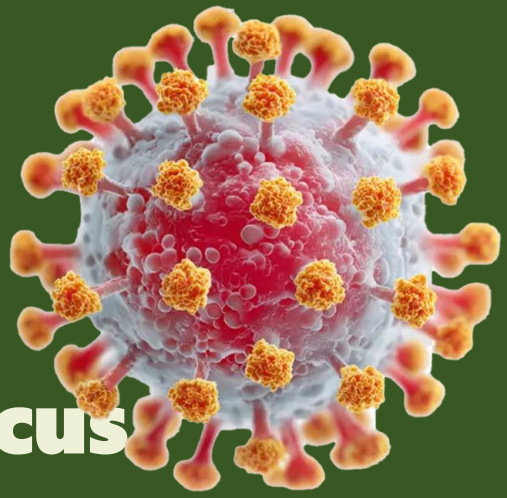


Rare complication of Herpes Zoster Ophthalmicus: orbital apex syndrome in an elderly diabetic patient

A case of Loghman Hakim Hospital

presenter : Dr. Minoosh Shabani, MD

Department of infectious disease , SBMU

A 83-year-old male with DM and HTN

presented to the infectious department of Loghman Hakim Hospital

with frozen left eye

For R/O of mucormycosis

• Dried and scabbed lesions on left frontal –to tip of nose

- Sudden loss of vision since 3 weeks ago
- Eye pain
- Ptosis
- Photophobia
- Periorbital and left frontal edema
- Nonspecific headache

PMHx

Type 2 diabetes , HTN

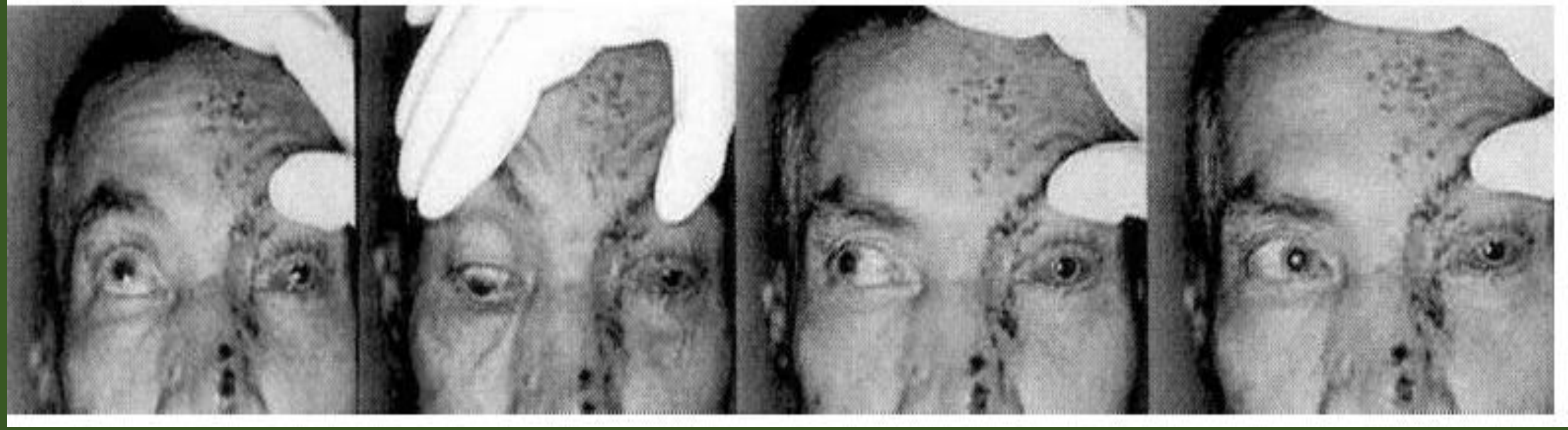
Shingles since 3 weeks ago (HZO)

Drug hx:

