necrotic changes in the brain parenchyma can also be present. Chest X-ray may reveal evidence of previous or current pulmonary affliction of TB. Common complications include stroke, hydrocephalus, optico-chiasmatic arachnoiditis and seizures. Anti-tubercular treatment initiation early on diagnosis is the standard treatment line.

On Imaging:

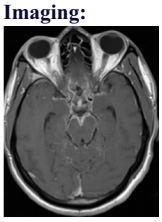

Fig: 1

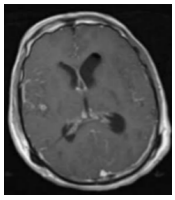

Fig: 2

Fig 1: Axial contrast enhanced T1-weighted image - thick meningeal enhancement at basal cisterns

Fig 2: Axial postcontrast T1-weighted image - small tuberculoma in right temporal region and hydrocephaly (more severe in left ventricle)

Ayurvedic View:
In *Ayurveda,* the symptomatology of TBM resembles the *sannipata jwara lakshana*[9].

Table. No. 1: Clinical features of TBM with respect to *sannipata jwara lakshana*

1. Kshane daha kshane sita	• High fever, or • Hypothermia, as in TB sepsis
2. Siroruja	• Severe headache
3. Moha, bhrama, pralapa	• Delirium and loss of consciousness
4. Aruchi, Tandra, srasthaangata, nidranasa, trishna	• Constitutional symptom in TB
5. Hrid vyadha	• Tachypnea / hypotension as in TB sepsis
6. Kasam, Pratatam kanta kujanam	• Respiratory distress in associated pulmonary TB
7. Srotopaka	• Systemic inflammatory response syndrome (SIRS) – as defense response to an infection
8. Doshaanaam chiraat paka	• Chronicity of TB
9. Marana	• TBM can be fatal, if untreated

The meninges, as per *Ayurvedic* view, can be considered as the *mastulunga* which is described by *Acharya Sushruta* as *majja dhatu* in *shira pradesha*[10]. According to *Vaidyaka sabda sindhu, majja* indicates *'suddha sneha'.* In classics, the appearance of this *mastaka majja* is elaborated as *sthyaana ghrtaakaara* and *ardhavileena ghrtaakaara*[11]. The etiopathogenesis of TBM can be understood as *agantujanidana* evolving to *tridoshakopa* with *majjadhatupaka* as a result of *dosha-dushya samurcchana.* As per *Madhava Nidana, majjagata jwara* includes certain features like *tamapravesa, saityam, vami, kasa* and *mahaswasa*[12] which typically resembles the clinical condition of TBM like delirium, loss of consciousness, hypothermia (as in sepsis), vomiting and respiratory distress (in extreme stage). *Madhavakara* has also explained *kantakubja,* one among the *sannipatajwara* that well resembles with the clinical features of meningitis. The *lakshana* includes *siroarti, kantagraha, moha, murccha*[13] which represent those symptoms manifested in acute TBM such as severe headache, neck stiffness, delirium and loss of consciousness.

Among the complications of TBM, stroke syndrome is common, manifesting as hemiparesis or rarely, paraparesis that can be well related with the *lakshana* of *balahani* mentioned in the *dhatupaka lakshana* by *Bhavamisra*[14]. The persistent inflammatory mechanisms occuring in TBM can thus be considered as *majjadhatupaka,* manifesting *balahani* as a sequelae. The common radiological findings such as tuberculoma and infarcts can be considered as *avarana* in *shira pradesha* that contributes to the presentation of *pakshaghata* with possible motor and sensory compromise. In the management of the same, considering the long-term use of ATT and consequent immune compromise, *sodhana karma* could be initiated for *sanchita dosha nirharana.* The *snehakalpana* for *sodhana* should be chosen taking into account the background of *prabala vyadhi, jwara, deerghakala oushadha sevana* and probable *koshtagni* and *dhatwagnimandya.* Owing to a *pittanubandha* in *rogasamprapti* and a lasting intestinal microbiome dysbiosis following ATT, *virechana karma* following *snehapana* becomes relevant. General treatment line of *vatavyadhi* incorporating *abhyanga* with *vata-pitta samaka* and *balya sneha* and mild *swedana karma* like *kwatha sidha ksheera dhara, shashtikasali pinda sweda* can be done. Initial *sodhana nasya* is expected to play a role in subsiding any remnant infarcts and a subsequent *brimhana nasya* can contribute to *mastishka poshana.* Among *vasti karma, yapanavasti* which has *rasayana guna* can be administered. Also, as per *Acharya Sushruta*, administration of ninth *vasti* reaches the *majjadhatu*[15], hence *karma vasti* or *kala vasti* also finds role in the management of TBM.

Scope Of *Ayurvedic* Intervention:
Implementation of directly-observed therapy short course (DOTS) is inevitable in the management of TBM. According to the Index-TB Guidelines (Guidelines on extra-pulmonary tuberculosis for India), TB meningitis is to be treated at the earliest with standard first-line ATT for a minimum of 9 months. It includes an intensive phase with RHZE – rifampicin (R), isoniazid (H), pyrazinamide (Z) and ethambutol (E) for 2 months with a continuation phase of atleast 7 months with RHE, currently being recommended to be extended for 12 months. In subjects of TBM with poor response to standard ATT, drug-resistant TBM is to be suspected. In addition, anti-tubercular drug induced hepatotoxicity (ATDH) also pose a major health threat in patients subjected to this treatment. In this background, the need of linking the pharmacological benefits of other streams of medicine with the conservative treatment becomes relevant for therapeutic betterment.

Studies reveal that while 2766 patients of pulmonary TB in a tertiary care hospital in Kolkata [1933-1947], put on modern anti-TB drugs, showed cure and death rate as 11.42 and 40.9 percent respectively, the supplementary administration of ayurvedic drugs altered the corresponding rates to 41.3% and 3.8% respectively[16]. In a study by *Debnath et al*, *Aswagandha* (*Withania somnifera* – 2 capsule of 500 mg each twice daily) and *Chyawanprash* (10 gram thrice daily) were administered adjunctively with ATT in 99 patients in which the treatment response revealed abated symptoms, improved body weight, normal erythrocyte sedimentation (ESR) value, marked change in IgA and IgM patterns and remarkable increase in bioavailability of isoniazid and pyrazinamide after 28 days of treatment[17]. These studies pave way to the scope that toxicity and allied ill effects of DOTS administered in TBM can be effectively challenged through *Ayurveda* interventions.

CONCLUSION:
Tuberculous meningitis (TBM), the most common CNS TB that critically affects the quality of life (QOL) of subjects who survive the disease, requires early diagnosis and ATT initiation to effectively check disease fatality and morbidity. For the emergence of any infectious disease, agent-host-environment interaction is a mandatory triad and breaking this chain can prevent disease transmission. Thus, measures to improve *vyadhikshamatwa* or host immunity becomes the prime need in the effort to control such *sankramika roga* which is regulated by many entities such as *bala (sahaja, kalaja and yuktikrita)* and *balavriddhikara bhava*, *trayopastambha*, *dinacharya, rtucharya* and *rtusodhana, agnirakshana*, *sadvritta* and *achararasayana.* Global initiatives such as the 'WHO End TB Strategy 2016-2035' are also on the rise with an eye on halting the incidence of TB.

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