Carboxypeptidase G2

Carboxypeptidase G enzymes hydrolyze the C-terminal glutamate moiety from folic acid and its analogues, such as methotrexate. Carboxypeptidase G2 (CPG2), is a dimeric zinc-dependent exopeptidase produced by Pseudomonas sp. strain RS-16. CPG2 has applications in cancer therapy: following its administration as an immunoconjugate, in which CPG2 is linked to an antibody to a tumour-specific antigen, it can enzymatically convert subsequently administered inactive prodrugs to cytotoxic drugs selectively at the tumour site. CPG2 has no significant amino acid sequence homology with proteins of known structure.

In the event of an intrathecal MTX overdose (OD), interventions recommended [1] :

ODs of up to 85 mg can be well tolerated with little sequelae; immediate LP with drainage of CSF can remove a substantial portion of the drug (removing 15 ml of CSF can eliminate ≈ 20–30% of the MTX within 2 hrs of OD). This can be followed by ventriculolumbar perfusion over several hours using 240 ml of warmed isotonic preservative-free saline entering through the ventricular reservoir and exiting through a External lumbar cerebrospinal fluid drainage. For major OD of > 500 mg, add intrathecal administration of 2,000 U of carboxypeptidase G2 (an enzyme that inactivates MTX). In cases of MTX OD, systemic toxicity should be prevented by treating with IV dexamethasone and IV (not IT) leucovorin.

1)
O'Marcaigh AS, Johnson CM, Smithson WA, et al. Successful Treatment of Intrathecal Methotrexate Overdose by Using Ventriculolumbar Perfusion and Intrathecal Instillation of Carboxypeptidase G2. Mayo Clin Proc. 1996; 71:161–165