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ANALYSIS OF PATHOLOGICAL ASPECTS OF VARIOUS BRAIN STEM SYNDROMES LIKELY TO OCCUR IN LOCALISED TBM

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Abstract:

Introduction: *Tuberculous meningitis (TBM) develops in 2 steps.* Mycobacterium tuberculosis *bacilli enter the host by droplet inhalation. Localized infection escalates within the lungs, with dissemination to the regional lymph nodes.* ***Objectives:*** *The main objective of the study is to analyze the pathological aspects of various brain stem syndromes likely to occur in localised TBM.* ***Methodology of the study:*** *This study was conducted in the Paediatric Department of DHQ hospital Narowal. In this study 30 children aged from 1 year to 13 years suspected of having tuberculous meningitis were included in the study. Tuberculosis may involve the different organs by primary infection when it causes infection of an unsensitised host.* ***Results:*** *Table 01 gives the various brain stem syndromes. The structures at the base of the brain and around the lateral and 3rd ventricles are commonly affected and hence their damage is expressed with development of different syndromes.* ***Conclusion:*** *It is concluded that there are many syndromes which are directly or indirectly associated with TBM. Tuberculous meningitis is the most common type of neurotuberculosis. However, more and more cases of modified clinical pictures are emerging because of BCG vaccination and often inadequate treatment of the disease.*

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INTRODUCTION:

Tuberculous meningitis (TBM) develops in 2 steps. *Mycobacterium tuberculosis* bacilli enter the host by droplet inhalation. Localized infection escalates within the lungs, with dissemination to the regional lymph nodes. In persons who develop TBM, bacilli seed to the meninges or brain parenchyma, resulting in the formation of small subpial or subependymal foci of metastatic caseous lesions, termed Rich foci [1]. Tuberculosis is an ancient disease that is known to have existed in prehistoric times. Tuberculosis is one of the commonest communicable diseases in a majority of the developing countries [2].1 It is caused by the Mycobacterium tuberculosis, which usually affects the lungs but may cause lesion in any organ or tissue of human body.

In more advanced countries the incidence has declined rapidly since the end of Second World War but disease is still present [3]. Decline in the incidence came due to improvement in socioeconomic condition of people, improved sanitation and housing, BCG vaccination, early case detection and treating the affected persons. However in developing countries tuberculosis is still a major health problem. In recent years there is resurgence of tuberculosis in Western countries due to AIDS, increasing number of immigrants from developing countries and increasing level of social deprivation in some inner city areas of the developed world [4].

Among infectious diseases tuberculosis is at present the leading cause of death. In 1990, 1.7 billion persons, (1/3 of the world population) were infected with Mycobacterium tuberculosis. Eight million new cases of tuberculosis (pulmonary and extra pulmonary) occur yearly with 2.9 millions deaths[5]. It has been predicted by Dolin (Dolin et al 1994) [5] that an estimated 88 million new cases of tuberculosis of which 8 million will be attributed to HIV infection will occur in the present decade (1990-2000) [6]. As children are only infected from infective adults, tuberculosis in children is a direct reflection of tuberculosis in adults. Tuberculosis continues to be a constant threat to the child population where-ever there is poverty, overcrowding and malnutrition. In studies of tuberculosis, a differentiation has to be made between tuberculous infection evident by a positive tuberculin test and tuberculous disease in which there is clinical, radiological or bacteriological evidence of infection. The great majority of infected people remain asymptomatic [7].

In Pakistan, tuberculosis is generalized and wide spread. There have been two prevalence surveys conducted in 1960-62 and 1974-78 with similar results. According to these surveys 54% of the entire population is infected and this infection rate goes as high as 80% in age groups of 20-29 years and above [8]. According to these surveys infection rate in children from 0-14 years of age was 25% in 1960-62 and 22% in 1974-78, 1.6% of the population above 10 years of age had chest radiograph suggestive of active cavitary or non cavitary pulmonary tuberculosis and 0.3% were sputum positive on microscopy and/or culture [7].

