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Intrathecal Methotrexate-Induced Myelopathy: A Reviews of Pathogenesis, Clinical Manifestations, And Management Strategies A Systematic Review

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Key Points

Question:
What are the pathogenesis, clinical manifestations, and management strategies for intrathecal methotrexate (IT-MTX)-induced myelopathy?
What preventive measures can reduce the risk of this rare but serious complication?

Findings:
IT-MTX-induced myelopathy manifests as progressive motor and sensory loss, impaired proprioception, absent deep tendon reflexes, sphincter dysfunction, and paraplegia/quadriplegia.
MRI findings include T2-weighted hyperintensities in the spinal cord's posterior column, resembling subacute combined degeneration but with normal vitamin B12 levels.
Treatment with corticosteroids, folate metabolism compounds (SAM, folic acid, cyanocobalamin) can lead to partial recovery, though many cases result in lasting neurological deficits.

Meaning:
IT-MTX-induced myelopathy is a rare but potentially irreversible complication. Early detection and intervention are essential, but current treatment options have limited effectiveness.
Further research is needed to refine preventive measures and explore novel therapeutic strategies.

Abstract

Importance:
Intrathecal methotrexate (IT-MTX) is a prophylaxis and treatment for CNS malignancies since it bypasses the BBB, suppresses DNA synthesis and tumor cells development while penetrating the meninges and persisting there. However, myelopathy is a rare but serious complication. Upon early intervention, it is reversible, but in some cases, it causes irreversible neurological deficits.

Objective:
This review aims to analyze, based on the current literature, the clinical presentation, pathophysiology, and management strategies for IT-MTX-induced myelopathy.

Evidence Review
We reviewed current literature focusing on IT-MTX-induced myelopathy. Data was collected from relevant studies including case-reports, autopsy studies, clinical reviews to MRI-imaging and histologic features. Our review explored IT-MTX-induced myelopathy pathophysiology causing neurological deficits, motor and sensory loss as well as therapeutic and preventative measures: cessation of chemotherapy and avoiding IT-MTX.

Findings
IT-MTX may cause progressive motor and sensory loss in bilateral lower extremities including impaired proprioception below T6 level, reduced temperature and vibration sensation, absent deep tendon reflexes, sphincter dysfunction, flaccid paralysis, paraplegia and quadriplegia. MRIs showed hyperintensities in the spinal cord posterior column on T2-weighted images resembling subacute combined degeneration but with elevated vitamin B12. Treatment using corticosteroids and folate metabolism compounds (S-adenosylmethionine (SAM), folic acid, cyanocobalamin) showed rapid recovery of lower extremities paralysis and mitigation of neurological sequelae. However, many patients revealed no improvement and lasting neurological dysfunction. Prevention includes avoiding concurrent IV and IT methotrexate, limiting the total IT methotrexate dose to 20, and ensuring minimum 2-week interval between CNS radiotherapy and IT-MTX.

Conclusions and Relevance:
This review reveals IT-MTX-induced myelopathy is rare but serious. Early intervention is crucial, but current treatment options have limited efficacy. Further research should improve preventive measures while seeking new therapies.

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