AMERICAN UVEITIS SOCIETY

Primary Central Nervous System Lymphoma

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Introduction

Primary central nervous system (CNS) lymphoma is a rare cancer that involves the central nervous system (brain, spinal cord, one or both eyes, and/or the coverings of the brain and optic nerve, also known as the meninges). The designation as a "lymphoma" reflects the fact that the cancerous cells are lymphocytes, a type of white blood cell. Primary CNS lymphoma affects all age groups, but is most commonly diagnosed in persons who are over 50 years of age. In addition, individuals who are immunosuppressed (have reduced functioning of the immune system) such as patients with AIDS or those taking certain drugs after organ transplantation, appear to be at increased risk.

History

Primary CNS lymphoma was first described in the 1920s. In the past, it has been known by various names including "perithelial sarcoma", "reticulum cell sarcoma" and "microglioma". However, since the 1970s, this cancer has been recognized as a form of lymphoma.

Disease Course

Patients with primary CNS lymphoma may develop a variety of symptoms, depending on the part of the CNS that is involved. For example, involvement of the brain may lead to headaches, personality changes, memory problems, drowsiness, weakness or numbness of a limb, and difficulty walking. Patients with eye involvement typically first experience seeing floating spots ("floaters"), which may progress to loss of vision. Symptoms related to the brain may come before, or after, the eye problems. Without treatment, these symptoms tend to progressively worsen. This cancer rarely metastasizes (invades other sites in the body), so signs such as enlarged lymph nodes, which occur in other forms of lymphoma, do not usually occur.

Diagnosis and Testing

The diagnosis of primary CNS lymphoma is often delayed. This reflects the fact that the cancer is rare and it mimics other more common problems, such as age-related memory loss or uveitis (inflammation in the eye). Often opinions from several ophthalmologists and neurosurgeons are

necessary to reach a final diagnosis. An MRI scan is the usual method for detection of primary CNS lymphoma affecting the brain and a detailed clinical examination will reveal lymphoma in the eye. Because the disease can affect both the brain and the eyes, a person with eye disease should be examined by a neurosurgeon and persons with brain disease should visit an ophthalmologist. A tissue biopsy is needed to make a definite diagnosis. If the eye is affected by cancer, the biopsy is taken from the eye, by a procedure known as a vitrectomy. Otherwise, a spinal tap or brain biopsy or both are required. Examination of this biopsy by a pathologist familiar with the disease is necessary to establish the diagnosis of primary CNS lymphoma. During the course of treatment, additional MRI scans, eye examinations and tissue biopsies may be required to judge effects on cancer growth.

Treatment

The optimal treatment for primary CNS lymphoma continues to be debated and is the subject of ongoing clinical trials. Surgery alone is not effective against this cancer, but, as detailed above, is required to establish the diagnosis. Treatment options include various forms of chemotherapy and/or radiotherapy. Although radiotherapy is highly successful in inducing a remission, the lymphoma usually recurs. Furthermore, there are serious complications, especially when higher doses—or repeated treatments—of radiation are used. These include dementia and leakage of the retinal blood vessels. Chemotherapy for primary CNS lymphoma poses different challenges. The brain and eye are protected from toxins circulating in the blood by a barrier of tightly joined cells. These "blood-brain" and "blood-eye" barriers also reduce the amount of chemotherapy drug that can enter the CNS or eye when the drug is given in the usual manner, by injection into a blood vessel or by mouth. Because of this, doses of chemotherapy must be very high, increasing the risk of drug side effects. A second option is the surgical insertion of a small tube that reaches into the fluid surrounding the spinal cord and brain, through which medicine can be injected (intrathecal chemotherapy). Another alternative, known as osmotic blood-brain barrier disruption, is available in selected international centers. This treatment involves the initial administration of a medicine that temporarily breaks down the blood-brain barrier, thereby allowing lower doses of systemic chemotherapy to be given and yet still achieve therapeutic levels of drug around the brain. This treatment requires administration under general anesthesia. These methods for delivering chemotherapy to the brain can be combined with local injections of chemotherapy drug into the eye (intraocular chemotherapy) to avoid the blood-eye barrier. Such treatment appears to be well tolerated and effective in clearing cancer cells from the eye.

Cause of Condition

The cause of primary CNS lymphoma is unknown. In particular, it is not understood why a lymphoma would involve the CNS first, a site that does not contain lymphocytes under normal circumstances. Researchers have suggested two theories for this puzzling situation. Perhaps the lymphoma develops within a focus of inflammation in the CNS, as may occur in other organ systems such as the gastrointestinal tract. Another possible explanation is that the cancerous lymphocytes develop elsewhere in the body, but acquire a receptor on their surface that draws them to a signal expressed only inside the CNS. In patients with AIDS, infection with the Epstein-Barr virus, which also causes infectious mononucleosis, or “mono”, is probably an important trigger for primary CNS lymphoma, although the reason for this is not understood.

Prognosis

Prior to the introduction of effective treatments, the outlook for an individual with primary CNS lymphoma was poor, with an average life expectancy without treatment of a few months.

However, with new treatment options, there is the opportunity for improvement of symptoms, including the recovery of vision. Life expectancy may be prolonged, with disease-free intervals of 3 years or longer.

Research and Future Outlook

Although primary CNS lymphoma is rare, active research is being conducted in a number of centers around the world to further improve the outlook for patients with this condition. Laboratory research is aimed at understanding the origin of the cancerous lymphocytes, as well as reasons for their localization in the eye and brain. Large clinical trials are underway to evaluate the safety and efficacy of the various therapeutic options currently available.