Background of the study

No age is immune to tuberculosis. It may affect any age ranging from intrauterine to upper limit of paediatric age. Incidence of infection increases as the age advances (Paediatrics and Child Health 1984). Tuberculosis can affect any tissue or system of body. Common presentations of tuberculosis are primary complex, tuberculous lymph adenitis and progressive primary disease. Due to introduction of BCG vaccination just after birth the clinical pattern of tuberculosis has changed[9].

Pathology of Neurotuberculosis

Neurotuberculosis is one of the serious complications of primary tuberculous infection. Tuberculous meningitis is its most dreaded form and is the main cause of death and disability in children. In a study by Dhariwal and Udain, of the 246 children who died at the Institute of Child Health, 16.5% died of tuberculosis.9 In an autopsy series in adults and children under 15 years of age studied from 1976 to 1987, deaths due to tuberculosis were 11.6% in adults (7676 cases) and 10.8% in 4080 children.10 CNS tuberculosis accounted for 65.5% of the total death. Tuberculous meningitis usually arises from the formation of a metastatic caseous lesion in the cerebral cortex or meninges that develops during the lymphohematogenous dissemination of the primary infection [1-5]. Tuberculous meningitis (TBM) the most dangerous form of extra pulmonary tuberculosis, occurs in 7-12% of tuberculosis patients in developing countries.

Objectives

The main objective of the study is to analyze the pathological aspects of various brain stem syndromes likely to occur in localised TBM.

METHODOLOGY OF THE STUDY:

This study was conducted in the Paediatric Department of DHQ hospital Narowal. In this study 30 children aged from 1 year to 13 years suspected of having tuberculous meningitis were included in the

study. Tuberculosis may involve the different organs by primary infection when it causes infection of an unsensitised host. Primary tuberculosis involves the following organs;

1. Lungs
2. Cervical lymph nodes including tonsils.
3. Gastrointestinal tract.
4. Skin.

Most common primary tuberculosis is of the lungs. From the lungs it may disseminate through lymphatics and blood stream to involve other organs of body as secondary infection. Lungs itself may be involved after healing of primary infection by reactivation of the primary lesion or reinfection from outside. This is called post primary pulmonary tuberculosis.

RESULTS:

Table 01 gives the various brain stem syndromes. The structures at the base of the brain and around the lateral and 3rd ventricles are commonly affected and hence their damage is expressed with development of different syndromes. Periventricular structures are likely to be damaged because of ventriculitis affecting the adjacent grey matter of thalamus. The hypothalamus is much more likely to be affected because of the exudate which is often dense at the base of the brain in the middle cranial fossa. The exudate itself can spread to the adjacent areas of hypothalamus or the dilated 3rd ventricle may compress upon various parts of hypothalamus and hypothalamic pituitary axis and rarely the red nucleus.

The thalamus and hypothalamus can be damaged by ischemia produced by the exudate compressing the various branches of the Circle of Willis particularly their small branches. The various syndromes can present as an isolated manifestation of a focal lesion. If there are multiple focal lesions, the clinical presentation may change but when there is a generalised Meningitis and involvement of brain, the syndromes are masked. However they may manifest during or after improvement of TBM with treatment and at times at the onset from a focal lesion.

Various syndromes which develop during the course of the disease are as follows;

1. Syndrome of inappropriate secretion of antidiuretic hormone (SIADH)

The supra-optic nucleus of the hypothalamus probably produces antidiuretic hormone (ADH) which stimulates absorption of water from distal portion of renal tubules independent of solutes. Neurons of supraoptic nucleus have osmoreceptors, which are very sensitive to changes in the salinity of the surrounding tissues and regulate the water metabolism of the body. Damage to these nuclei causes diabetes insipidus and the patient gets polyuria and polydypsia. The polyuria occur only if cortisol is present. Operative removal of neurohypophysis does not prevent diabetes inspidus because ADH producing nuclei promote the hormone to enter the circulating blood directly.

SIADH is common in TBM occuring in almost 67% of cases.55 However unless it is severe it can be easily missed.

