Neoplastic meningitis is a late, difficult-to-treat complication found in 5% of all patients with cancer. As patients with cancer live longer and as the use expands of antibody therapies that typically do not cross the blood–brain barrier, one may expect that the prevalence of neoplastic meningitis will increase in the future.

Clinical suspicion must be high because early treatment may improve prognosis. The method of diagnosis has remained the same over the years and is based on cytology and biochemistry of the cerebrospinal fluid (CSF; with flow cytometry for hematological malignancies), gadolinium-enhanced magnetic resonance imaging of the entire neuraxis, and multifocality of neurological symptoms. For the differential diagnosis, the clinician must always keep in mind infectious forms of meningitis, paraneoplastic syndromes, and autoimmune diseases, because these conditions may coexist or mimic neoplastic meningitis.

Neurosurgeons may be consulted for neoplastic meningitis management, which may include placement of a ventricular-access device (for intrathecal chemotherapy) or a shunt for CSF diversion, because many patients have increased intracranial pressure due to communicating or obstructive hydrocephalus. When a shunt is placed, a programmable valve will allow for the intrathecal administration of chemotherapy by increasing pressure for several hours after infusion. Neurosurgeons should attempt to avoid iatrogenic neoplastic meningitis due to the spillage of tumor cells during brain and spinal cord tumor piecemeal resections.

Radiotherapy is reserved for patients with bulky disease and as an adjunct to improve CSF flow abnormalities and help with the distribution of chemotherapeutic agents. Regional chemotherapy may use methotrexate, but systemic myeloablative chemotherapy with or without stem cell transplantation or targeted agents (BRAF inhibitors) may also be utilized.

In spite of a poor overall prognosis, some patients with neoplastic meningitis live longer, especially those with hematopoietic malignancies. However, many unanswered questions still remain, particularly with regard to methods of measuring outcomes and the role of chemoprophylaxis in patients with leukemias and lymphomas. “Liquid” biopsy also holds promise as a future diagnostic tool by detecting circulating tumor DNA in the CSF.

This issue of Cancer Control attempts to review the literature on the subject of neoplastic meningitis, focusing on establishing the diagnosis early, maintaining a high index of suspicion for this complication among patients with cancer, describing potential treatments on the horizon, and identifying the multidisciplinary approach required to manage the disease.

In their article, Dr Filis and colleagues discuss key points on the physiology of CSF as well as the diagnostic and treatment options for hydrocephalus. Of particular interest to all clinicians, Dr Rigakos and coauthors comprehensively review the clinical presentations, differential diagnosis, and radiographical findings of patients with neoplastic meningitis — which remains woefully underdiagnosed.

Dr Le Rhun and others examine neoplastic meningitis secondary to solid malignancies, which typically have a short median survival of a few months. In those cases, determining whom to treat can be challenging.

Dr Murthy and colleagues review neoplastic meningitis with primary or secondary central nervous system involvement by leukemia or lymphoma. They emphasize aggressive, preventive strategies, the early diagnosis of high-risk patients, and systematic therapies that can penetrate the blood–brain barrier.

Dr Sahebjam and others examine experimental treatments for neoplastic meningitis from solid malignancies. In particular, they summarize the role of BRAF inhibitors in melanomas, epidermal growth factor receptor–tyrosine kinase inhibitors in lung carcinomas, and trastuzumab in ERBB2-positive breast cancer.

Dr Volkov and coauthors discuss the use of the Ommaya reservoir for the intrathecal administration of chemotherapy and shunting devices for hydrocephaly as well as their respective complications.

Diagnostic difficulties exist for neoplastic meningitis — including the lack of new diagnostic tools — as well as frustration from clinicians because of poor prognoses despite aggressive treatment, so neoplastic meningitis can be thought of as one of the few “last frontiers” of oncology to be conquered. To do so will require innovation and wisdom across a multidisciplinary team.
In the same vein, we hope you enjoy and benefit from reading this issue of *Cancer Control.*

Frank D. Vrionis, MD, PhD  
Neuro-Oncology Program  
H. Lee Moffitt Cancer Center & Research Institute  
Tampa, Florida  
fvrionis@brrh.com

*Dr Vrionis is now affiliated with the Marcus Neuroscience Institute, Boca Raton Regional Hospital and the Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, Florida.*

**References**