

ARROCase

Orbital MALT

Stephen Rosenberg, MD

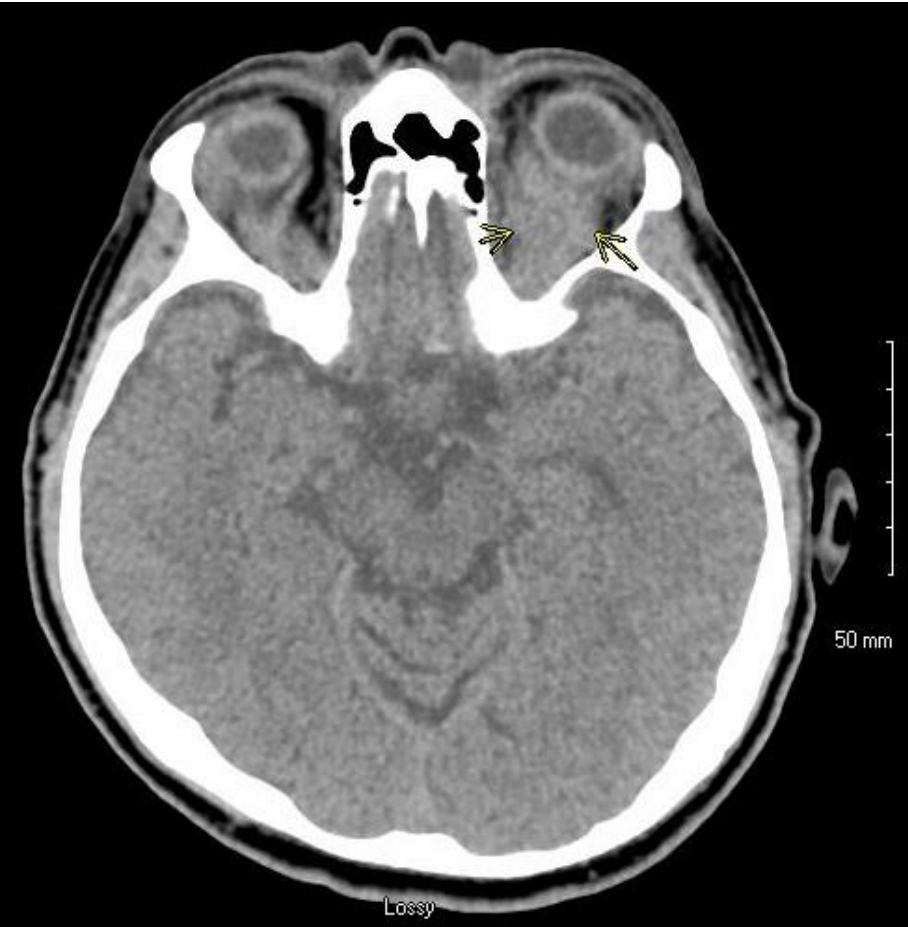
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History

- 56 year old gentlemen with a history of ESRD secondary to hypertensive nephropathy. Recently transplant rejection and dialysis dependent admitted to UW secondary to AMS and fever.
- **CT scan of the head during work up showed homogenous left orbital soft tissue mass associated with left proptosis. Subtle similar findings in the right orbit. Bilateral preseptal soft tissue thickening involving the eyelids.**
- Subsequently seen by Ophthalmology who indicated that corrected vision 20/25 R eye and 20/30 L eye. +2 diffuse injection of the left eye. No abnormalities on dilated fundoscopic exam.