2. Persistent Pyrexia

Often children with TBM improve with TBM but later on start getting persistent high fever. This is probably due to the damage to the rostral hypothalamus particularly preoptic area which regulate, body temperature.

3. Unilateral contralateral hemiballismus

This is commonly seen in children with TBM when he has hemiplegia on one side and hemiballismus on the opposite side. With improvement in hemiplegia and the ballismic movements often become bilateral. This is due to damage to the subthalamic nucleus by the exudate tracking up from the base of the brain.

Table 01: Various Brain stem syndromes likely to occur in localised TBM with involvement of vessels

Syndrome	Artery affected	Structures involved	Manifestation
Medial	Paramedian	Emerging fibres	Ipsilateral
hemiparalysis	Branches	of the 12th nerve	
Syndromes	Paramedian	Pontine gaze centre,	Paralysis of gaze
medulla			
Inferior	branches	near or in nucleus of the 6th nerve	side of lesions
to	Paramedian	Medial longitudinal	Internuclear
pons	branches		fasciculus
Superior	Anterior inferior		Emerging fibres of
pons	cerebellar		the 7th nerve
Inferior		the 7th nerve paralysis	Ipsilateral facial cerebellar

DISCUSSION:

Tuberculous meningitis complicates about 0.3% of untreated primary infections in children. It is most common in children between 6 months and 4 years of age. Occasionally, tuberculous meningitis may occur many years after the primary infections, when rupture of one or more of the subependymal tubercles discharges tubercle bacilli into the subarachnoid space [10]. The clinical progression of tuberculous meningitis may be rapid or gradual. Rapid progression tends to occur more often in infants and young children, who may experience symptoms for only several days before the onset of acute hydrocephalus, seizures and cerebral edema [11-13].

The most severe complication of tuberculosis is infection of the central nervous system, which is invariably fatal if appropriate therapy is not administered promptly[14]. Outcome of tuberculous meningitis is strongly associated with the stage of disease at presentation. In this study 66.03% children presented in Stage III and 32.07% in Stage II and 1.88% in Stage I and the mortality was 75.47% among them mainly those who presented in Stage III. Our findings correspond to many other authors [15].

The nervous system is damaged by a number of pathological mechanisms in neurotuberculosis:

1. Meningeal exudate: This mainly occurs at the base of the brain. The exudate per se can involve a number of structures at the base of the brain with resultant clinical manifestations [16].

2. Obstruction of CSF pathway: Hydrocephalus is mostly due to obstruction of the CSF pathway of the basal cisterns but can occur at the level of interventricular formina, aqueduct of Sylvius a foramina of Lusaka and Magendie [17]. At times the obstruction occurs at multiple levels. Hydrocephalus is one of the most common mechanisms of brain damage by causing myelin depletion, axonal degeneration and neuronal fall out initially in cerebral white matter and later in the cortex.

3. Large vessels: Varying degrees of involvement and occlusion of large vessels in the Circle of Willis and that of middle cerebral artery in the Sylvian fissure by the exudate leads to ischemic foci in the brain. With complete occlusion of the artery, there is infarction with severe brain edema around it [18].

4. Small arteries: Small arteries particularly lenticulostriate vessels have small areas of infarction in the region supplied by them. These small lesions lead to focal lacunar infarcts with edema around them which clinically may present with localized encephalopathy and can be detected in neuro CT Scan as hypodense areas. They are better appreciated in MRI of the brain.

5. Nerves: Engulfment and/or destruction of the cranial nerves particularly 2nd, 3rd, 4th, 6th and 7th with resultant multiple cranial nerve palsies [19].

6. Other structures: Extension of the basal meningeal exudate into the brain with damage to various structures, for example, involvement of nucleus subthalamicus and their pathways results in ballismic movements. Less commonly damage to hypothalamic nuclei in the floor of the 3rd ventricle results in leukolomy or frontal lobe syndrome [20].

