Complete oculomotor nerve palsy with pupillary involvement is a neuro-ophthalmologic emergency because it is commonly caused by a compressive aneurysm at the junction of the posterior communicating artery and the internal carotid artery. If left untreated, this condition can be potentially fatal within days. The present report describes a 45-year-old African American woman with human immunodeficiency virus who presented with complaint of new-onset nonspecific headache, acute onset of complete oculomotor nerve palsy, and a dilated pupil of the right eye. Results of standard work-up for aneurysm and other etiologic factors were negative. Ten days after presentation, papulovesicular eruptions occurred over the V1 and V2 dermatomes, revealing herpes zoster ophthalmicus. The present case may be the first to identify a patient with complete ophthalmoplegia with pupil involvement as a pre-eruptive manifestation of herpes zoster. The literature on epidemiology, pathogenesis, clinical presentation, diagnosis, and current treatment options for this rare form of shingles are reviewed.

**Report of Case**

A 45-year-old African American woman with human immunodeficiency virus (HIV) was admitted to the internal medicine service at Interfaith Medical Center in Brooklyn, NY. She presented with new-onset headache on the right side and complete ptosis of the right eye, for which the ophthalmology service was consulted.

The patient’s medical history was significant for HIV infection with a recent CD4 cell count of 8. She had chronic anemia, schizophrenia, and herpes zoster, and she had Whipple procedure for pancreatic cancer. She completed a review of systems and denied blurry vision, diplopia, eye pain, neck pain, fever, and paresthesia. Family, social, and surgical history were noncontributory. The patient had no known medication allergies. Her medications and dietary supplements included epoetin alfa, azithromycin, sulfamethoxazole and trimethoprim, omeprazole, olanzapine, fluconazole, and iron, multivitamins, and folic acid.

Physical examination at the bedside revealed that the patient was alert and properly oriented (ie, to person, place, and time). She was in no acute distress. Her blood pressure was 100/63 mm Hg; pulse, 80 beats per minute; respiration, 20 breaths per minute; and body temperature, 37°C.

On further examination, she had complete ptosis of the right eye (OD) with normal periorbital and facial skin appearance. No rash was present, and the left eye (OS) appeared normal. The patient had uncorrected near visual acuity (20/200 OD, 20/100 OS). The pupils were anisocoric and unequally reactive to light. In dim light, the pupils were 6 mm OD and 4 mm OS. In bright light, they were 5.5 mm OD and 2 mm OS. The reaction of the pupil OD was sluggish, whereas the pupil OS was brisk. There was no relative afferent pupilary reaction. Extraocular motility OD revealed absence of adduction, infraduction, and supraduction. Extraocular motility OS was full. Confrontational visual field appeared full in both eyes. Globes were equally soft by palpation. The irises in both eyes were...
normal. There were no cotton-wool spots or retinal hemorrhages.

Meningitis was suspected because of the patient’s initial complaint of headache and her immunodeficient status. Results from a computed tomography scan without contrast of head and orbits were normal. A lumbar puncture was performed, and analysis of cerebral spinal fluid (CSF) revealed clear fluid, no red blood cells, no white blood cells, normal glucose level (61 mg/dL), and normal gram stain and culture. Further tests for opportunistic infections were done, but results from polymerase chain reaction (PCR) of CSF for tuberculosis, cryptococcus, cytomegalovirus, and venereal disease were all negative. Blood cultures and direct antiglobulin were also normal. The complete blood cell count was nonspecific for infections, and the comprehensive metabolic profile was normal (Figure 2). However, her laboratory results revealed substantial hyponatremia.

Because of the patient’s complete oculomotor nerve palsy with pupillary involvement, further neuroimaging was required to rule out a compressive lesion. Magnetic resonance imaging of the brain with and without gadolinium dye were normal (Figure 3). Because there was no obvious compressive lesion, a magnetic resonance angiography of the brain was ordered and showed a 50% diameter reduction in the distal right and left middle cerebral arteries (Figure 4). However, no aneurysms were found. An internal right carotid cerebral angiogram (Figure 5) showed a normal right internal carotid artery, left vertebral artery, and basilar artery—the branches of which were without demonstrable aneurysm, extravasations of contrast, or mass affecting the arteries. Specifically, there was no evidence of a posterior communicating artery aneurysm.

About 10 days after the initial presentation, papulovesicular rashes broke out over the right V1 and V2 dermatomes (Figure 6). In light of the absence of compressive lesions, aneurysm, lymphoma, cardiovascular risk factors, and demyelinating process, the complete oculomotor nerve palsy with dilated pupil was likely caused by herpes zoster. With this classic clinical presentation of herpes zoster, intravenous acyclovir was recommended to the patient. She refused this treatment, so oral valacyclovir (1000 mg twice daily) was administered instead. The patient was observed for 2 additional days before discharge to an outside assisted-living psychiatric facility.