antidiabetic agents, losartan, valacyclovir , eye drops

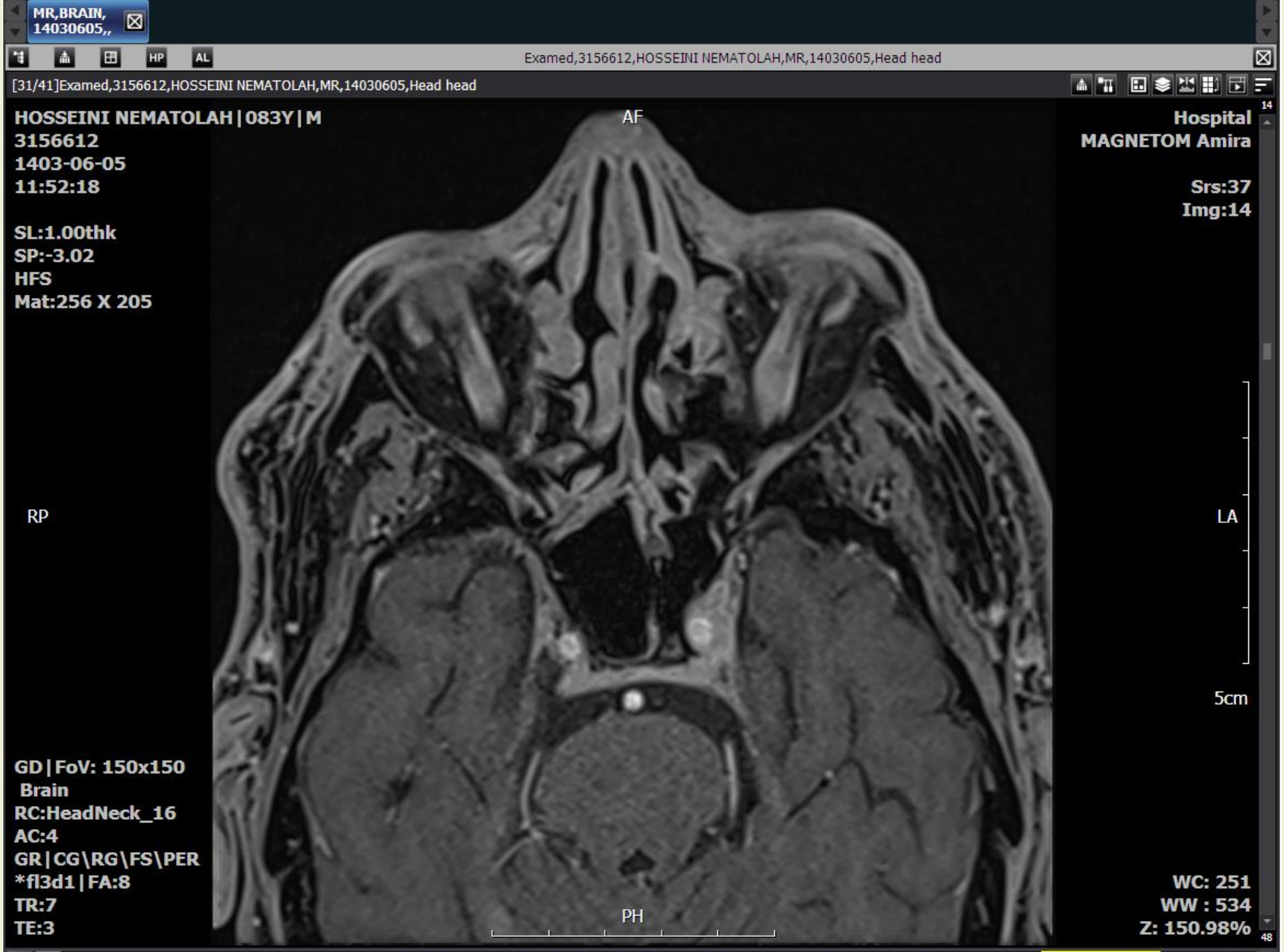
Physical exam

- Normal vital signs
- Dried and scabbed lesions were present on face
- Frozen eye
- Red eye
- Normal size pupil with Poor light reaction*
- Oral and nasal cavities were normal
- w/o anesthesia !