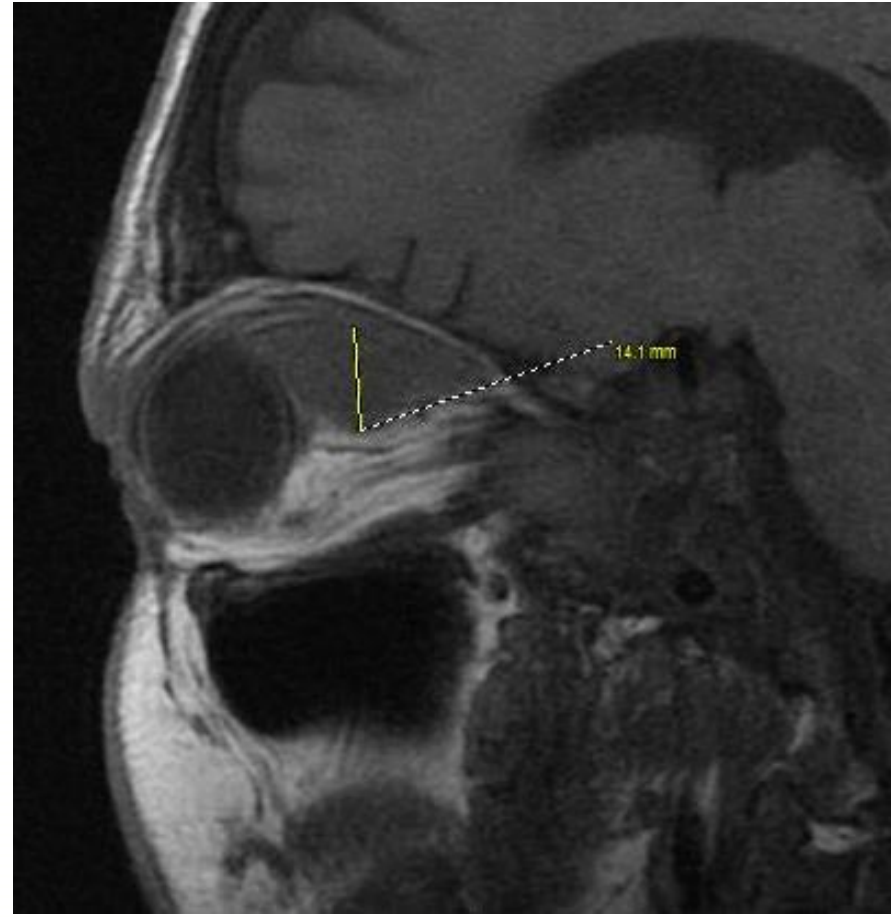
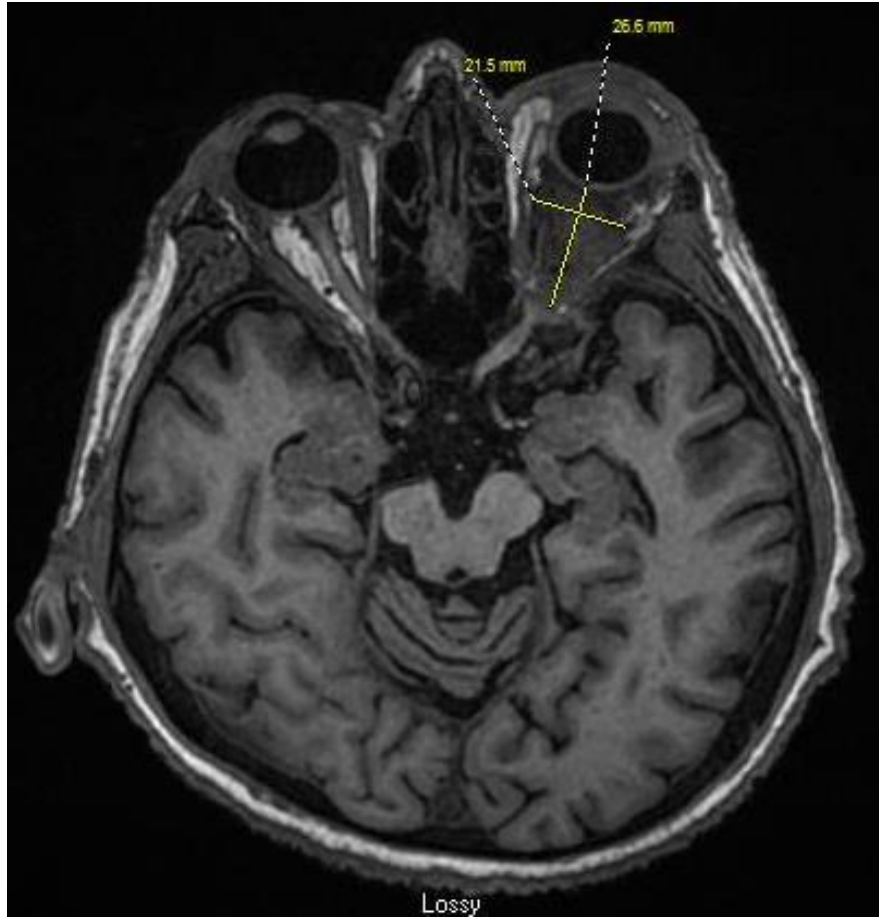
Imaging