Although the patient was lost to follow-up, her prognosis for recovery from the complete ophthalmoplegia as a result of herpes zoster ophthalmicus is good. Research has shown that improvement from complete ophthalmoplegia following herpes zoster ophthalmicus can be seen within 2 months. Complete to near resolution generally occurs within 18 months.2

Discussion
Herpes zoster (shingles) results from the reactivation of dormant varicella zoster (chicken pox) mostly in thoracic and cranial sensory ganglia. This condition affects approximately 1 million people in the United States annually and causes significant morbidity. About 15% to 25% of all cases of herpes zoster involve the trigeminal nerve, also known as herpes...
thermore, patients with HIV are 15 to 25 times more likely to have herpes zoster.2-5

Pathogenesis
The varicella zoster virus is a double-stranded DNA virus that causes two distinct clinical entities: primary varicella and herpes zoster. Varicella zoster virus is transmitted via airborne and direct contact.

During primary varicella infection, the virus invades the cutaneous ends of sensory nerves and causes acute febrile exanthamous illness. It then migrates to the dorsal root ganglia of the spinal column and cranial nerve ganglia, where it becomes latent. It typically remains dormant for decades unless the immune system is compromised.6

Reactivation of the virus has been linked to patients with cell-mediated immunity. The decline of varicella antibodies occurs naturally in aging and can be induced by immunosuppressive conditions caused by illness or medication.

The reactivated virus in a sensory ganglion causes inflammation of the neuronal axons and results in shingles of the associated dermatome. Sensory nerves of the thoracic dermatomes are most commonly affected, followed by cranial nerves.

Varicella zoster infection is more severe in patients who

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**CASE REPORT**

**Complete Blood Cell Count**
- White blood cell count, 7400/μL
- Hemoglobin, 12.3 g/dL
- Hematocrit, 37%
- Platelets, 82 × 10^9/L
- Neutrophils-segmented, 84.5%
- Neutrophils-band, <10%
- Lymphocytes, 7.1%
- Monocytes, 8.2%
- Eosinophils, 0.1%
- Basophils, 0.1%

**Comprehensive Metabolic Profile**
- Sodium, 133.2 mmol/L
- Potassium, 3.78 mmol/L
- Chloride, 102.5 mmol/L
- Bicarbonate, 26.3 mmol/L
- Blood urea nitrogen, 8 mg/dL
- Creatinine, 0.7 mg/dL
- Glucose, 101 mg/dL
- Calcium, 8.7 mg/dL
- Aspartate aminotransferase, 51 U/L
- Alanine aminotransferase, 30 U/L
- Alkaline phosphate, 159 U/L
- Total bilirubin, 0.5 mg/dL
- Total protein, 6.4 g/dL
- Albumin, 2.5 g/dL
- Globulin, 3.9 g/dL
- Prothrombin time, 11.2 sec
- International normalized ratio, 0.83

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**Figure 2.** Laboratory results for a 45-year-old African American woman with human immunodeficiency virus presenting with ptosis and complaint of headache on the right side.

**Figure 3.** Axial view of the brain and orbits as shown in a magnetic resonance imaging scan without gadolinium contrast of a 45-year-old African American woman with human immunodeficiency virus. The patient presented with new-onset headache and ptosis of the right eye. The scan did not reveal any obvious compressive lesion, which was suspected to be the cause of the patient’s oculomotor nerve palsy.

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zoster ophthalmicus, of which 11% to 29% of patients present with ophthalmoplegia.2-6

**Epidemiology**
About 99% of adults with a history of chicken pox and up to 90% of those without have serology that is positive for varicella zoster.2-5 Age and immunoincompliance are the main risk factors. The lifetime risk of herpes zoster is estimated to be 10% to 20%, though patients older than 85 years have an incidence rate of 50%.2-5 Patients with immunodeficient conditions such as HIV or AIDS, cancer, or autoimmune diseases show greater prevalence of herpes zoster than the general population.
are immunosuppressed, elderly, pregnant, or neonates. The virus can cause a wide spectrum of disorders, including typical herpes zoster, recurrent herpes zoster, chronic disseminated herpes zoster, and visceral dissemination.

Several mechanisms of ophthalmoplegia as described in the present report have been postulated:

- oculomotor nerve involvement caused by inflammation of the trigeminal nerve spreading to the cavernous sinus or the superior orbital suture
- microinfarction of cranial nerves from occlusive vasculitis; suggests the presence of chronic inflammatory cells infiltrating the long posterior ciliary vessels and nerves
- meningeal inflammation at certain locations of cranial pathways
- as described in autopsies, the pattern of onset and rate of recovery point to a demyelinating process

Clinical Presentation

Herpes zoster usually evolves in three distinct stages: prodromal, acute, and chronic. Some patients may present with overlapping stages.