Ophthalmologic exam

- Visual acuity of left eye : finger count
- Keratitis
- Anterior uveitis
- Negative marcus gunn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WW : 534
Z: 150.98%
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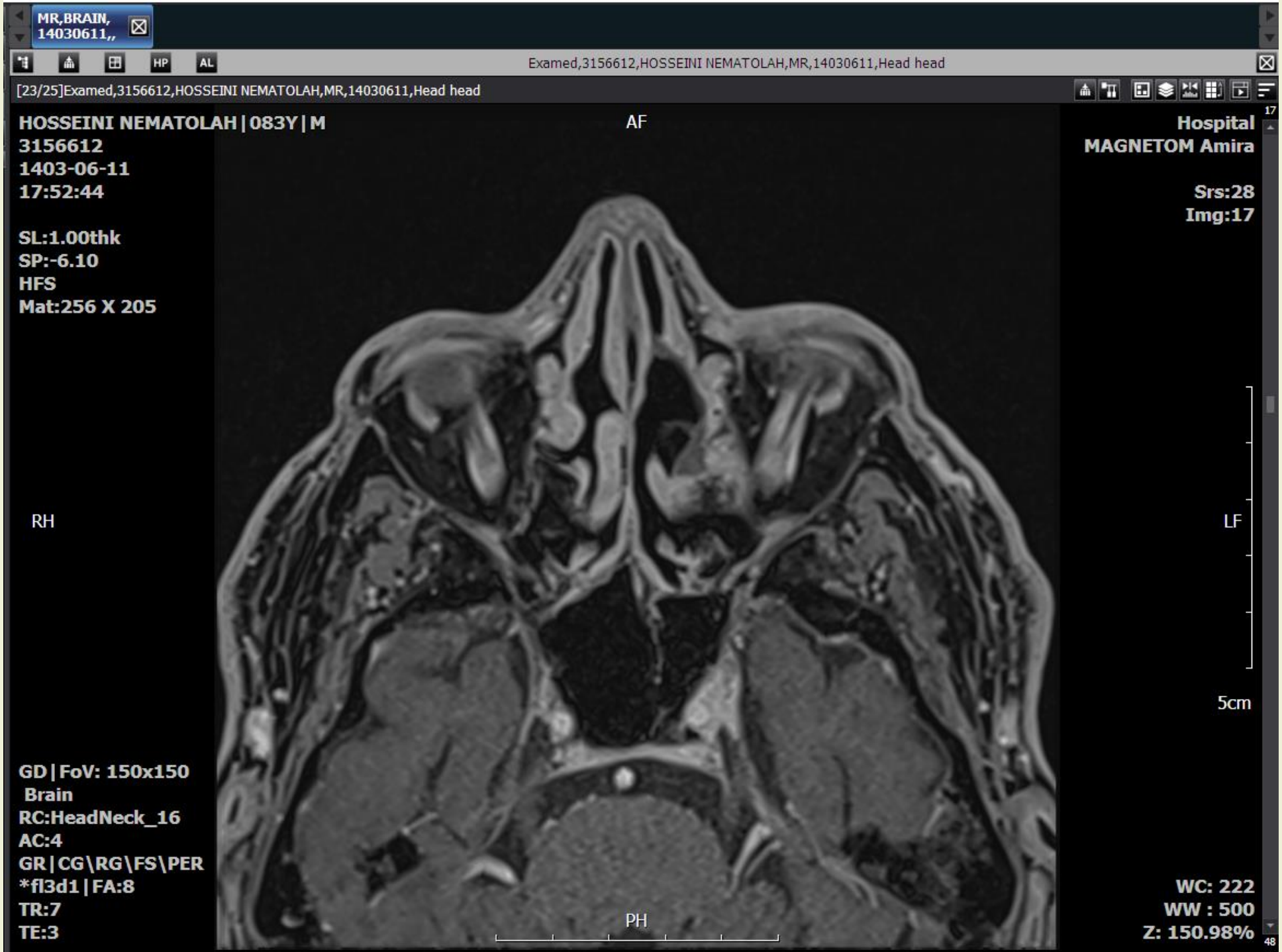
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WC: 222