History

- Patient's AMS improved during hospitalization secondary to adjustment of home opiate & benzodiazepines.
- Fever work up was unremarkable, including blood cultures. Antibiotics discontinued.
- **MRI of the Orbits revealed infiltrative bilateral soft tissue masses involving the left greater than right orbits with abnormal infiltration and thickening of the preseptal soft tissues/conjunctiva.**

Imaging



History

PMH: ESRD, Rheumatic Fever, Acute rejection of kidney transplant, Hydronephrosis, Neutropenia, Pericardial effusion, Community-acquired pneumonia, GERD, Hypothyroidism, Depression, Anxiety, Valve with AV fistula infection, Secondary hyperparathyroidism, Hypertension

PSH: Renal transplant, Renal Biopsy, Knee arthroscopy, Cystoscopy, Parathyroidectomy

ROS: He denies any diplopia or blurry vision. He has noticed keratoconjunctivitis sicca. Additionally, he notes pruritus in the left eye for at least 5 to 6 months. No headaches, chest pain, or other systemic symptoms.

Family History: No history of malignancy

Medications: Tylenol, Atenolol, Calcitriol, Calcium carbonate, Klonopin, Lunesta, Heparin, Fosrenol, Synthroid, MTV, Zoloft

Differential Diagnosis

- Lymphoma
- Lymphoproliferative disease (including post transplant disorder in this patient)
- Idiopathic orbital inflammatory disease
- Cellulitis
- Metastatic disease
- Vascular or lymphatic malformation
- Sarcoidosis
- Granulomatosis with polyangiitis

History (continued)

- A left extensive superior and posterior orbitotomy with biopsy of the posterior orbital mass and orbital fat was performed.
- Pathology consistent **with low-grade B-cell lymphoma**, most consistent with a **marginal zone lymphoma**.
- Patient underwent complete systemic staging with a CT chest, abdomen, and pelvis which showed no metastatic disease.
- No significant elevation in Chlamydia psittaci antibodies.

