**Neuro-Ophthalmic Manifestations of Cancer**

Kelly A. Malloy, OD, FAAO, Diplomate

**COURSE DESCRIPTION:** This course discusses the variety of ways cancer causes neuro-ophthalmic disorders. A case-based approach shows clinical presentations of varied primary brain cancers and metastases, both in the setting of known cancer as well as the initial manifestation. Discussions regarding work-up, diagnosis, treatment and appropriate referral are included.

**COURSE OBJECTIVES:**

1. To become more familiar with the various types of primary brain cancers and metastases.
2. To understand better which types of cancer are most likely to metastasize to brain, bone, etc.
3. To realize that a new onset neurologic deficit in a patient with a history of cancer should be worked-up to rule out a metastasis.
4. To understand the potential importance of the optometrist's role in diagnosing both a primary brain cancer and metastatic disease.
5. To understand the necessary work-up when dealing with metastatic disease.
6. To become more familiar with the types of treatment used for both primary cancers as well as metastatic disease.

**COURSE OUTLINE:**

I. PRIMARY BRAIN TUMORS
   a. Arise from brain tissue, spinal cord, or meninges
   b. Four main types of brain tumors

      i. CARCINOMA – Cancers that are epithelial in origin.
         1. Adenocarcinoma
         2. Etc

      ii. SARCOMA –Cancer of connective or supportive tissue. The type depends on the cell type from which the tumor originates

         1. Osteosarcoma (bone)
         2. Chondrosarcoma (cartilage)
         3. Liposarcoma (fat)
         4. Leiomyosarcoma (smooth muscle)
         5. Rhabdomyosarcoma (skeletal muscle)

6. Etc.

iii. GLIOMAS - the most common type of brain tumor in adults, responsible for about 42% of all adult brain tumors. Arise from brain or spine tissue.

1. ASTROCYTOMAS
    a. Grade I – Pilocytic Astrocytoma
        i. Slow growing, with little tendency to infiltrate surrounding brain tissue. Most common in children and adolescents
    b. Grade II – Diffuse Astrocytoma
        i. Fairly slow-growing, with some tendency to infiltrate surrounding brain tissue. Mostly seen in young adults
    c. Grade III- Anaplastic /Malignant Astrocytoma
        i. These tumors grow rather quickly and infiltrate surrounding brain tissue
    d. Grade IV-Glioblastoma Multiforme
        i. An extremely aggressive and lethal form of brain cancer. Unfortunately, it is the most common form of brain tumor in adults, accounting for 67% of all astrocytomas

2. OLIGODENDROGLIOMAS - make up 4% of brain tumors, mostly affect people over 45 years of age

3. EPENDYMOMAS - rare and make up 2% of all brain tumors, however they are the most common brain tumor in children. They generally don't affect healthy brain tissue and don't spread beyond the ependyma.

iv. MENINGIOMAS - One-quarter of all brain and spinal tumors are meningiomas, and up to 85% of them are benign. Account for about 27 percent of all primary brain tumors
    1. Benign
    2. Atypical
        a. About 5% of al meningiomas
        b. exhibit increased tissue and cell abnormalities. These tumors grow at a faster rate than benign meningiomas and on occasion can invade the brain. Atypical meningiomas have a higher likelihood of recurrence than benign meningiomas
    3. Anaplastic or Malignant –
        a. About 3-5% of al meningiomas

b. increased cellular abnormalities, and grow at a faster rate than either benign or atypical meningiomas. Malignant meningiomas are the most likely to invade the brain and metastasize to other organs in the body, and tend to recur more often than the other two types

v. ACOUSTIC NEUROMAS / SCHWANNOMAS - typically benign
    1. Tumors arising from the nerve sheath or Schwann cells (in acoustic neroma)

vi. MEDULLOBLASTOMA
    1. Form of primitive neuroectodermal tumor (PNET)
    2. common brain tumor in children
    3. usually diagnosed before the age of 10
    4. arise from fetal cells that remain in the cerebellum after birth
    5. Can grow quickly and metastasize

vii. HEMATOLOGIC MALIGNANCIES
    1. Leukemia
    2. Lymphoma
    3. Myeloma

II. METASTATIC DISEASE

a. Most common sites for metastases
    i. Bone
    ii. Lung
    iii. Liver
    iv. Lymph Nodes
    v. Brain
    vi. Leptomeninges

b. BRAIN METASTASES
    i. among the most common mass lesions in the brain
    ii. increased incidence traced to an increase in the median survival of patients with cancer because of modern therapies, increased availability of advanced imaging techniques for early detection, and vigilant surveillance protocols for monitoring recurrence. In addition, most systemic treatments (eg, the use of chemotherapeutic agents, which may penetrate the brain poorly) can transiently weaken the blood-brain barrier (BBB) and allow systemic disease to be seeded in the CNS, leaving the brain a safe haven for tumor growth
    iii. Radiology appearance
        1. usually at the junction of the gray/white matter
        2. often with surrounding edema
        3. dural based mets may mimic meningioma
        4. often enhance with contrast
            a. solid enhancing