WW : 500
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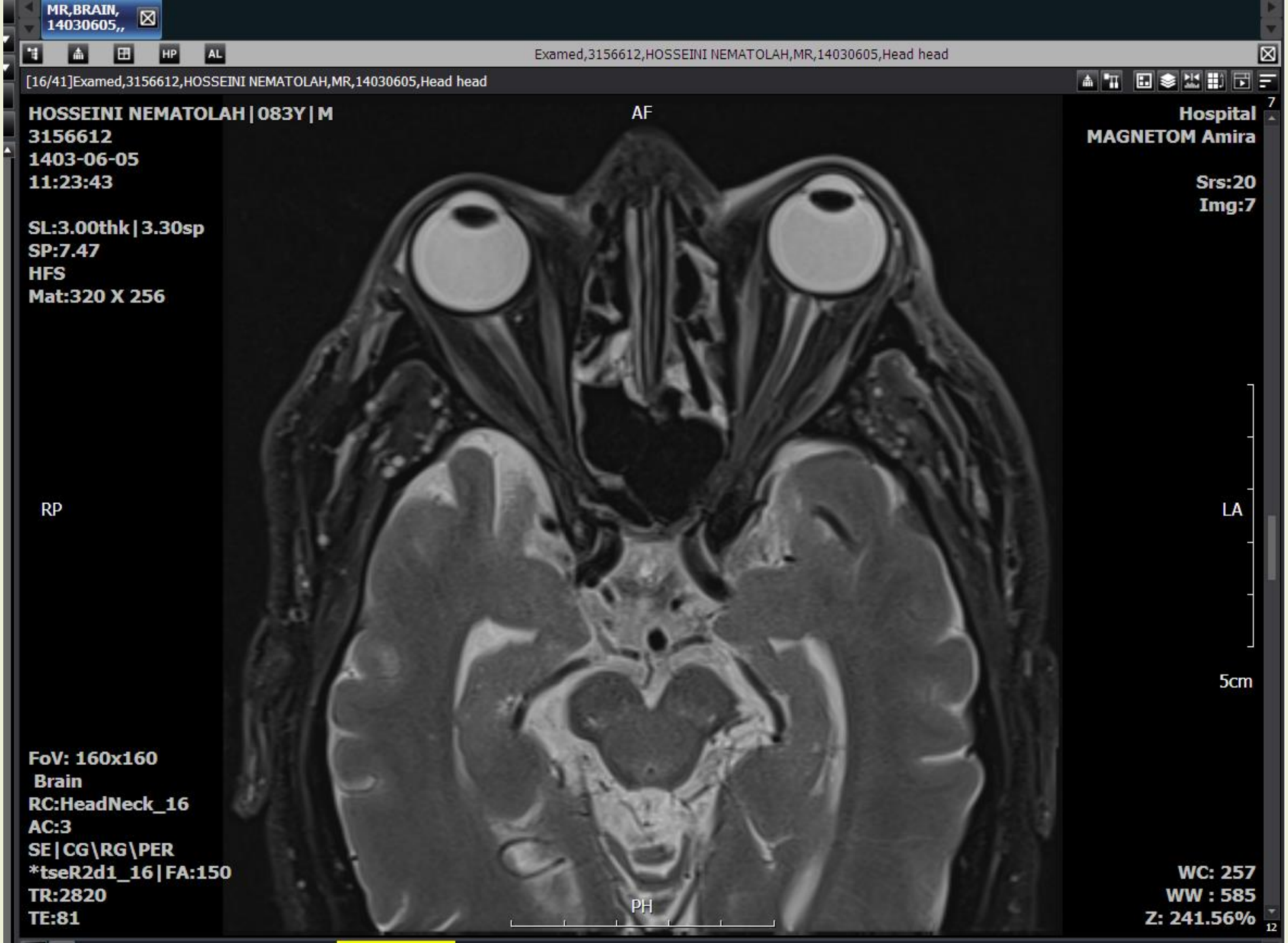
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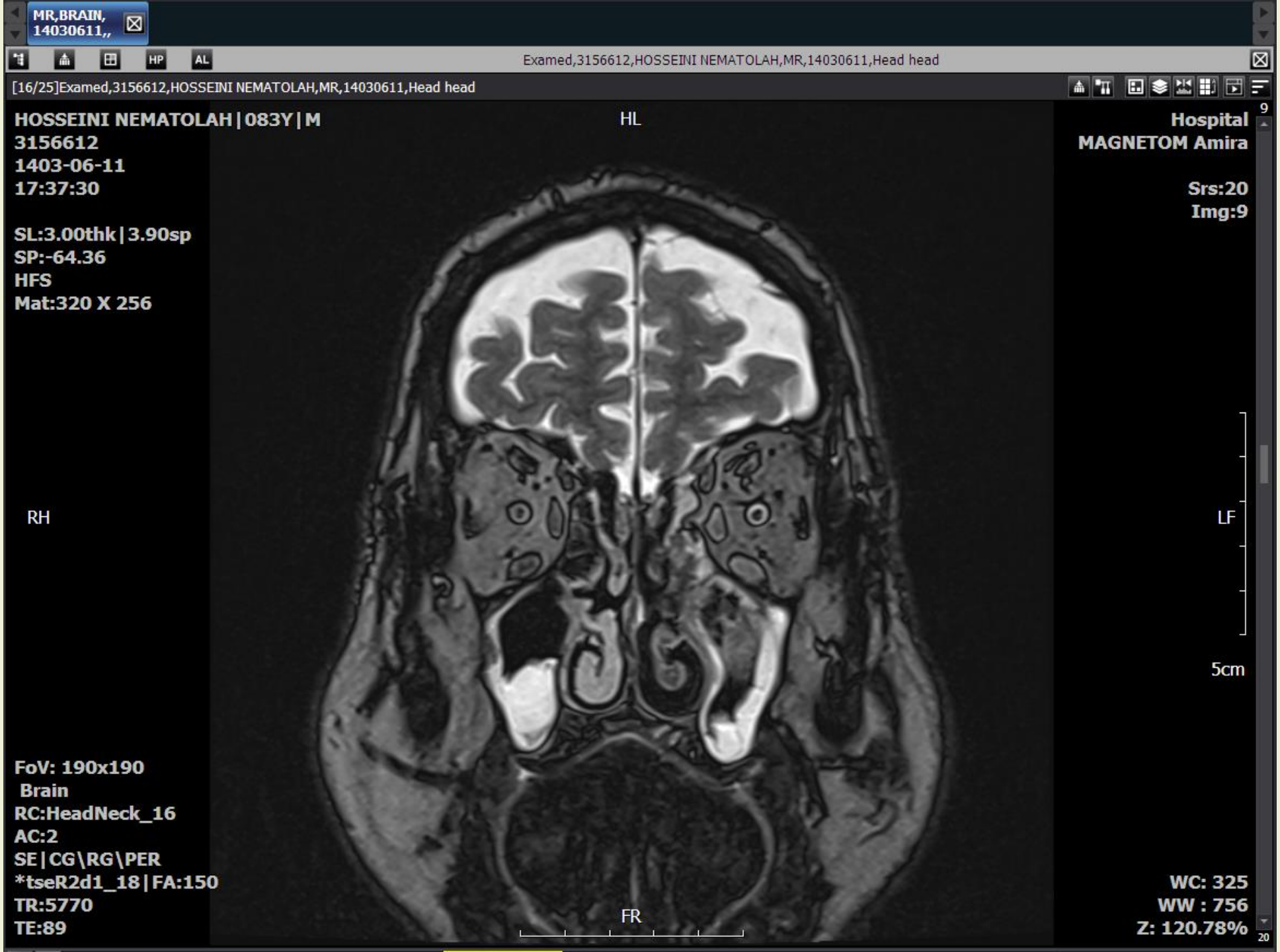
TE:81
PH
WC: 257
WW : 585
Z: 241.56%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*tseR2d1_18|FA:150
TR:5770
TE:89
WC: 325
WW : 756
Z: 120.78%