In the prodromal stage, the patient may experience flu-like symptoms, dysesthesia, burning, itching, tingling, boring, photophobia, or prickly or knife-like sensations in skin area of the affected dermatome. These sensory changes are believed to be the result of nerve fiber degeneration and usually precede skin eruptions from a few hours to 1 week.

The acute stage is characterized by skin eruptions. The rash progresses from erythematous macules to clusters of papules and clear vesicles within 24 hours. It then evolves into pustules within 1 week. These pustules will rupture and crust by day 10. However, the lesions heal within 4 weeks, leaving hyper- or hypopigmented scarring.
The chronic stage is most commonly manifested by postherpetic neuralgia (PHN) after the skin manifestations have resolved. This condition occurs in 9% to 34% of all zoster patients, though it affects 50% to 75% of elderly patients with herpes zoster. It is the third most common cause of neuropathic pain after low back pain and diabetic neuropathy and has been described as constant deep pain, recurrent shooting pain, and allodynia. It typically resolves within 2 months in 50% of patients and within 1 year in 70% to 80% of patients.

Herpes zoster ophthalmicus involves the ophthalmic division of the trigeminal nerve (Figure 7). The ophthalmic branch is subdivided into frontal, nasociliary, and lacrimal branches. As the nasociliary branch innervates the globe and nose, a lesion at the tip of the nose, commonly referred to as Hutchinson’s sign, is a good clinical indicator of possible ocular involvement. However, one-third of patients with ocular involvement do not have Hutchinson’s sign.

In herpes zoster ophthalmicus, numerous ocular structures can be involved:

- **Eyelids**—Resolution of skin and adnexal inflammation can leave cicatricial lagophthalmos.
- **Conjunctiva**—Chemosis and circumcorneal injection usually resolve within 1 week.
- **Episclera and Sclera**—Inflammation causes localized dilation of deep vessels and associated pain.
- **Cornea**—Inflammation causes pseudodendrites and decreases corneal sensitivity. Varicella DNA can still be detected up to 34 days after rash onset.

### Anterior chamber reaction
Uveitis occurs in response to viral antigens in the iris and ciliary body and is usually associated with increased intraocular pressure and sectoral iris atrophy. Secondary glaucoma can be caused by inflammation of the uvea and the trabecular meshwork.

### Cranial nerve
Palsy or paresis can be caused by one of the mechanisms previously discussed.

### Optic nerve
Neuritis may cause permanent visual loss.

### Retina
Aggressive posterior inflammation can lead to acute retinal necrosis or progressive outer retinal necrosis, which have guarded visual prognosis. While herpes zoster ophthalmicus is generally a localized condition, systemic involvement is more serious. Severely immunocompromised patients have a 40% risk of visceral dissemination, which can affect the liver, lungs, and brain.

### Diagnosis
Myriad clinical conditions mimic the prodromal sensations of herpes zoster ophthalmicus: trigeminal neuralgia, maxillary sinusitis, myocardial pain, and atypical facial pain. Also, acneiform eruptions, candidiasis, cellulitis, contact dermatitis, erysipelas, folliculitis, insect bites, lichen striatus, varicella, and herpes simplex may mimic the skin lesions. The key factor in the differential diagnosis of herpes zoster is that it affects a specific dermatome.

With the recognition of the common signs and symptoms, herpes zoster can be easily recognized and accurately diagnosed. Atypical presentations and other disseminated forms require diagnostic work-up to prevent potentially life-threatening complications.
threating complications. Because varicella virus is labile, viral culture has a low yield. Tzanck test, direct fluorescence assay, and PCR are more capable of detecting the virus in fluid and tissues. Furthermore, direct fluorescence assay and PCR are more specific and sensitive and allow differentiation of herpes simplex from herpes zoster.

**Treatment Options**

The goal of therapy is to limit the severity of acute and chronic pain, hasten the healing process, and reduce the chances of dissemination. Antiviral therapies in the form of acyclovir, valacyclovir hydrochloride, and famciclovir are approved by the US Food and Drug Administration for the management of herpes zoster, as follows:

- acyclovir, 800 mg orally five times daily for 7 to 10 days
- famciclovir, 500 mg orally three times daily for 7 days
- valacyclovir, 1000 mg orally three times daily for 7 days

Antiviral therapy is substantially more effective if begun within the first 72 hours of rash onset. It induces prompt resolution of skin lesions, diminishes viral shedding, lessens lesion formation, and decreases corneal and uveal involvement. All three medications are generally safe but may require dosage adjustment for patients with renal insufficiency.

