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The Eyes as a Window to the Brain: a Teaching Case Report of Misdiagnosed Glioblastoma

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Abstract

Glioblastomas [also called glioblastoma multiforme (GBM)] are malignant grade-IV tumors. The tumors consist predominantly of abnormal astrocytic cells but contain a mix of cell types. Glioblastomas are the most common and most malignant of the glial tumors. While GBM is not the most common brain tumor, it is the deadliest. Median survival time with standard therapy is 14-15 months after diagnosis. In a disease with poor prognosis and rapid progression, early tumor detection is necessary for making timely treatment decisions. Optometrists are in a position to detect early signs of tumors such as GBM and improve the survival rate. Clinical evaluation — thorough review of symptoms including seizures, headaches, weight loss, dizziness, muscle weakness and visual field loss — is crucial for these patients. New or worsening visual field defects may indicate the presence or progression of glioblastoma and should prompt further testing and investigation. We identify a case, previously misdiagnosed as glaucoma, in which careful history and Humphrey visual field testing predated neuroimaging findings of glioblastoma located in an unusual part of the brain.

Key Words: *grade-IV tumors, glioblastoma, optic pathway, neurological symptoms, Humphrey visual field defects, neuroimaging*

Background

Glioblastoma [also known as glioblastoma multiforme (GBM)] is a type of glioma or astrocytoma, cancer that forms from star-shaped cells in the brain called astrocytes. Gliomas account for 40-50% of all primary and metastatic intracranial tumors with glioblastoma being the most common type.[1,2]

The World Health Organization (WHO) classification grades astrocytic tumors from grade-I to grade-IV, and GBM is often referred to as a grade-IV astrocytoma. These are the most invasive type of glial tumors, rapidly growing and commonly spreading into nearby brain tissue.

In adults, GBM can be found in many parts of the brain but occurs most often in the cerebral hemispheres, especially in the frontal and temporal lobes of the brain, with 3% of lesions arising occipitally. GBM is a devastating brain cancer that typically results in death in the first 15 months after diagnosis.[3-6]

Glioblastoma can present with variable symptoms depending on the anatomical location of the mass. These may include persistent headaches, vomiting, loss of appetite, changes in mood and personality, changes in the ability to think and learn, new onset of seizures and speech difficulty of gradual onset. Neurological symptoms can be subtle or partially to entirely absent.

Ocular manifestations of gliomas and GBM are variable and similar to those of other space-occupying lesions and may include visual field loss. Recognizing pertinent neuro-ophthalmic signs and symptoms

and appropriate ocular testing including perimetry are crucial for an immediate neurological evaluation and early detection of possible tumor growth.[2,7-9]

The following case report describes the visual symptoms and visual field testing results associated with an occipital lesion related to glioblastoma, previously misdiagnosed as glaucoma. For optometry third- and fourth-year students and residents, the case report can reinforce clinical competence in neuro-ophthalmic care. It focuses on the proper approach to early diagnosis and management of patients with intracranial masses.

Student Discussion Guide

Case presentation

A 43-year-old Hispanic male was referred by his primary care physician concerning visual loss. The patient reported a previous diagnosis of glaucoma by an ophthalmologist in another country where he had recently traveled. The purpose of his visit was primarily to receive a second opinion about the diagnosis. He reported that while traveling in that country, he experienced an episode of headache more to the right side of his head without other symptoms, except for a disturbance in his peripheral vision. He decided to visit an emergency clinic, where he was prescribed analgesics for pain and was discharged with a diagnosis of borderline hypertension and a referral to ophthalmology. The ophthalmologist diagnosed glaucoma and recommended medical treatment with a scheduled follow-up visit. The patient's only complaint at the time of the first visit was blurry peripheral vision with no headaches or other symptoms.

Medical history revealed borderline hypertension controlled by diet and exercise. The patient was not taking any medications. Family medical history was positive for hypertension. Ocular history included myopia and astigmatism, for which the patient used glasses since he was 11 years old. His family ocular history was insignificant. He had no allergies to medications. Social history revealed sporadic, approximately once a month, alcohol consumption and no history of smoking.