Imaging

- Brain and Orbit MRI :

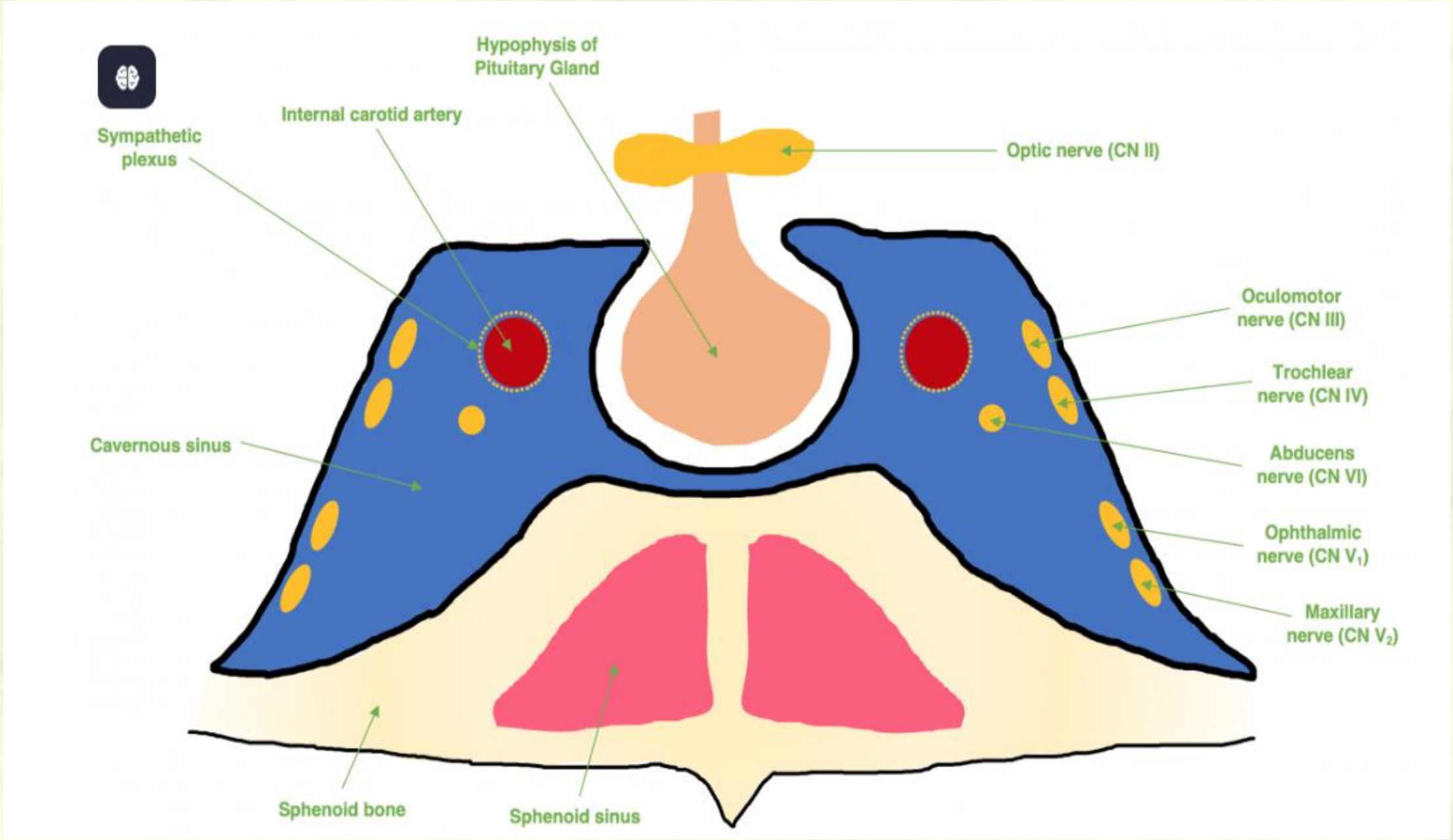
left eye rectus muscles ,cavernous sinus, trigeminal nerve enhancement

