

Acute Onset Isolated Sixth Nerve Palsy Secondary to a Metastatic Brain Lesion

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Abstract

Introduction: A sixth nerve palsy causes binocular horizontal diplopia due to a paretic lateral rectus muscle, particularly in the direction of the involved muscle. Over the age of 50, vasculopathic (diabetes and hypertension) etiology is most common. Monitoring until resolution is typically the course of treatment. Further testing may be required, when indicated by systemic findings.

Case Report: A 55-year-old male presented with recent onset diplopia and restricted ocular motility left eye in left gaze. He denied headache, pain, or recent injury. There were no signs or symptoms of transient ischemic attacks/stroke, flashes, floaters, vision loss, or any other ocular symptoms. Further questioning found no jaw claudication, recent weight loss, temporal pain, or other associated signs of giant cell arteritis. Medical history revealed hypertension and prostate cancer. An MRI of the brain confirmed an enhancing clival mass adjacent to Meckle's cave consistent with metastatic disease. An immediate referral to oncology was made. The patient's PET scan revealed multiple metastatic lesions throughout his body. The patient is currently being treated with extensive chemotherapy and radiation. Visually, the patient continues to improve subjectively through use of a head turn and patching as needed. Objectively, the patient's deviation remained relatively stable through four months before being lost to follow-up. In this case, the patient showed subjective improvement due to learned behaviors and patching but little, if any, objective improvement was seen.

Discussion: The two most common etiologies for sixth nerve palsy are vasculopathic and unknown, followed more rarely by traumatic and metastatic events. This patient presented with a brain neoplasm involving the left petrous apex and clivus. It is at this bony extension where the sixth nerve runs most medially and compression forces can result in nerve palsy. Although a metastatic etiology of sixth nerve palsy is less common, a patient presenting with such a history warrants earlier additional testing.

Key Words

abducens nerve palsy, clivus, metastatic disease, prostate cancer, sixth nerve palsy calisthenics, strabismus, traumatic brain injury, vision therapy

Introduction

Sixth nerve palsies arise from a variety of etiologies, the two most common being vascular (18-37%) and undetermined (21-30%).¹⁻⁴ When combined, these two causes account for the majority of isolated sixth nerve palsies seen clinically. It has been speculated that vasculopathic nerve palsies are caused by an arterial infarct of the microvasculature resulting in a localized demyelinating event of the adjacent cranial nerve. These localized demyelinating events are thought to result in minimal axonal degeneration and therefore recover relatively completely upon remyelination.⁵ Because this remyelination process is time dependent, most isolated sixth nerve palsies are simply followed for a period of time before further testing is indicated. If improvement is not seen within one to three months, or if new findings such as persistent pain or other cranial nerve involvement occur, further imaging such as MRI or CT scans should be performed.¹⁻⁴

Due to its long course through the brain, the abducens nerve (CN VI) is also vulnerable to both traumatic disruption and metastatic disease, the next two most common causes for an isolated sixth nerve palsy.¹⁻⁴ The abducens nerve enters the cavernous sinus adjacent to the internal carotid artery and more medial than the other cranial nerves (II, IV, V1 and V2). Therefore, CN VI is most vulnerable to the compression forces of an enlarging metastatic lesion. For this reason, CN VI can be the first, if not only, cranial nerve involved.^{1, 6-9}

Case Report

A 55-year-old male presented with double vision that started the previous evening while watching television. He associated the double vision with an initial dose of hydrocodone he took the previous day and thought perhaps it was a side effect of the medication. The diplopia was constant and worse in left gaze. The patient denied headache, pain, or recent injury. He also denied signs and symptoms of transient ischemic attack/stroke, flashes, floaters, vision loss, or any other ocular symp-

Table 1. Oncology History

Date	Finding/Treatment
September 2009	Bony metastases first noted
January 2010	Gonadotropin-Releasing Hormone (GnRH) agonist Goserelin started (Goserelin is a palliative treatment of advanced prostate cancer)
February 2010	L neck mass biopsy showed adenocarcinoma with prostate origin
August 2010	L CN VI palsy with clivus region expansile lesion
August 2010	Rising PSA
August 2010	Bicalutamide added and radiation therapy began (anti-androgen)
August 2010	Osteoblastic metastatic lesion of L hip – radiation therapy starting

toms. Further questioning uncovered no jaw claudication, recent weight loss, temporal pain, or other associated signs of giant cell arteritis.