Best-corrected visual acuity measured 20/20 OD and 20/20 OS. Pupils were equal in size and reacted normally to light and accommodation. Color vision measured with Hardy-Rand-Rittler plates was normal for both eyes. Extraocular muscle movements were full in each eye. The cover test confirmed absence of strabismus or any abnormal heterophoria. Confrontation visual field testing showed field loss on the patient's right side in both eyes. Anterior segment evaluation was unremarkable. Intraocular pressure measured 20 mmHg OD and 19 mmHg OS. Posterior segment evaluation showed a normal-size disc OD and OS with cup to disc ratio of 0.4/0.4 OD and OS. The optic nerves showed no elevation and had a positive spontaneous venous pulsation without glaucomatous appearance. The macula in both eyes appeared normal with positive foveal reflex, and the rest of the posterior pole and peripheral retina were unremarkable.

Humphrey visual field (HVF) testing performed the same day showed right homonymous hemianopsia with evident macular sparing **(Figures 1 and 2)**.

Figure 1. Automated Humphrey visual field test of the left eye showing hemianopic field loss with macular sparing.
Click to enlarge

Figure 2. Automated Humphrey visual field of the right eye showing hemianopic field loss with macular sparing.
Click to enlarge

Blood pressure measured 130/90. Neurological evaluation revealed full orientation to time and place. The patient showed no motor or sensory dysfunction. Evaluation of cranial nerves 1 to 12 was normal. Coordination and balance proved to be normal.

The patient was referred to his primary care provider for hypertension evaluation. Computerized tomography (CT) without contrast was immediately ordered. The CT scan showed an intra-axial oval-shaped mass with partial fluid component at the left occipital lobe measuring approximately 5 cm long, 7.7 cm anterior-posterior and 2.7 cm transversely with minimal surrounding edema and some mass effect and midline shift to the left lateral ventricle **(Figure 3)**.

The patient was immediately seen by a neurologist at a hospital facility, and magnetic resonance imaging (MRI) with and without contrast was ordered. The MRI showed a cystic mass with the same measurements as seen on the previous CT scan consistent with cystic glioma **(Figures 4 and 5)**.

Figure 3. Axial CT scan showing hypodense large cystic lesion in occipital lobe region. Click to enlarge

Figure 4. Axial MRI T1-weighted image without contrast showing large hypodense heterogeneous lesion consistent with a cystic glioma. Click to enlarge

Figure 5. Axial MRI T2-weighted image showing heterogeneous lesion having high signal with surrounding edema consistent with a cystic glioma. Click to enlarge

After being evaluated by a neurosurgeon, the patient underwent tumor resection surgery. The operation revealed an occipito-parietal tumor. The pathology of the tumor showed glioblastoma of the NOS (not otherwise specified) type (WHO grade-IV). Following brain surgery, the patient received radiation therapy and oral chemotherapy with temozolomide.

While the patient continued the oral chemotherapy, he also received the new treatment modality of tumor treating fields (TTF). Six months after the surgical resection, the patient was stable and had returned to his daily activities.

Educator's Guide

Key concepts

1. Critical thinking in diagnosis and clinical approach in primary eye care
2. The pathophysiology of the brain, its space-occupying lesions and the impact on the eyes
3. The importance of early detection of brain lesions such as GBM, which can contribute to timely treatment decisions and improve the patient's survival period
4. The importance of ensuring that patients understand their current situation and the seriousness of the matter at hand
5. The significance of ocular signs and visual field testing results in developing the diagnosis of brain tumor
6. With prompt and appropriate detection, treatment and referral, optometric physicians can play a significant role in reducing the risk of permanent vision impairment associated with brain tumors and improve the patient survival rate

Learning objectives

1. Learn the importance of recognizing systemic neurological signs and symptoms
2. Understand the importance of visual field interpretation in the detection of neurological conditions
3. Learn to differentiate life-threatening situations based on patient presentation
4. Develop a basic understanding of the types of headaches associated with intracranial tumors as well as the differential diagnosis of pain
5. Gain knowledge on the differential diagnosis of optic nerve appearance in glaucomatous vs. neurological clinical presentations
6. Gain a basic understanding of glioblastoma including signs, symptoms, necessary testing and available treatment options
7. Gain expertise in patient education and management when urgent care is required