Minimal change in optic nerve

- MRA/MRV : normal

- **FESS** : ok

- **Pathology** : No fungal elements
  No granuloma
  No necrosis


Hypophysis of Pituitary Gland
Internal carotid artery
Sympathetic plexus
Optic nerve (CN II)
Oculomotor nerve (CN III)
Trochlear nerve (CN IV)
Cavernous sinus
Abducens nerve (CN VI)
Ophthalmic nerve (CN V1)
Maxillary nerve (CN V2)
Sphenoid bone
Sphenoid sinus

- Cranial palsy of III- IV- VI and first division of cranial nerve V confirm the diagnosis of OAS or SOFS !!

1- if we consider Perineuritis and myositis without intracranial involvement confirm of OAS

2- w/o optic nerve involvement confirm of SOFS

Lab data

- **CBC :** mild anemia
- **HbA1C :** 7
- **CSF :** mildly elevated protein; no pleocytosis.

- **HIV :** negative
- **Rheumatologic factors*** (R/O autoimmune dis. and GPA) **:** normal
- TFT and other lab data were normal

Interventions

- Valacyclovir continued; corticosteroid* started
- Bethametasone eye drop for Anterior segment inflammation
- Topical homatropine 2% eye drop
- Lubricant drop for keratopathy
- Also received oral pregabalin for neuralgia

- Vision improved at 2 weeks; ocular motility partially recovered; tapering steroid ongoing (during 10 days)

Follow up

- Multidisciplinary follow-up; consider repeat assessment if symptoms recur; optimize glucose control
- After 2 months fully recovered eye movements- w/o ptosis but yet blurred vision
- After one year as before

Manifestations of HZO

- *can be classified by anatomical area:*

1-Periocular region: Unilateral radicular pain and vesicular rash

2-Conjunctiva

3-Anterior segment: Episcleritis, scleritis, punctate epithelial keratitis, "pseudodendritic" keratitis, neurotrophic keratopathy

4-Uvea: Iritis, iris atrophy, iridocyclitis, and panuveitis

5-Vitreous and retina: acute retinal necrosis, ..and progressive outer retinal necrosis

6-Neuro-ophthalmological: Optic neuritis and ophthalmoplegia

- Ocular manifestations in **20–70% of HZO**, with involvement of any ocular structure
- Neurologic complications: most common PHN but cranial nerves (II-to- VII , stroke , myelitis , meningoencephalitis
- Nerve palsies in **5–3O% of HZO** although complete ophthalmoplegia is rare

Superior orbital fissure syn.

Orbital apex syndrome

Cavernous sinus syn.

OAS (orbital apex syndrome)

- Marked ophthalmoplegia and vision loss*
- There is often an afferent pupillary defect**
- Etiologies include:
    1- vascular (e.g., carotid cavernous fistula)
    2- inflammatory (e.g., giant cell arteritis, Wegener's disease)
    3- neoplastic (e.g., lymphoma, head and neck cancers)
    4- infectious***

SOFS (superior orbital fissure syndrome)

- If the infection is localized immediately anterior to the orbital apex, a "superior orbital fissure syndrome" may occur

- This syndrome has the same cranial neuropathies as orbital apex syndrome except there is no involvement of the optic nerve

(CSS) cavernous sinus syndrome

• If the infection is posterior to the orbital apex, a “cavernous sinus syndrome” may occur. This has the same cranial neuropathies as orbital apex syndrome except with the added involvement of the second division of cranial nerve V*

• because the cavernous sinus is a venous plexus that extends to the opposite side, bilateral cranial neuropathies are typical.

• The superior orbital fissure, orbital apex, and cavernous sinus are contiguous, and the etiologies are similar

• Infectious etiologies for all of these syndromes include fungi, bacteria such as *S. aureus,* streptococci including *S. anginosus (milleri),* gram-negative bacilli, syphilis, and herpes zoster.

J Neuro-Ophthalmol, Vol. 29, No. 4, 2009

Complete Unilateral Ophthalmoplegia in Herpes Zoster Ophthalmicus

Srinivasan Sanjay, MBBS, MRCS(Edin), Errol Wei'en Chan, MBBS, Lekha Gopal, MBBS, FRCS(Edin), Smita Rane Hegde, MBBS, MS(Ophthal), and Benjamin Chong-Ming Chang, MB, BCh, BAO, FRCS(Irel), FRCS(Edin), FRCOphth(Lond)

