Carcinomatous Meningitis Diagnosis

Carcinomatous Meningitis Diagnosis is made with positive Cerebrospinal fluid cytology results, subarachnoid metastases identified on radiologic studies, or a history and physical examination suggestive of Carcinomatous Meningitis along with abnormal CSF findings.

Current methods for detection of leptomeningeal disease is the combined use of cranio-spinal MRI, and cerebrospinal fluid cytology from a post-operative lumbar puncture. Low et al., hypothesized that CSF taken at the start of surgery, either from an external ventricular drain or neuroendoscope will have equal sensitivity for positive tumour cells, in comparison to lumbar puncture. Secondary hypotheses include positive correlation between CSF cytology and MRI findings of LMD. From a clinical perspective, the key aim of the study was for affected paediatric patients to avoid an additional procedure of a lumbar puncture, often performed under anaesthesia after neurosurgical intervention.

This is single-institution, retrospective study of paediatric patients diagnosed with malignant brain tumours. Its main aim was to compare cytological data from CSF collected at the time of surgery versus data from an interval lumbar puncture. In addition, MRI imaging of the same cohort of patients was examined for leptomeningeal disease and corroborated against CSF tumour cytology findings.

Thirty patients are recruited for this study. Data analysis demonstrates a statistically significant association between our intra-operative CSF and LP sampling. Furthermore, our results also show for significant correlation between evidence of leptomeningeal disease on MRI findings versus intra-operative CSF positivity for tumour cells.

Although this is a retrospective study with a limited population, our data concurs with potential to avoid an additional procedure for the paediatric patient diagnosed with a malignant brain tumour [1)].

Imaging studies

Gadolinium-enhanced multiplanar MRI is the preferred imaging modality over CT because of its sensitivity and specificity

MRI findings considered diagnostic of LC include leptomeningeal enhancement of the brain, spinal cord, cauda equina, or subependymal areas, which extend into the sulci of the cerebrum or folia of the cerebellum MRI of the spinal cord can show nerve-root thickening, cord enlargement, intraparenchymal and subarachnoid nodules, or epidural compression

Cerebral Spinal Fluid

The standard diagnostic procedure

Positive CSF cytology is found on the initial lumbar puncture in 50-70% and in nearly all cases after 3 attempts

Increased CSF pressure and elevated CSF protein are also commonly found.

CSF findings typically include the following:

High CSF pressure (greater than 25 cmH2O) is observed in about 50% of CM patients [2].

Pleocytosis is detected in 33-79% of CM [3].

White blood cells are mostly lymphocytes, but eosinophils are also identified in lymphomas and leukemia. The presence of RBCs or xanthochromia in CM may develop due to a traumatic tap. The protein level in CSF is elevated in about 80% of the cases [4].

The normal range of protein in CSF is between 15-45 mg/dl, and elevated values are due to proteins produced by the tumor cells or breakdown of the blood-brain barrier.

Repeat CSF cytology is done if the first sample is negative and if clinical suspicion remains high. This increases the sensitivity to 80% [5]

Moreover, higher volumes of CSF (>10 ml) also improves yield. The sensitivity of CSF cytology for the diagnosis of CM ranges from 80 to 95%, but the specificity is very high. The standardization of the method for CSF collection is an indispensable requirement. An appropriate site (producing symptoms preferably) and sufficient volume (minimum 10 ml) are the prerequisites for the spinal tap. Analysis of CSF via lumbar puncture (LP) and CSF tested from an indwelling catheter produces varying results.

Although CSF cytology is the gold standard for diagnosis, immunohistochemical staining of the cells is recommended, particularly if the primary site of the tumor remains unknown. Flow cytometry is a rapid, quantifiable measure of a specific type of cell with certain characteristics such as cancer cells that are associated with specific antigens. It provides a highly sensitive method for the detection of hematological malignancies. FISH (fluorescent in situ hybridization) is a cytogenetic technique for localizing particular DNA sequences or genes and may yield information on metastatic lesions but with a lower sensitivity [6].

PCR (polymerase chain reaction) is used to identify immunoglobulin gene arrangements in malignant cells, specifically for lymphoma. Hence the study of cytological, morphological, molecular, and cytogenetic characteristics is vital for identification of the tumor type and, at times, the prognosis [7].

Tumor markers have a role in making an early diagnosis and monitoring response to treatment. However, it may also be imperative in determining the prognosis. The nonspecific markers include LDH (lactate dehydrogenase), beta-2 microglobulin, and specific markers include AFP (alpha-fetoprotein), BHCG (beta-human chorionic gonadotropin), and CEA (carcinoembryonic antigen). CSF value of more than 1% of the serum level of these markers is diagnostic [8].

A study done at Memorial Sloan-Kettering Cancer Center demonstrated that patients with CM from breast cancer, lung cancer, and melanoma have abnormal levels of at least one tumor marker in CSF in 74-90% of the cases [9].

CEA is helpful in adenocarcinoma of the lung, AFP in germ cell tumors, and Beta-2 microglobulin in hematological malignancies. The pro-angiogenic factor VEGF (vascular endothelial growth factor) in CSF also has a diagnostic significance. The VEGF index, defined as the ratio of CSF/serum VEGF concentration to CSF/serum albumin levels, is found to be higher in CM and is a promising reliable diagnostic tool [10]. Moreover, the detection of several tumor markers in CSF can increase sensitivity, specificity, and predictive value [11].

Cerebrospinal fluid glucose for Carcinomatous Meningitis Diagnosis

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