Discussion questions

1. Basic knowledge and concepts related to the case:

    a. Describe the cell type of glioblastoma tumor, localization of the tumor in the brain and its general pathophysiology
    b. Describe the epidemiological characteristics of glioblastoma
    c. Describe the method of grading and genetic identity clues for glioblastoma
    d. Describe systemic and ocular symptoms related to glioblastoma
    e. Emphasize the importance of visual field testing in the diagnosis and monitoring of brain tumors such as glioblastoma

2. Differential diagnosis, treatment, prognosis:

    a. What are the likely diagnoses and differentials based on a patient's presenting signs, symptoms and chief complaint?
    b. List types of neuroimaging diagnostic techniques used
    c. List available treatment options for glioblastoma and emphasize the importance of inherent resistance to conventional therapy
    d. Describe the poor prognosis in glioblastoma cases

3. Critical-thinking concepts:

    a. Primary care optometrist's role in the detection and management of patients with intracranial masses, emphasizing the importance of baseline visual field testing in patients with a particular type of neurological symptoms
    b. The importance of the optometrist's role in the appropriate communication with a patient while delivering news of a lethal tumor and ensuring that the patient understands his or her current eye health condition

Literature review

Table 1. Click to enlarge

There are more than 120 types of brain and central nervous system (CNS) tumors. Today, most medical institutions use the WHO classification system to identify brain tumors. The WHO classifies brain tumors by cell origin and how the cells behave, from the least aggressive (benign) to the most aggressive (malignant). Some tumor types are assigned a grade, ranging from grade-I (least malignant) to grade-IV (most malignant), which signifies the rate of growth. There are variations in grading systems, depending on the tumor type. The classification and grade of an individual tumor help predict its likely behavior.

Glioblastomas are glial tumors but specifically belong to the diffuse astrocytic and oligodendroglial tumor categories[3,4] **(Table 1)**.

Discussion

Teaching methodology

The case can be taught as a direct PowerPoint ground rounds seminar presented by the attending resident to third- and fourth-year students. At the end of the presentation the participants work together in small groups or individually and read the information explained in the case discussion. Their learning experience is based upon reading each discussion question and trying to respond in writing. Learning objectives can be assessed during a summative evaluation of participant correct responses against a set of predetermined answers provided in the discussion. This teaching/learning experience will:

- Allow the application of theoretical concepts to be demonstrated, thus bridging the gap between theory and practice
- Encourage active learning
- Provide an opportunity for the development of key skills such as communication, group working and problem solving
- Increase the students' enjoyment of the topic and hence their desire to learn

What are the definition and general pathophysiologic concepts of glioblastoma?

GBM are malignant grade-IV tumors in which a large portion of tumor cells are reproducing and dividing at any given time. They are nourished by an ample and abnormal tumor vessel blood supply. The tumors are predominantly made up of abnormal astrocytic cells, but also contain a mix of different cell types (including blood vessels) and areas of dead cells (necrosis).[2,7] Glioblastomas are infiltrative and invade nearby regions of the brain. They can also sometimes spread to the opposite side of the brain through connection fibers (corpus callosum). It is exceedingly rare for glioblastomas to spread outside of the brain.

Primary glioblastomas may arise de novo, meaning they begin as grade-IV tumors with no evidence of a lower-grade precursor. De novo tumors are the most common form of glioblastoma (90%) and tend to be more aggressive and tend to affect older patients. Alternatively, secondary glioblastomas may progress from lower-grade astrocytic tumors (grade-II and grade-III) and evolve into grade-IV tumors over time. In general, these tumors tend to be slower growing initially, but can become aggressively progressive. They tend to occur in younger patients and they have a predilection for the frontal lobes.

Glioblastomas are usually diagnosed as either isocitrate dehydrogenase (IDH)-wild type or IDH-mutant. IDH-wild type glioblastomas are more common, tend to be more aggressive, and have worse prognosis than IDH-mutant glioblastomas. IDH-wild type are generally primary tumors while IDH-mutant are secondary.[3,4,10,11]

What are the prevalence and incidence of glioblastoma?

The National Cancer Institute estimates that 22,850 adults (12,630 men and 10,220 women) were diagnosed with brain and other nervous system cancers in 2015. It also estimates that 15,320 of these diagnoses resulted in death.

Glioblastoma has an incidence of 2-3 per 100,000 adults per year and accounts for 52% of all primary brain tumors. Overall, GBM accounts for 17% of all tumors of the brain (primary and metastatic). Caucasians are affected more frequently than other ethnicities. These tumors tend to occur in adults age 45-70. Between 2005 and 2009, the median age for death from cancer of the brain and other areas of

the central nervous system was 64.[1,7]

What are the grading and genetic identity of glioblastoma?