CONCLUSION:

It is concluded that there are many syndromes which are directly or indirectly associated with TBM. Tuberculous meningitis is the most common type of neurotuberculosis. However, more and more cases of modified clinical pictures are emerging because of BCG vaccination and often inadequate treatment of the disease.

REFERENCES:

1. Rook GAW. The role of vit D in tuberculosis. Am Rev Resp Dis 1988; 138: 768-770.
2. Khomenko AG, Litvinov VI, Chukanova V PandPospelov LE. Tuberculosis in patients with various HLA phenotype. Tubercle 1990; 71:187-92.
3. Moreno C, Taverne J, Mehlert A. Lipoarabinomannan from mycobacterium tuberculosis induces the production of tumour necrosis factor from human and anurine macrophages. Cli Exp Immunol 1989; 76: 240-245.
4. Ridley DS, Ridley MJ. Rationale for the histological spectrum of tuberculosis. A basis for classification. Pathology 1992; 19: 198-192.
5. Festenstein F, Grange JM. Tuberculosis and the acquired immune deficiency syndrome. J App bacteriol 1991; 71:19-30.
6. Burn CG, Finlay Kh. The role of hypersensitivity in the production of experimental meningitis. J Exp Med 1932; 56:203-21.
7. Tendon Pn, Singh B, Mohapatra LN et al. Experimental tuberculosis of the central nervous system. Neurol India 1970; 18;81.
8. Wisniewski hm, Bloom BR. Primary demyelination as a non specific consequence of a cell mediated immune reaction. J Exp Med 1975; 141:346-59.
9. Chandramukhi A, Nayak P. Subacute and chronic meningitis in children. An Immunological study of cerebrospinal fluid. Indian J Pediatr 1990; 57:685-91.
10. Tandon PN, Bhatia R, Bhargana S. Tuberculous meningitis. In: Hand Book of Neurology and Microbial Diseases, Vol.8(52). Ed Harris AA. Ansterdam, Elseiver Science Publisher 1988; pp 195-226.

11. Joishy KN, Sant MV. Experience with the laboratory diagnosis of tuberculous meningitis in children. In: Tuberculosis of nervous system. Eds Kapila CC, Dastur DK, Singh B, Tandon PN. Monograph on the proceedings of the symposium, Bombay, India 1974; pp 117-19.
12. Rowland LP. Various brain-stem syndromes likely to occur in localised TBM with involvement of vessels. In: Principles of Neural Sciences. Eds Kandal ER, Schwartz JH, New York, Elsevier-North Publishers, holland 1981; pp 419-30.
13. Menon RK, Sharma V, Siddique MH et al. Study of syndromes of inappropriate antidivertic hormone secretion (SIADH) in meningoencephalitis using a highly sensitive ADH assay abstract of 18th National Conference of Indian Academy of Pediatrics, Hyderabad 1981; p 111.
14. Vani PM, Parekh VC, Dastur DK. Neurological and related syndromes of CNS tuberculosis, clinical features and pathogenesis. J Neurol 1971; 14:341-57.
15. Chari CR, Chitra Rao NS. Transient Neurological deficit as a presentation of tuberculosis of central nervous system. Neurol 1987; 37:1884-85.
16. Udani Pm, Parekh UC, Dastur DK. Neurological and related syndrome in neuro-tuberculosis in children: Further observation. In: Tuberculosis of nervous system. Ed Kaplla CC, Dastur Dk, Singh B, Tandon Pn. Monograph on the proceedings of the symposium. Bombay, India 1974; 37-49.
17. Wright S. Applied physiology. 7th edition, London, Oxford Univ Press 1942; 190;666.
18. Teoh R, Humphries J, Chan JCN et al. Internuclear ophthalmoplegia in tuberculosis meningitis. tubercle 1989; 70:61-64.
19. Udani Pm, Dastur DK. CNS tuberculosis. In: text Book of pediatrics with special references to problems of child health in developing countries. Ed Udani PM, New Dehli Jaypee Bros 1991.
20. Park JE, Park K. Textbook of preventive and social medicine 12th ed. Jabalpur BanarsidasBhanot Publishers 1989; 131-40.