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MMP-9 – the prominent mediator of neurological damage in tuberculous meningitis.

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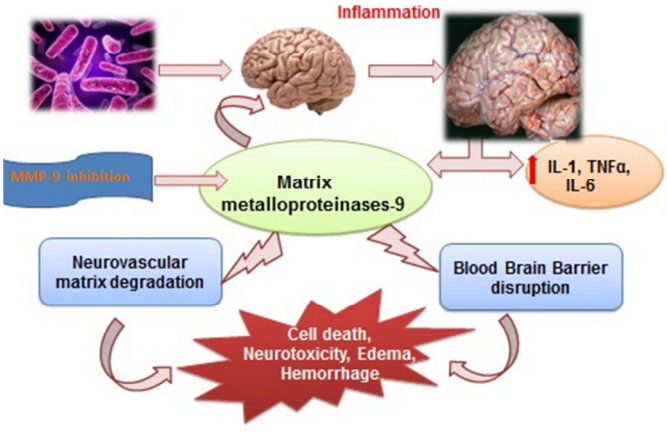
TBM (Tuberculous meningitis) is severe form of tuberculosis causing death of one third of the affected individuals or leaving two-third of the survivors disabled[1]. The main cause of disabilities and death is the neurological destruction mainly caused by immense inflammatory response.[2] MMP-9 (Matrix metalloproteinase-9) is produced by the central nervous system in a variety of inflammatory conditions and has a role in the breakdown of extracellular matrix and blood–brain barrier. [3].Moreover, the correlation between tuberculosis infection and MMP-9 is an earlier known fact.[4, 5] Methodology & Theoretical Orientation: This study was designed to evaluate the role of MMP-9 in advancement of TBM and therapeutic role of targeting MMP-9 against TBM. In this study, the levels of MMP-9 and its inhibitor, TIMP-1(tissue inhibitor of metalloproteinases-1), were screened using zymography and reverse zymography in cerebrospinal fluid and serum of tuberculous meningitis patients at different stages of the disease. Further, role of MMP-9 as therapeutic target was studied in C6 glioma cells and mouse model of TBM infected with Mycobacterium tuberculosis H37Rv. Infected cells and mice were treated with dexamethasone or SB-3CT (specific inhibitor of MMP-9) in combination with conventional antitubercular drugs. Findings: MMP-9 levels in patients were increased as the disease progressed to advanced stages. The infection lead to increased MMP-9 levels in C6 glioma cells and mice. The specific inhibition of MMP-9 by SB-3CT augmented bacillary clearance when used along with antitubercular drugs in both infected C6 glioma cells and mice model of TBM.



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