b. ring-enhancing

iv. Sites of Origin
    1. Lung
    2. Breast
    3. Melanoma
    4. Lymphoma
    5. Renal
    6. Colorectal
    7. Osteosarcoma
    8. Head/Neck Cancers

v. Location of Brain metastases
    1. Based on blood supply, since the metastases occurs through the bloodstream
        a. Cerebrum (80-85%)
        b. Cerebellum (10-15%)
            i. Renal cancer
            ii. GI cancer
            iii. Pelvic cancer
        c. Brainstem (3-5%)

vi. Number of Brain metastases
    1. If there appears to be an isolated brain metastasis on CT, there are often found to be multiple mets on MRI
    2. Isolated
        a. Thyroid cancer
        b. Colon cancer
        c. Renal cancer
    3. Multiple
        a. Melanoma
        b. Lung cancer
        c. Breast cancer

c. BONE METASTASIS
    i. Primary bone cancers are rare
    ii. Associated with lytic lesions and pain
    iii. Sites of Origin
        1. Prostate
        2. Breast
        3. Lung
    iv. Sites of metastases (to cause neuro-ophthalmic disorder)
        1. Clivus
        2. Skull base

d. LEPTOMENINGEAL CARCINOMATOSIS / NEOPLASTIC MENINGITIS
    i. invasion to and subsequent proliferation of neoplastic cells in the subarachnoid space
    ii. substantial rates of morbidity and mortality
    iii. MRI with contrast can detect leptomeningeal enhancement
    iv. Diagnosis confirmed with CSF cytometry
    v. Sites of origin
        1. Lung
        2. Breast
        3. Melanoma
        4. Medulloblastoma
    vi. Because the leptomeninges cover the cranial nerve roots, tumor seeding of the cranial nerves is not uncommon.
    vii. Can cause symptoms either from encasement of the nerve or by direct invasion with subsequent axonal destruction and demyelination. – Can have cranial nerve palsies
    viii. Symptoms include headache (50%), nausea, vomiting, seizues

III. OTHER MALIGNANCY ASSOCIATED PRESENTATIONS - Depends on cancer type and treatment type
    a. Hematologic
    b. Anemia
    c. Thrombo-embolic complications
    d. Pleural Effusion
    e. Radiation optic neuropathy / retinopathy
    f. Many others

IV. PARANEOPLASTIC SYNDROME
    a. rare disorders that are triggered by an altered immune system response to a neoplasm. They are defined as clinical syndromes involving nonmetastatic systemic effects that accompany malignant disease
    b. collections of symptoms that result from substances produced by the tumor, and they occur remotely from the tumor itself.
    c. Because of their complexity and variety, the clinical presentations of these syndromes may vary greatly. Usually, paraneoplastic syndromes are divided into the following categories:
        i. miscellaneous (nonspecific)
        ii. rheumatologic
        iii. renal
        iv. gastrointestinal
        v. hematologic
        vi. cutaneous
        vii. endocrine
        viii. neuromuscular
            1. may include Myasthenia gravis

V. CLINICAL PRESENTATION (SIGNS / SYMPTOMS)
    a. Depending on location of metastases

i. Increased intracranial pressure
    1. Papilledema
    2. CN VI palsy
ii. Cranial Nerve Palsies
    1. CN II, III, IV, V, VI, others
iii. Headache
iv. Seizures
v. Ataxia
vi. Focal Weakness / Numbness
vii. Mental Status Change

VI. WORK-UP:
- a. Neuro-Imaging
    - i. MRI
        1. Brain
            - a. With contrast if possible
                - i. Primary brain cancer
                - ii. Metastatic disease
                    1. To brain
                    2. To bone
                        - a. Clivus
                        - b. Skull base
                        - c. Vertebrae
    - ii. CT scan
        1. Chest – to look for primary cancer
        2. Abdomen– to look for primary cancer
        3. Pelvis– to look for primary cancer
        4. Brain
            - a. if MRI contraindicated
            - b. Good to detect hemorrhage into the metastatic lesion
            - c. All with contrast if possible, but contrast not necessary to look for hemorrhage (more common with melanoma)
- b. Lumbar Puncture
    - i. Used to diagnose leptomeningeal carcinomatosis or carcinomatous meningitis

VII. TREATMENT:
- a. Radiation
- b. Chemotherapy
- c. Surgery

VIII. REFERRALS:
- a. Neuro-surgery
- b. Oncology
- c. Radiation-Oncology
- d. Others