Abstract: Based on a review of 20 well-documented cases reported in the English literature between 1968 and 2008, herpes zoster ophthalmicus (HZO) may rarely be associated with complete unilateral ophthalmoplegia, defined here as impaired ocular ductions in all 4 directions within 3 months of onset of manifestations of HZO. Ophthalmoplegia occurred equally in immune-competent and immune-incompetent individuals. HZO preceded ophthalmoplegia in 75% by a mean interval of 9.5 days and a range of 2 to 60 days, occurred simultaneously with ophthalmoplegia in 20%, and followed by 2 days the onset of ophthalmoplegia in only 5%. Concurrent conjunctival inflammation, keratitis, or anterior uveitis was present in 90%. Lumbar puncture showed features of aseptic meningitis in 88%, slightly more than the 40%−50% found in patients with HZO without ophthalmoplegia. On orbit/brain imaging, abnormal enlargement of the extraocular muscles was present in 33%, and orbital soft tissue swelling was present in 17%. Enhancement of ocular motor cranial nerves was not reported. Complete or near-complete resolution of ophthalmoplegia occurred in 65% within a range of 2 weeks to 1.5 years (mean 4.4 months). A single autopsy report described granulomatous angiitis of the meninges and large vessels in the anterior cerebral circulation, as well as periaxial infarction in the optic nerve, pons, and medulla but without viral inclusion bodies or antigen. Unsettled issues are whether the pathogenesis is direct viral invasion or an immune reaction to the virus, whether the impaired ocular ductions are based on myopathic or neuropathic injury, whether there are predisposing factors to the combination of HZO and complete ophthalmoplegia, and whether treatment is effective.

Department of Ophthalmology and Visual Sciences (SS, EWC, LG, H, BC-MC), Alexandra Hospital, Singapore; Eye Clinic (SS, EWC, , SRH, BC-MC), Jurong Medical Centre, Singapore; and Department Ophthalmology (BC-MC), KK Women's and Children's Hospital,

(*J Neuro-Ophthalmol* 2009;29:325−337)

Herpes zoster ophthalmicus (HZO) refers to involvement of the ophthalmic division of the trigeminal nerve from reactivation of latent varicella zoster virus (VZV) harbored in the trigeminal sensory ganglion. It is characterized by an acute dermatomal eruption that evolves through papular, vesiculobullous, pustular, and crusting stages over days to 3 weeks. The zoster rash is often accompanied by periocular pain and neurosensory disturbances in the first trigeminal division.

Ocular manifestations are observed in 20%−70% of patients with HZO, with involvement of every ocular structure (1). Postherpetic neuralgia is the most common neurologic sequela, but other neurologic complications, including cranial nerve palsies, stroke, myelitis, meningoencephalitis, and polyneuropathy, have also been reported (1,2).

Ocular motor cranial nerve palsies are reported in 5%−31% of patients, but the occurrence of complete unilateral ophthalmoplegia, defined here as concurrent unilateral impairment of ocular ductions in all directions, is rarer (2,3). In 1948, Edgerton (3) summarized 40 cases of unilateral ophthalmoplegia associated with HZO reported up to 1940. A review by Chang-Godinich et al (4) in 1997 included 16 cases reported from 1968 to 1997 and provided a comprehensive evaluation of this condition. However, that review did not include cases reported between 1948 and 1968 or 2 cases (5,6) reported much later with unusual clinical features. In addition, some of the reports included (7,9−11) contained very brief clinical information on the presentation, outcomes, and underlying systemic diseases, limiting a discussion on these aspects of this condition.

In this review the risk and prognostic factors, diagnostic utility of lumbar puncture and neuroimaging

- A literature search was conducted on articles published in the last 60 years
- In this review the risk and prognostic factors, diagnostic utility of lumbar puncture and neuroimaging studies, efficacy of different treatment modalities, and the pathophysiologic basis of this condition in the light of recent neuroimaging findings be addressed

- There were 9 men and 11 women
- Nine patients were receiving medical immunosuppression*
- **Most patients (55%) had not received treatment before the onset of ophthalmoplegia**.

- HZO preceded the onset of ophthalmoplegia in 15 patients

- anterior segment involvement in 18 patients
- Posterior segment in 4 patients

- optic neuropathy in the context of an orbital apex syndrome in 4 patients (20%)

- An ipsilateral lower motor neuron facial nerve palsy in 1 patient
- meningitis or encephalitis in 5 patients

Therapy was initiated in 18 patients

- 3 patients with acyclovir
- 2 patients with systemic corticosteroids
- 13 patients with a combination of acyclovir (or valacyclovir) and systemic corticosteroids

- At the end of the follow-up period, complete or near-complete resolution of ophthalmoplegia was observed in 13 patients (65%) , the time interval to resolution having a range of 2 weeks to 1.5 years

In the remaining patients its outcome could not be determined because of inadequate documentation

- Based on this review, one cannot determine whether the clinical outcome was influenced by treatment.

