Explaining Leptomeningeal Metastases

Guest post by Seema Nagpal, MD, a Clinical Assistant Professor of Neurology in the Division of Neuro-oncology at Stanford University School of Medicine

Leptomeningeal metastases, also known as “LM”, carcinomatous meningitis, or neoplastic meningitis, are cancer metastases that have spread to the coating of the brain. Rather than growing as a ball, leptomeningeal metastases form a thin layer along the meninges. LM may occur with or without brain metastases, but is generally a complication that occurs after cancer has spread from its primary site to other organs.

LM can be a frightening diagnosis for patients and for doctors, alike. While we do not have a cure for LM, new drugs and a multi-disciplinary approach can dramatically alter outcomes. Doctors who see patients with LM are seeing longer and better survivals than we have in the past. Many of us can tell you about patients who have lived a number of years after coming to us very ill. Though this won’t be the case for every patient, seeing a doctor who treats LM frequently can assure you are getting information about all of the options. Clinical trials often exclude patients with LM, but this is also slowly changing, so be sure to check with your doctor and with clinicaltrials.gov if you are interested.

Symptoms of LM

The symptoms of LM can come from the brain, the nerves exiting the brain, or nerves exiting the spinal cord. The most common symptom is persistent headache, frequently accompanied by nausea. These symptoms may be worse in the morning and get slightly better through the day. Other symptoms can include double vision, difficulty walking, numbness or weakness not explained by other problems, and neck stiffness.

Diagnosis

Because symptoms of LM are varied and may be vague, LM can be tricky to diagnose. Patients and doctors need to be aware of this complication and consider a work-up for LM if symptoms are otherwise unexplained. MRI of the brain and spinal cord with contrast can be helpful in many cases, but may not be as accurate in patients with blood cancers as it is in solid organ cancers. MRIs should be performed with a high quality scanner and the radiologist should be aware of the possible diagnosis.

For some patients, the combination of MRI and symptoms is enough to make the diagnosis of LM. In patients where there is some doubt, the test that confirms diagnosis is a lumbar puncture or spinal tap. Despite the scary name, it’s usually performed in a doctor’s office using the same anesthetic your dentist uses. Patients go home within 20 minutes to 1 hour of the procedure. Again, the doctor performing the lumbar puncture needs to be aware of the possible diagnosis so that enough fluid can be tested and so that the sample can be tested right away (or it’s not accurate). Unfortunately, even in the best hands, a single lumbar puncture may only make the diagnosis 70% of the time. Sometimes, 2 lumbar punctures are
needed. We are working on tests for DNA and RNA in the spinal fluid that may help make testing the spinal fluid more accurate.

Treatment

Treating LM is very individualized. The choice of treatment depends on the type of cancer, the patients’ symptoms and how well controlled the cancer is outside of the central nervous system. There are 3 general approaches. Most of the time, we use a combination of these, along with direct symptoms management, to help patients live better and longer:

1. **Systemic Chemotherapy** with central nervous system penetration: Most drugs do not enter the central nervous system due to the “blood-brain-barrier.” However, some drugs are able to enter the nervous system and effectively treat metastases in both the brain and leptomeninges. Patients with blood cancers who develop LM may receive high doses of methotrexate. Patients with specific types of lung cancer may get alternate dose regimens of oral drugs like erlotinib (Tarceva), or receive pemetrexed (Alimta) in combination with bevacizumab (Avastin). Patients with melanoma may receive vemurafenib (Zelboraf). Centers who see more patients with LM frequently have other alternatives they use for patients.

2. **Radiation** can be used to slow disease and relieve symptoms. This may mean whole brain radiation or radiation to specific areas of the spine.

3. **“Intrathecal Chemotherapy”** is chemotherapy that is given directly into the fluid that surrounds the brain and spinal cord. Usually, patients will have a port, called an Ommaya, surgically placed into the brain prior to this chemotherapy.

Symptom Management

The symptoms of LM are varied, depending on the most effected areas of the nervous system. For patients suffering nausea and vomiting from elevated pressure in the brain, a shunt from the brain to the abdomen can help reduce pressure. Medications that reduce irritation to the coating of the brain or decrease spinal fluid production can also help. I see my patients with LM often and frequently in conjunction with our supportive care oncologists. Controlling symptoms is important not only to quality of life, but can also increase survival.

Summary

This is a very basic overview of leptomeningeal metastases, or metastases to the coating of the brain. LM can cause a number of bothersome and vague symptoms, such as nausea or difficulty walking. Diagnosis can be tricky, but is usually made with MRI and a lumbar puncture. While LM is not curable, a multi-disciplinary treatment approach that includes a supportive care specialist and a doctor who sees many patients with LM can improve quality of life as well as survival.