The patient's medical history was positive for hypertension and metastatic prostate cancer. Best-corrected visual acuity was 20/20 OD and OS. Pupils were equal, round, and reactive to light with no afferent pupillary defect. Confrontation fields were full in all quadrants. Extra-ocular motility testing showed the left eye was unable to abduct across the midline while the right eye had full range of motion. The patient also noted diplopia in all quadrants of left gaze. Cover test revealed an esotropic deviation with 25 base-out prism required to fuse the target in left gaze, 10 base-out in primary gaze, and 2 base-out for fusion in right gaze. Maddox rod revealed no vertical component. All other cranial nerves were tested and were within normal limits. Blood pressure measured 142/112 mmHg at this visit.

The biomicroscopy examination yielded ocular pressures of 15 OD and 16 OS with Goldmann tonometry, corneal arcus, deep and quiet anterior chamber, flat and intact iris, and early nuclear sclerosis. Funduscopy evaluation revealed 0.50 cup/disc ratio with spontaneous venous pulsation, clear and flat macula, mild vessel crossing changes, and flat and intact peripheral retina OU.

An assessment was made of an isolated sixth nerve palsy OS, hypertension with mild retinopathy, and pre-surgical cataracts OU. Other differential diagnoses to be considered included: vasculopathic, trauma, neoplasm, thyroid-related orbitopathy, myasthenia gravis, orbital inflammatory pseudotumor, giant cell arteritis, Duane syndrome type 1, and convergence spasm. The patient was given a patch to help deal with the double vision while further testing was completed. Given the patient's history of metastatic disease, the plan was to refer the patient for an MRI of the orbits and brain with and without contrast the same day. The MRI findings (Figure 1) showed an expansile heterogeneously enhancing mass involving the clivus and left petrous apex. Meckel's cave and the left internal auditory canal were involved.

There was a mass effect and displacement of the left internal carotid artery and abducens nerve. No hemorrhage, hematoma, intra/extra axial fluid collection, hydrocephalus, or acute in-

Figure 1: Imaging of the brain showing an enhancing mass that is consistent with osseous metastatic disease.

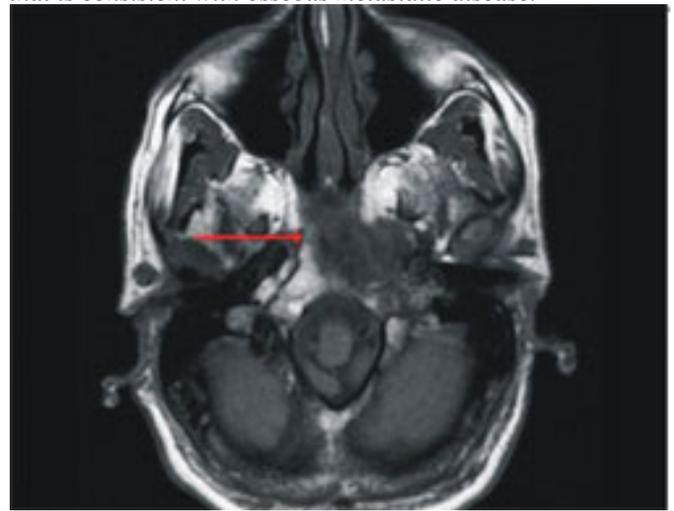
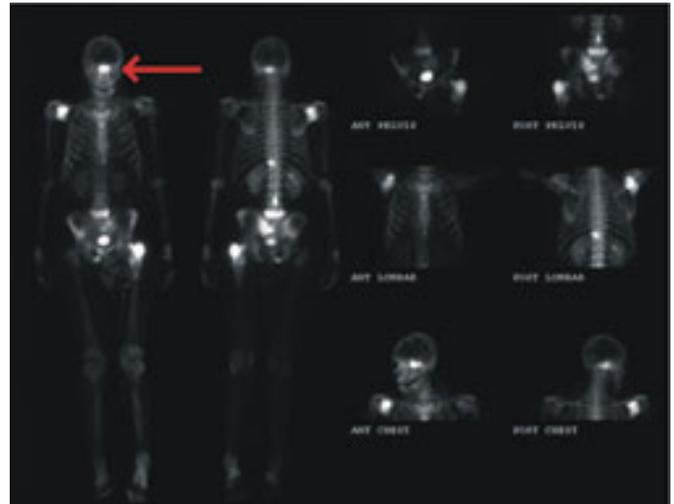


Figure 2: Positron Emission Tomography (PET) scan identifying the locations of the other metastatic lesions. Note the lesion located in the base of the skull adjacent to where the abducens nerve transverses.



fart was noted. Prior to the MRI findings, the patient had an appointment scheduled with oncology at a later date; however, that appointment was moved up so the patient could be seen in two days instead. At the oncology visit, further imaging was performed including a PET (Positron Emission Tomography) scan (Figure 2).

