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[Intrathecal infusion of the antineoplastic agents for meningeal dissemination]

[Article in Japanese]

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One of the specific forms of progression of malignant tumors of the central nervous system is meningeal dissemination. Meningeal dissemination is a condition in which tumor cells migrate to the brain surface and sub arachnoid space via cerebrospinal fluid and then infiltrate there. This condition can arise from both primary and metastatic brain tumors, with reported incidences of 4.2% for primary tumors and 5.1% for metastatic tumors. Meningeal dissemination frequently arises from germinoma, medulloblastoma, ependymoma and glioblastoma in cases of primary brain tumors and frequently arises from breast cancer, lung cancer and gastric cancer in cases of metastatic brain tumors, known as meningeal carcinomatosis. The prognosis of meningeal dissemination is poor, and conventional treatments such as systemic chemotherapy and radiation therapy are ineffective. Intrathecal infusion of anti neoplastic agents is one of the options for treatment of meningeal dissemination. The advantage of intrathecal chemotherapy is that the anti neoplastic agent is rapidly diffused in the sub arachnoid space, and its duration of activity is long due to its slow clearance and metabolism. Routes of administration include infusion into the lateral ventricle by puncture of the Ommaya reservoir, infusion into the sub arachnoid space by lumbar puncture, or both of these procedures performed alternately or simultaneously, and methods of infusion include bolus injection and ventriculo lumbar perfusion. Commonly used drugs include methotrexate (MTX), cytarabine (Ara-C), and 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-1-(2-chloroethyl)- 1-nitrosourea hydrochloride (ACNU), and some new drugs have also begun to be used clinically. Although there are differences depending on the histological type of the tumor, the anti neoplastic agent administered and the method of administration, the response rate is about 40-80% and mean survival time is about 4-25 months. Although side effects of the anti neoplastic agents are not as severe as with agents used for systemic chemotherapy, specific side effects include nonspecific drug-induced meningitis or ventriculitis, transient or permanent paralysis and leukoencephalopathy. These side effects can be alleviated by reducing the dose or discontinuing the anti neoplastic agents, and a small dose of an adrenocorticosteroid is sometimes administered simultaneously. Bacterial meningitis is another complication and requires discontinuation of anti neoplastic agents, removal of the Ommaya reservoir, or systemic or intrathecal administration of antibiotic agents. Although meningeal dissemination is a rare metastatic condition with a poor prognosis, there have been some reports of successful treatment using this method, which is expected to be widely used in the future.

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