TUBERCULOUS MENINGITIS (REPORT)

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The last decade has witnessed a worldwide revival of tuberculosis (TB) due to significant demographic changes as well as the HIV infection boom. The same tendency has been manifest in Romania.

Tuberculous meningitis (TB) is the most severe form of extrapulmonary TB and represents 5-7% of all the TB localisations.

Mycobacterian tuberculosis (Koch Bacillus - KB) reaches the neuraxis either through hematogenic dissemination in primary TB infection from a previous TB focus or through direct intrarachidian insemination from Pott morbus. Cerebromeningeal tuberculous localization takes place at the pia mater level, the arachnoidea, choroidal plexus and the superficial structures of the central nervous system.

Favourable factors of TM are: a) poor socio-economic conditions; b) consumptive, chronic disease (diabetes, cirosis, etilism, neoplasias, hematologic and autoimmunitary disease); c) HIV infection; d) immunosuppresive therapy; e) untreated TB focus.

TM is a granulomatous meningitis with the following morphopathologic aspects: a) meningeal inflammation; b) inflammation of the choroidal plexus and of the ventricular ependimary epithelium; c) inflammation of the cerebral arteries (arteritis with fibrinoid necrosis), with the possibility of secondary trombosis and appearance of cerebral microinfarctions; d) cerebral tubercules with localisation mostly on the

cerebral trunk, the thalamus and cerebral hemispheres; e) cerebral edema of various degrees and expansion.

From immunopatogenic point of view, there are two basic mechanisms in TM: a) monocyte/macrophage and T-lymphocyte systems activation with citokine release (TNF-α, IL-1, IL-2) in the CSF; b) temporary reversible depression of cellular immunity through TCD_4 lymphocite decrease - especially in severe forms, irrespective of the immunodeficiency induced by other causes, HIV infection including.

TM start can be: a) "classical"; b) "appearantly sudden"; c) "atypic". "Classical" clinical picture of TM includes: a) prolonged fever with various characters and values, which can sometimes be the only symptom, especially in neonates; b) complete or partial meningeal syndrome - represents most faithfully the specific group of symptoms; c) encephallous affection - frequently marked by consciousness disorders (from dizziness to confusion and different degrees of coma), neurologic focus signs, hypothalamic syndrome, signs of cerebral trunk, focussed or generalized convulsive crises; d) cranial nerve paralyses, especially of no. III, VI, VII; e) medular affection manifest as paraparesis/paraplegia. "Atypic" clinical picture appears especially in small children or in old ages. Severe clinical picture is present especially in immunodefficient patients (HIV infected) who rapidly develop hydrocephaly or tubercules associated with other infections of the central nervous system. Intracranial Hypertension syndrome (IHS) determined by cerebral edema and/or hydrocephaly is often met in TM. According to the presence/absence of neurologic signs, TM includes the following stages: stage I - without clinical focus signs; stage II - with minimal neurologic focus signs, cranial nerve paresis, mental confusion; stage III - with obvious focus signs, motion deficiency, comatous state.

Classical CSF modifications in TM are defined by: a) clear aspect; b) presence of fibrin veils; c) low plecytosis (ten, thousands of small adult lymphocytes); d) proteorachia with increased values over 1 g/l; e) low levels of glycorachia; f) decreased clorrachia; g) increased lactic acid values between 3-6 mmol/L; h) moderately low pH; i) increased lacticdehidrogenase; j) C-reactive protein moderately increased; k) increased immunoglobuline; l) presence of citokine; m) decreased O_2 partial pressure. "Atypic" CSF can reveal: a) opalescent/xanthocromic aspect; b) pleocytosis. Conventional bacteriologic exam of CSF in TM consists of: a) KB direct identification from the Z-N coloured CSF on Loewenstein cultures, positive in 4-6 weeks' time, or through guinea pig CSF-innoculation - with positive results in 14-21 days. Among the modern techniques og KB identification in CSF, there are: a) radiometry - through C_{14} marked - CO_2, measured in liquids; b) new techniques of mollecular biology: hybridization and ADN amplification through "Polimerase chain

reaction"; c) immunodiagnosis with ELISA method; d) with monoclonal antibodies.

Complementary TM examinations: a) examination of the fundus of the eye can reveal edema of papillary stasis and presence of pathognomonic choroid tubercules; b) pulmonary X-ray vizualizes TB focuses; c) IDR tuberculine in case of viral context; d) computer tomograph cranio-medular examination or magnetic resonance provide evolutive data or is used in severe/atypical cases: i.e. cerebral ventricule dilatation, hypodense/lacunar periventricular zones, cerebral tubercules, especially in the basal nuclei.

TM differs from all the clear CSF - meningitides especially from those with basal localization and prolonged evolution. The TM forms with encephalitis affection will differentiate from the cerebral abscesses and from those with cranial nerve affection; and HIC syndrome will be different from the expansive processes of posterior cerebral fossa. MT treatment with anti-TB drugs will take into consideration: a) diffusibility through hematoencephalic barrier; b) present-day multiresistance of KB; c) patient's reactivity; d) optimum CSF concentrations. Triple or quadruple combinations are applied over a long period. Anti-TB medicines are administered even in case of TM suspicion. Current anti-TB drugs include: a) NIH with bactericid effects penetrates the CSF in 20% concentrations relative to the plasmatic level; b) RMP with bactericid effect on all types of KB, penetrates the CSF to a lesser degree than NIH but through prolonged administration offers useful concentration; c) PZM - has good diffusibility and realizes efficient concentrations; d) EMB is active on KB from macrophages and the NIH resistant and realizes a CSF concentration of 30% relative to the plasmatic values. Duration of treatment is established in connection with KB resistance and immunologic status of the patient:6-9 months for the immunocompetent compared to the 9-12 months for the immunodepressed. New anti-TB drugs: a) Fluoroquinolone of the second generation (Ofloxacine, Pefloxacin, Ciprofloxacin) and third generation (Sparfloxacin) have satisfactory CSF penetration and is active on the BK from macrophages and is associated with anti-TB drugs; b) Azytromicin and Claritromicin are active on multiresistant KB jeducts modest CSF penetration their use in TM is limited. Corticotherapy is associated to anti-TB drugs for various seasons:a) diminishes immunopathologic reactions from the meningeal inflammation; b) controls cerebral edema and cetebral arterites; c) prevents blockage through CSF circulation; d) intensifies anti-TB drugs and facilitates their penetration in the CSF and tubercules. Dexametazone is administered in the first 4-6 days and then hydrocortizone sodiumsuccinate for maximum 14-21 days. Adjuvant treatment in TM is directed: a) against cerebral edema; b) towards efficient respiration through

assisted ventillation in severe forms; c) towards neurosurgical treatment of hydrocephalus (ventriculo-peritoneal shunt) and cerebral tubercules.