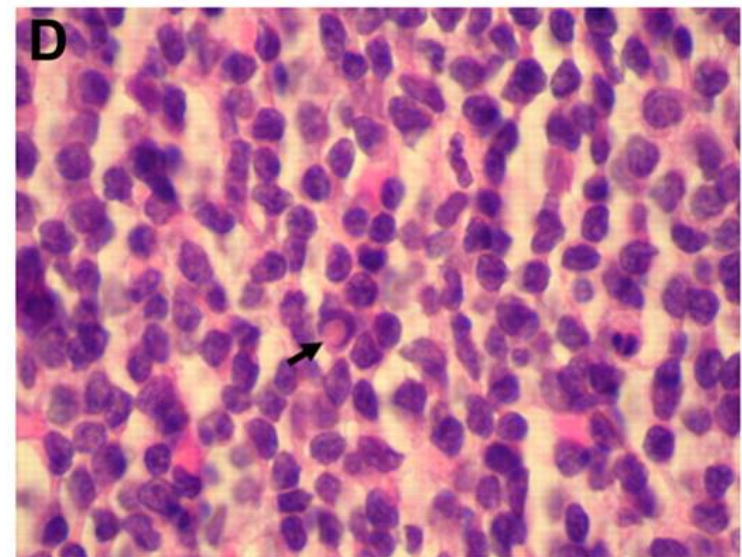
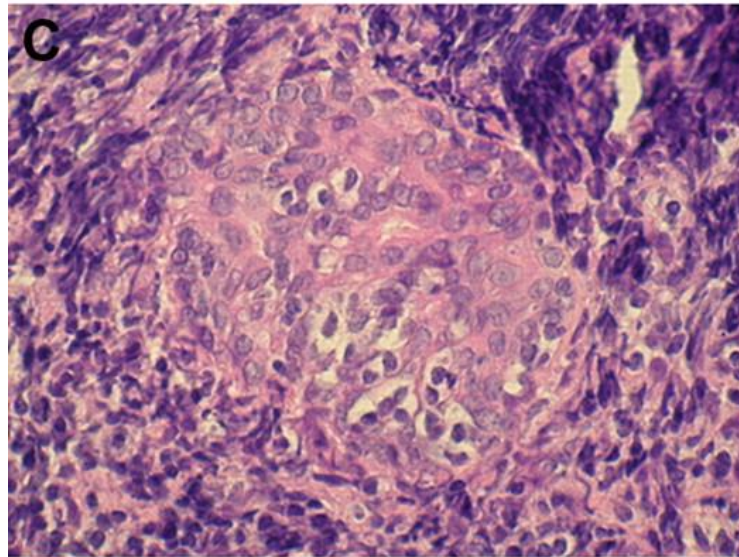
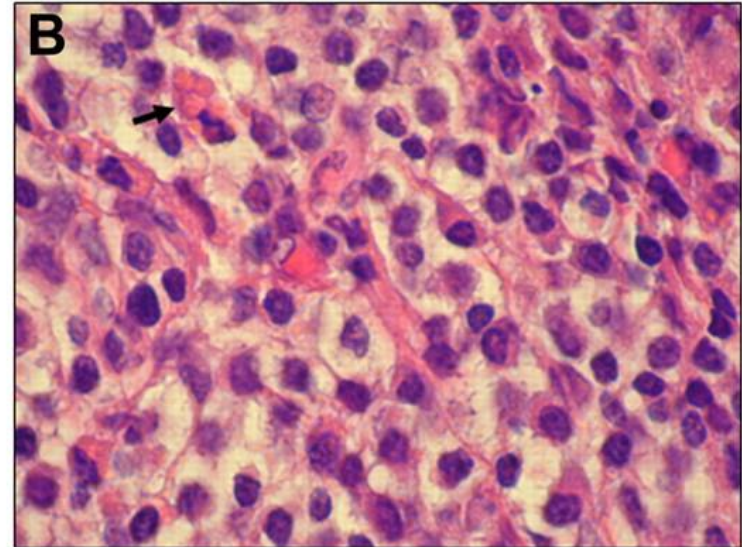
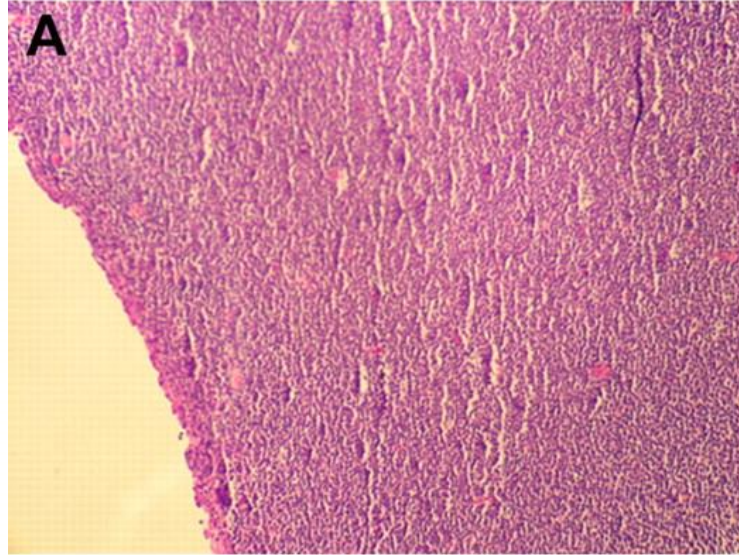
Mucosa Associated Lymphoid Tissue (MALT) Lymphoma

- MALT lymphomas are often secondary to chronic inflammation (autoimmune or infectious etiology).
- The most common locations for MALT Lymphomas are the GI tract (stomach>small intestine>colon). Other locations include: lung, thyroid, salivary gland, tonsil, breast, or **orbit**.
- MALT lymphomas **typically arise from the marginal zone** of lymphoid follicle.
- Typically these malignancies are low grade B-cell lymphomas that are **CD20+, CD35+, CD5-, and CD10-**.