- Because the number of cases with complete unilateral ophthalmoplegia is small, meaningful conclusions is difficult to stablish

PATHOPHYSIOLOGY

1- Perivascular and perineural inflammation

2- Cytopathic damage to the virus to neural tissue and direct spread* of HZV

3- Cranial nerve compression: Caused by edema of the orbital soft tissue

4- Microinfarct of the cranial nerves

Journal of Neuro-Ophthalmology

The Official Journal of the North American Neuro-Ophthalmology Society

ORIGINAL CONTRIBUTION

Orbital Apex Syndrome Secondary to Herpes Zoster Ophthalmicus

Verhaeghe, Florent MD; Villain, Max MD, PhD; Labauge, Pierre MD, PhD; Daien, Vincent MD, PhD

Author Information

Journal of Neuro-Ophthalmology 36(2):p 147-151, June 2016. | **DOI:** 10.1097/WNO.0000000000000349

Abstract

- a literature for articles from 1966 to August 2015
- We added our case to 14 other published reports of OAS due to HZO

- The mean age : 68 years - women [73%]
- The risk of OAS increased with immunosuppressive disease or therapy*
- CSF was documented in 4 cases, revealing lymphocytic meningitis
- Although a search for VZV-DNA by PCR may be done with CSF analysis, the diagnosis of OAS due to HZO is primarily based on clinical findings
- All reported patients were treated with systemic acyclovir and steroids except 2 cases

Treatment duration is empiric and patients are commonly on antivirals and steroids for 2–6 months, depending on clinical recovery

More than half of the patients (n = 9, 60.0%) showed partially recovered visual acuity, but complete resolution was rare (n = 4)

May 2025

REVIEW

Treatment Efficacy in Herpes Zoster Ophthalmoplegia: A Systematic Review and Meta-Analysis of Case Reports and Series

Mansoor Shahriari[1,2] | Sadra Ashrafi[1] | Seyyed Morteza Hosseini Imeni[1,2] | Saeed Mohammad Soleymani[2,3] | Hadi Esmaily[2,3]

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Keywords: antiviral agents | herpes zoster ophthalmicus | steroids | Varicella zoster virus

ABSTRACT

Varicella zoster virus (VZV) causes herpes zoster ophthalmicus (HZO), a disease resulting from VZV reactivation in the eye branch of the trigeminal nerve, primarily affecting the elderly or immunocompromised. Current research on the relative prevalence of ocular HZO is limited to case series and reports. This study aims to conduct a systematic review and meta-analysis comparing the effects of antiviral drugs, corticosteroids, and their combination in published cases of ophthalmoplegic HZO. We reviewed the Scopus, PubMed, and Google Scholar databases for HZO-related studies, analysing all case reports and case series interventional studies. Our initial search yielded 14,100 articles, with 92 articles encompassing 111 patients included in the final analysis. Steroid treatment showed a greater improvement in visual score compared to antiviral treatment (β = 0.80, 95% CI = 0.10, 1.50 = 1.10, p = 0.024). We found no significant relationship between treatment type and extraocular movement improvement ($p > 0.05$). While corticosteroid administration timing did not correlate with extraocular movement improvement (p = 0.108), increased acyclovir duration was associated with 3.64 times higher odds of improvement (OR = 3.64, 95% CI = 1.004, 13.23, p = 0.049). Patients with myositis had 19.42 times higher odds of skin involvement after orbital symptoms compared to those with orbital apex syndrome (OAS) (OR = 19.42, 95% CI = 1.16, 325.05, p = 0.039). Our findings suggest corticosteroid treatment may be more effective for visual outcomes than antiviral drugs or combination therapy. Additionally, longer antiviral therapy duration is linked to better extraocular motor outcomes. Most ophthalmoplegic HZO patients exhibited signs of aseptic meningitis in cerebrospinal fluid (CSF) examinations.

1 | Introduction

Varicella-zoster virus (VZV), a double-stranded DNA virus, causes herpes zoster ophthalmicus (HZO). HZO results from VZV reactivation of the ophthalmic division of the trigeminal

patients, that is, HIV patients [4, 5]. The risk of reactivation of VZV is greatest at 80 years of age. The additional risk factors include organ or hemopoietic stem cell transplantation, cancer (including haematologic malignancy), chemotherapy, moderate immune suppression especially from antirheumatic drugs

- 14,100 articles, including all case report and series

- - We **found no significant relationship between treatment type and extraocular movement improvement**
- While corticosteroid administration timing did not correlate with extraocular movement improvement (*p* = 0.108**), increased acyclovir duration** was associated with 3.64 times higher odds of improvement

- corticosteroid treatment may be more effective for visual outcomes than antiviral drugs or combination therapy
- Additionally, longer antiviral therapy duration is linked to better extraocular motor outcomes

OAS may be due to immunoreactions against inactive or replicating viral antigens, nerve damage, direct cytopathic effects of the virus, ischemia due to occlusive vasculitis, or most likely from a combination of these factors

Thanks for your attention