After detection of a brain tumor on CT or MRI scan, the tumor tissue is biopsied. The analysis of the tissue under the microscope is used to assign the tumor a named grade and to provide answers to the following questions:

- From what type of brain cell did the tumor arise? (The name of the tumor is derived from this)
- Are there any signs of rapid growth in the tumor cells?
- Are there any specific genetic mutations within the tumor that can help with prognosis and/or provide a target for therapy?

The tumor name and grade help determine treatment options and provide important information about prognosis.[4,5,12]

Glioblastomas are diagnosed and classified as IDH mutations. Among these mutations, three types have been determined: IDH-wild type, IDH-mutant and, rarely, glioblastoma NOS when IDH status cannot be determined.

IDH-wild type glioblastomas include chromosomal genetic abnormalities related to chromosomes 7, 9, 10 and 13. Mutations of genes can occur in IDH-wild type glioblastomas and most commonly include:

- Phosphatase and tensin homolog (PTEN) gene, a tumor suppressor
- Epidermal growth factor receptor (EGFR) gene, which affects the cell membranes and stimulates cell division
- Telomerase reverse transcriptase (TERT) gene, which when mutated allows cancer cells continue to multiply and divide

IDH-mutant glioblastomas have mutated IDH1 and IDH2 genes. These mutations alter the cell energy requirements and cell function. Also, alteration or damage of chromosome 19 is related to this type of tumor. Finally, the gene p53, a tumor suppressor, can become mutated and lead to tumor growth.[7,10,11]

What are the systemic and ocular symptoms related to glioblastoma?

Neurological symptoms vary depending on the anatomical location of the tumor. Symptoms of glioblastoma may appear slowly and be subtle at first. Patients may present with headaches, confusion, memory loss, motor weakness and seizures. Other patient complaints include nausea, personality changes, difficulty concentrating, hemiparesis and aphasia.
It is important to recognize headaches related to brain tumors. The nature of a brain tumor headache is different from the nature of a tension or migraine headache in various ways such as:[2,7]

- Waking up frequently with a headache
- Headaches that wake a person up at night
- Headache pain that changes as the person changes positions
- Headache pain that does not respond to standard pain relievers
- Headaches that last days or weeks at a time and then disappear
- Headaches accompanied by various symptoms such as unexplained weight loss, increased pressure in the back of the head, dizziness or loss of balance, seizures, hearing loss, sudden inability to speak, weakness or numbness of one side of the body and uncharacteristic moodiness and anger

Ocular manifestations of gliomas and GBM are similar to those of common space-occupying lesions and

may include any of the following:[2,7]

- Blurred vision
- Visual field loss (defects correlate with site of tumor: homonymous hemianopsias)
- Spatial neglect
- Cranial nerve palsies
- Optic disc edema and atrophy
- Pupillary abnormalities, including relative afferent pupil defect
- Gaze-induced nystagmus

Most commonly, glioblastomas originate in the frontal and temporal lobes, with 3% of lesions arising occipitally. Symptomatology varies based on tumor location. Lesions affecting the occipital lobe can present with a wide array of visual symptoms, including peripheral vision loss, visual hallucinations and several forms of visual agnosia. Masses that affect the temporal lobe often manifest with memory impairment, auditory hallucinations, spatial disorientation and peripheral vision loss. Parietal lobe tumors may cause impaired speech, lack of recognition, spatial disorders and decreased eye-hand coordination.[2,7]

What is the importance of visual field testing in the detection and monitoring of glioblastoma?