Orbital/Ocular Adnexal Lymphoma

- Lymphomas are the most frequent tumor of the ocular adnexa.
- Ocular Lymphomas:
 - 1) Marginal Zone Lymphoma of MALT (~40-80%)
 - 2) Follicular Lymphoma (~20%)
 - 3) Diffuse Large B-Cell Lymphoma (~8%)
 - 4) Mantle cell, small lymphocytic, lymphoplasmacytic (these are less common)
- **t(11;18)(q21;q21) is seen in 15-40% of patients with Orbital MALT.** Fusing *API2* (apoptosis inhibitor 2) gene on chromosome 11 and the *MALT1* gene on chromosome 18.

Pathology



Stefanovic A. and Lossos I. Blood 2009;114:501-510

Orbital MALT

- Patients often present between 5th – 7th decade
- Female predominance (1.5-2.0:1.0).
- **10-15% of patients present with bilateral orbital disease.**
- Most frequent sites: Orbit (40%), Conjunctiva (35-40%), Lacrimal gland (10-15%), and Eyelid.
- ***Chlamydia psittaci*** identified in **~25% of orbital MALT** on meta-analysis.
- *Chlamydia psittaci* association with orbital MALT lymphoma **varies by region:**
 - Common in Italy, Austria, Germany, and parts of the US

Husain., et. al. Cancer 2007; 110:809-815

Ferreri., et. al. JCO 2012; 30(24):2988-2994

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Patient Presentation

- Patients with Orbital MALT often present with 1 or more of the following:
 - Proptosis
 - Orbital lesion (salmon-colored conjunctival mass)
 - Pain (vitritis/uveitis)
 - Blurred vision
 - Floaters

Work-up and Evaluation

- Physical exam including ophthalmologic exam (fundoscopy, slit lamp exam).
- Lab work: CBC, LFTs, ESR, BM biopsy, Chlamydia psittaci antibodies/PCR, CSF as clinically indicated.
- Imaging: MRI Brain/Orbits, CT C/A/P or PET/CT.

Staging

- Ann Arbor Staging System:
 - Stage I: Localized to 1 eye
 - Stage II: Cancer within two separate regions (same side of the diaphragm)
 - Stage III: Disease on both sides of the diaphragm
 - Stage IV: Diffuse or disseminated involvement in ≥ 1 extralymphatic organ (i.e. bone marrow, liver).
- E: Extralymphatic organ or site

Case Management

- May consider trial of medical treatment if positive for *Chlamydia psittaci* infection.
 - Would not pursue medical management if symptomatic (i.e. visual changes)
 - 100 mg Doxycycline BID for 3 weeks
 - Response assessment 3-4 weeks after treatment
- Radiation therapy considered definitive therapy.
 - Definitive radiation treatment is 24-30 Gy
 - 2 Gy x 2 fractions shows good response (CR=85%), consider in palliative setting

Radiation Therapy Approaches

- Partial Orbit vs. Whole Orbit:
 - Higher rates of local failure with partial orbit irradiation (33% vs. 0%)
- Typically CTV includes all of orbital bony borders in addition to any extra-orbital disease.
- PTV expansion is 3-5 mm.
- If disease confined to conjunctiva/eyelid may consider sparing rest of orbit.
- IMRT or Superior/Inferior Wedge pair to spare contralateral orbit.
- Doses: 24-25 Gy at 1.5-2.0 Gy/fraction.
 - **Small fraction size important to minimize toxicity.**