A PET scan measures vital functions such as blood flow, oxygen use, and glucose metabolism. This allows doctors to identify abnormally from normally functioning cells. The PET scan noted in Figure 2 shows the areas of metastasis and abnormal function. The oncology history of our patient can be found in Table 1.

At his follow-up visit two months later, he reported subjective improvement but not resolution of his double vision. He had, at that time, developed a head turn to minimize his diplopia, which still neutralized with 12 base-out prism in primary gaze. Additionally, he used the patch from the previous visit for relief as needed. The examination findings two months later showed similar findings of 12 base-out prism for fusion in primary gaze. Again, the patient reported a subjective improvement. The patient was then lost to follow-up. By this

point, a lack of spontaneous resolution warranted further testing, but the early MRI results had already elicited an etiology and the patient was being treated by oncology.

Discussion

Our patient presented with an acute isolated abducens nerve palsy from a metastatic brain tumor involving the clivus and left petrous apex. The close proximity to the bony clivus makes CN VI vulnerable to chordomas and metastatic cancer near this region.¹⁰ Of the neoplasms causing CN VI palsy in adults, the most common were found to be metastatic tumors.¹ Several approaches for treating clivus metastases include trans-sphenoidal surgery, stereotactic radiosurgery, or treating the primary cancer with chemotherapy and/or radiation.¹¹

In this patient's case, the metastatic lesion was secondary to prostate cancer. Prostate cancer is one of the leading causes of morbidity and mortality for men.¹²⁻¹⁴ Metastasis to the brain from prostate cancer as a primary site is rare, occurring in 2.4% of patients. These metastases can be associated with cranial nerve palsies secondary to compression or infiltration of the affected nerves.^{2, 3, 15}

For many years, PSA (prostate-specific antigen) testing was used as a screening test for prostate carcinoma; however, due to the test's high false positive detection rates, the effectiveness of the test is controversial. When a positive PSA screening has occurred, the additional testing and treatment involves invasive procedures and increased morbidity. The main treatments for prostate carcinoma include radiation therapy with androgen deprivation therapy or radical prostatectomy if indicated.^{13,14}

A patient presenting with a CN VI palsy requires a careful history, appropriate testing, and referral. Patients with a history of vascular disease alone are typically followed for spontaneous resolution of their diplopia. However, consultation with their primary care provider, cardiologist, or endocrinologist is helpful for controlling the underlying etiology and decreasing the chances of other manifestations of their disease process. Those presenting with a history of trauma may be referred to radiology for a CT scan, MRI, or magnetic resonance angiogram immediately to rule out signs of skull or brain trauma. As with our patient, those with a history of cancer should also be referred for an MRI to rule out metastatic disease and, as warrants, to oncology. Patients with symptoms of giant cell arteritis require immediate blood work and referral to ophthalmology for consideration of a temporal artery biopsy. Those with symptoms of myasthenia gravis may require a neurology evaluation and tensilon testing. Any thyroid orbitopathy findings should be referred to internal medicine or endocrinology for further blood work and evaluation.

It should be noted that while this patient stated subjective improvement through learned behaviors and patching, he demonstrated little objective improvement. Due to the etiology, resolution of the diplopia might have corresponded to the metastatic lesion's response to chemotherapy and radiation. Should the patient have remained symptomatic, Fresnel prisms could have been used pending final determination of residual esotropia. While patching was the initial approach to treat the patient's diplopia, occlusion using Bangerter foils should have been considered as recent literature supports it as an alternative to complete occlusion for a multitude of condi-

tions.^{16,17} Eye movement activities could have been initiated as deficiency of saccades, smooth pursuit movements, vergence, and optokinetic nystagmus have been shown to improve and even resolve with treatment.^{18,19}

Conclusion

In patients over the age of 50, vasculopathic (diabetes and hypertension) etiology is the most common cause of an isolated CN VI palsy, and monitoring until resolution is the usual treatment. If more than one cranial nerve becomes involved, further imaging and evaluation is indicated. If there is an existing cancer history, metastasis must be ruled out. Working with other health care providers to manage the underlying conditions, along with careful follow-up to treat the patient's diplopia through prism, patching, and taught behaviors can help these individuals through a potentially trying experience.

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