In many cases, neurological symptoms are absent, with visual field loss being the only manifestation. Functional studies provide a clinical context for imaging findings, increasing the predictive value of a positive imaging result. For example, HVF testing is a functional study that adds sensitivity to detecting disease evidence and progression of tumors involving the optic pathway. This fundamental concept is well-known but often overlooked in the era of increasingly sophisticated imaging techniques. Over-reliance on imaging that does not fit with clinical findings may lead to delayed treatment, inappropriate treatment or unnecessary tests.[8,13] While imaging has played, and will continue to play, a vital role in detection and monitoring of glioblastomas, the use of accurate tools to assess clinical status should be similarly emphasized. HVF testing may prove to be useful for early detection and monitoring clinical signs of progression, as up to 50% of patients with lesions in the optic pathway show visual field defects. While HVF testing can be prone to error, well-documented reliable studies show a clear pattern of visual changes can alert clinicians to the need for prompt work-up. In the absence of highly accurate and early neuroimaging identification of tumor presence and progression, HVF testing is useful as an adjunctive clinical evaluation.[8,9] In the case presented here, HVF showed clear, right homonymous field defects in the setting of minor visual complaints before the MRI positive findings. Therefore, for rapidly growing tumors occurring near optic pathways, such as glioblastoma, we recommend prompt neuro-ophthalmological evaluation with HVF testing. Evidence of progressive visual field deficits requires mandatory clinical monitoring and should prompt further systemic assessment and consideration of changes in treatment regimens.

What are the differential diagnoses and how may neuroimaging aid in diagnosis?

Common differentials for intracranial masses include astrocytoma, chordoma, CNS lymphoma, glioma and medulloblastoma. Also, posterior cerebral artery infarcts and hemorrhages in the infero-medial aspect of the occipital area should be included in the differential diagnosis. A biopsy is needed to determine a definite diagnosis. Key findings for all differentials are visual field defects, visual and auditory hallucinations, memory loss, visual agnosia and headaches.

Modern imaging techniques can accurately pinpoint the location of brain tumors. Diagnostic tools include CT and MRI. The latter is more sensitive and is the modality of choice.[5,12] CT scanning can be reliable in the diagnosis of the tumor; however, it may miss small tumors. Also, lesions such as brain abscess, infarct with hemorrhage and large demyelinating lesions may look similar on CT and mimic glioblastoma.

Nonenhanced CT scan findings may show a heterogeneous and not well-marginated mass with internal areas of low or high attenuation indicating necrosis or hemorrhage, respectively. Enhanced CT scans show improvement of imaging results such as irregularity and inhomogeneity.[5,12] MRI gives a higher degree of confidence in the diagnosis and is more sensitive in identifying location and size of brain tumors. In the case of glioblastoma, because the lesion is infiltrative, tumor cells are detected well beyond the area of abnormal signal intensity shown on MRIs. Techniques such as perfusion weighted imaging used in MRI demonstrate a heterogeneous mass with low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. Necrotic foci, neovascularity and peritumoral vasogenic edema are significantly enhanced after the administration of gadolinium-based contrast material. Intraoperative MRI may also be useful for guiding tissue biopsies and tumor removal.[12]

Magnetic resonance spectroscopy is used to examine the tumor's chemical profile. Positron emission tomography (PET) helps detect tumor recurrence. Differentiation between residual or recurrent tumor and postoperative edema or scarring is often difficult on MRI and CT scans. PET scanning is useful in cases of active tumor, which show high metabolic activity, and in cases of scarring or edema, which usually show no increased activity at all. [12,5]

What are the treatment options for glioblastoma?

Standard treatment is surgical resection followed by radiation therapy or combined radiation therapy and chemotherapy. If the tumor is inoperable, radiation or radiation/chemotherapy can be administered.[10,14,5] Treatment requires effective teamwork from neurosurgeons, neuro-oncologists, radiation oncologists, physician assistants, social workers, psychologists and nurses.

Glioblastoma's capacity to wildly invade and infiltrate healthy surrounding brain tissue makes complete resection impossible.[16] However, improvements in neuroimaging have helped to make better distinctions between tumor types and between tumor and healthy cells. After surgery, radiation therapy is used to kill leftover tumor cells and try to prevent recurrence.[14,15,19] Temozolomide and bevacizumab are used in chemotherapy.[18-23] In 1997, the U.S. Food and Drug Administration (FDA) approved polifeprosan 20 with carmustine implant, an alkylating agent that is surgically implanted as a wafer after surgical resection and allows for drug delivery directly to the tumor site.