The efficacy of antiviral therapy for PHN is still inconclusive. However, famciclovir and valacyclovir have proven therapeutically equal or better than acyclovir in alleviating symptoms. Generally, patients with PHN require treatment during the acute phase of herpes zoster with antivirals or tricyclic antidepressants. These medications can significantly reduce the incidence, severity, and duration of PHN. Desipramine hydrochloride and nortriptyline hydrochloride are the most commonly recommended tricyclic antidepressants for PHN. However, a full discussion of the medical treatment of PHN is beyond the scope of the present report.

A live attenuated herpes zoster vaccine for individuals older than 60 years has recently been approved by the US Food and Drug Administration. This vaccine has been shown to reduce substantially the incidence of herpes zoster by 51.3% and the occurrence of PHN by 66.5% in addition to management of herpes zoster elsewhere in the body, specific ophtalmic care is warranted because herpes zoster ophthalmicus can affect different layers and components of the eye.

**Skin, lashes, and conjunctiva**—A cool and wet compress and cleansing of the skin lesions followed by topical antibiotics (eg, neomycin, bacitracin, polymixin B) should be applied to protect the ocular surface from keratitis and conjunctivitis. Systemic steroids can be added to control significant edema and pain while oral antivirals are used. Reducing the soft tissue edema within the orbit helps prevent orbital apex syndrome, which can cause catastrophic consequences as the second, third, fourth, sixth, and ophthalmic division of the trigeminal nerves pass through the optic foramen and superior orbital fissure at the apex of the orbit.

**Cornea, sclera, and iris**—Topical steroids (eg, 0.125%-1% prednisolone) may be used between two and six times daily under the care of an ophthalmologist for the treatment of patients with keratitis, episcleritis, scleritis, or iritis. In addition, mydriatics and cycloplegics, such as cyclopentolate 1% or homatropine 5% can be added for ocular pain and photophobia control. However, topical antivirals have proven ineffective.

**Optic disk**—Prostaglandin inhibitors and pilocarpine are contraindicated in managing secondary glaucoma caused by herpes zoster because prostaglandin inhibitors induce inflammation and pilocarpine may promote synchaia. Therefore, β-blockers, α-adrenergics, and carbonic anhydrase inhibitors are the medications of choice.

**Retina**—Acute retinal necrosis requires intravenous acyclovir, foscarnet sodium, or both. Additional uses of oral famciclovir or valacyclovir accompanied by systemic steroids and anticoagulants have been used successfully to reduce intraocular inflammation, vasculopathy, and neuropathy. The suggested antiviral regimen for acute retinal necrosis is 10 to 15 mg per kilogram of body weight twice a day for 2 weeks, followed by 1 g twice a day for 4 to 6 weeks.

Laser photocoagulation is also used to prevent retinal detachment from retinal necrosis. Progressive outer retinal necrosis requires the same treatment regimen recommended for acute retinal necrosis. However, an intravitreal injection of ganciclovir sodium and laser photocoagulation may also be required to limit retinal damage.

**Conclusion**

The present case is very unusual in that a 45-year-old woman’s complete isolated unilateral oculomotor nerve palsy was a pre-eruptive stage of herpes zoster ophthalmicus. The common differential diagnoses for isolated oculomotor nerve palsies involving the pupil include a posterior communicating artery aneurysm; compressive lesion; ischemic microvascular disease, which is associated with diabetes mellitus and hypertension; tumor; or trauma. Uncal herniation, cavernous sinus mass lesions, orbital lesions, herpes zoster, and leukemia are less common causes. Onset of a oculomotor nerve palsy with pupil involvement, especially associated with pain, warrants magnetic resonance imaging, which produces high resolution images and can detect lesions smaller than 1 mm. However, because this imaging technique does not always detect small aneurysms, further testing may be needed if there is high clinical suspicion. Cerebral angiogram is still the “gold standard” for aneurysm testing.

The recovery prognosis from external ophthalmoplegia of the patient in the present report is good. Improvement from complete ophthalmoplegia following herpes zoster can be seen within 2 months, with complete to near resolution within
18 months. The patient’s sudden onset of oculomotor nerve palsy with pupillary involvement 10 days before the cutaneous eruptions suggests herpes zoster as the etiologic cause in the present case with an initial sign of pupil-involving oculomotor palsy. Oculomotor nerve ophthalmoplegia is a very rare complication of herpes zoster ophthalmicus. In 16 reported cases, ophthalmoplegia developed 2 months after herpes zoster rash occurred.2

The case described in the present report may be the first to identify a complete oculomotor nerve ophthalmoplegia with pupil involvement as a pre-eruptive manifestation of herpes zoster. Primary care physicians and neurologists must be cognizant of the initial signs and symptoms of herpes zoster ophthalmicus and refer these patients to an ophthalmologist when ocular involvement is suspected.

Acknowledgment
We thank Vincent N. Tran, BS, graphic designer at Digital Canvas, Inc, for the trigeminal dermatome graphic.

References