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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 cross-sectional study was conducted in Services Hospital Lahore during March 2019 to December 2019. 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 million 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].

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 cross-sectional study was conducted in Services Hospital Lahore during March 2019 to December 2019. 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 Syndromes	Branches	of the 12th nerve	
	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].

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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