In addition, the medical device treatment TTF has been approved for adult patients with newly diagnosed and recurrent glioblastoma. The device is applied with electrodes placed on a patient's scalp. It delivers alternating electric fields that exert variable but specific toxicity in proliferating cancerous cells, thus disrupting tumor growth. The TTF device must be worn by the patient for at least 18-20 hours a day during 4-6 weeks. This innovative treatment usually follows radiation therapy and surgery. FDA has approved the device for glioblastoma patients age 22 and older.[17,20,24] Several clinical trials are being conducted to determine the efficacy of glioblastoma treatments. These trials include immunotherapy, antiangiogenic therapy, gene and viral therapy, cancer stem cell therapy and targeted therapy.[20,25]

What is the prognosis for glioblastoma-type tumors?

The average survival time for adults with IDH-wild type glioblastoma is approximately 11-15 months. Younger age at diagnosis (less than 50 years) and complete surgical removal of the tumor can be essential factors for an improved prognosis. Biopsy results after surgery related to molecular markers can also play a role in prognosis. Patients with IDH-mutant glioblastoma have a better prognosis with average survival time of 26-30 months. Molecular biomarkers can also become important factors in the effectiveness of chemotherapy and consequently alter the prognosis. Such a marker is methylguanine-DNA-methyltransferase (MGMT), which involves the methylation of the genes. MGMT becomes valuable and vital for the stability of the genes within the cells. A methylated gene becomes inactivated thus making cancer cells more sensitive to the available chemotherapy drugs. Adults with glioblastoma NOS

have a similar prognosis to those with the IDH-wild type tumor, but several factors such as age, location, degree of necrosis, degree of enhancement, biomarkers and the patient's general health status prior to the diagnosis play an important role in the survival rate.[7,11,16]

What is the optometrist's role in the detection of tumors such as glioblastomas?

The eyes are unique windows into overall health. The eye is the only place in the body through which veins, arteries and a cranial nerve can be observed without surgery. As such, the eyes can reveal information about many health conditions, including tumors.

Optometrists need to realize that their eye exam format should always include tests of peripheral vision and muscle function because these tests can often be the first line of detection of a brain tumor. Brain tumors, depending on their location, can cause loss of peripheral vision or damage the nerves that supply the muscles of the eyes resulting in abnormal eye movements, double vision or other changes in vision.

How important is patient education as part of the patient's management?

Early on, eye doctors need to solidify their relationship with patients. By building rapport based on warmth and trust, optometrists can establish a good foundation for any difficult conversation that may become necessary. Bad news comes to everyone at some point, and if optometrists deliver it using their own feelings, they can be a powerful support. It is important to understand that a doctor can never feel the way patients feel or truly understand their emotions, but can comfort them as if he or she were sharing the same emotions. The doctor must always understand the patient's perspective in a situation. As a patient asks questions such as "Will things get worse?" the doctor needs to be clear about what is meant by worse, rather than assume that the patient's concept of worse is the same.

The optometrist should never protect patients from the facts. The most serious mistakes in delivering bad news may be avoiding or not fully relaying the severity of the situation. It's natural to feel sympathy for patients and want to give them hope. Even a glimmer of hope is important. However, honesty is most important so that the appropriate care can be accomplished. It is necessary to let patients understand that the doctor will accompany them throughout this difficult process. Finally, optometrists need to know their patients, which requires listening to them and being sensitive to the fears and cultural beliefs that may cause them to refuse a particular treatment.[26]

Conclusion

GBM is the most common and deadliest of malignant primary brain tumors in adults and among a group of tumors referred to as gliomas/astrocytomas. Classified as grade-IV (most serious) astrocytoma, GBM develops from the lineage of star-shaped glial cells, called astrocytes, which support nerve cells. Glioblastoma develops primarily in the cerebral hemispheres but can develop in other parts of the brain, brainstem or spinal cord. Because of its lethality and its variable genetic integrity, glioblastoma can respond differently to aggressive therapies, making treatment extremely difficult and challenging. Early detection can be vital and may help in prolonging the patient's survival period. GBM can present with various neurological symptoms and ocular manifestations, and recognition of such expressions can be crucial in the early detection of possible tumor growth.

As primary eyecare providers, it is important for optometrists to pay close attention to unusual visual symptoms experienced by patients, as these symptoms can be useful in the diagnosis, localization and co-management of patients with intracranial masses. For rapidly growing tumors occurring near optic pathways, such as glioblastoma, prompt neuro-ophthalmological evaluation with visual field testing is recommended. HVF testing may very well be a first step toward bridging the gap between functional and imaging identification of tumor presence or progression involving the optic pathways.

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