Kaushik., et al. Int J Radiation Oncol Biol Phys. 2012. 84(5): 1145-1150

Tran., et al. Leukemia & Lymphoma. 2013. 54(3): 491-496

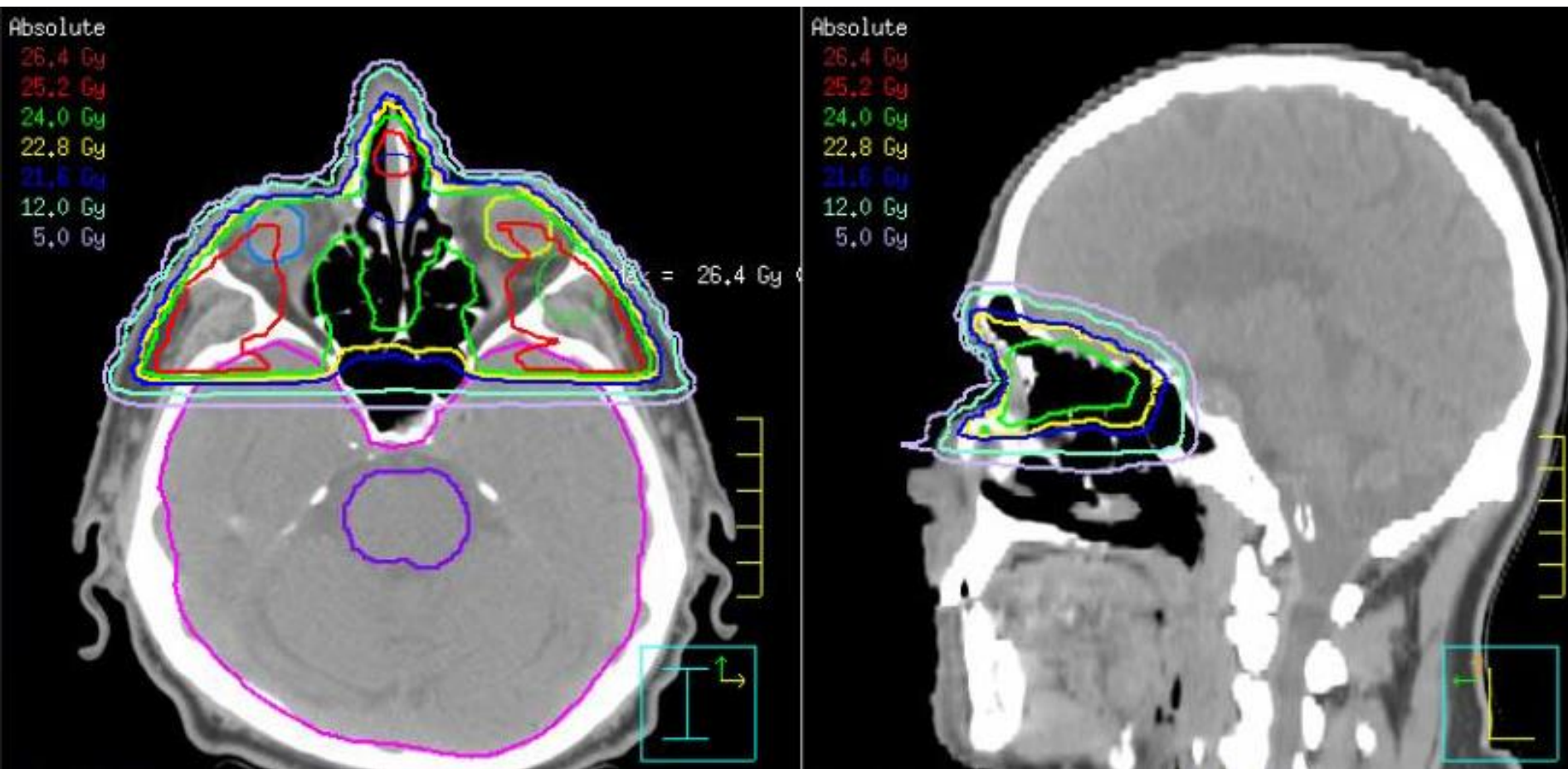
Pfeffer., et al. Int J Radiation Oncol Biol Phys. 2004. 60(2): 527-530

Yahalom., et al. Int J Radiation Oncol Biol Phys. 2015. 92(1): 11-21

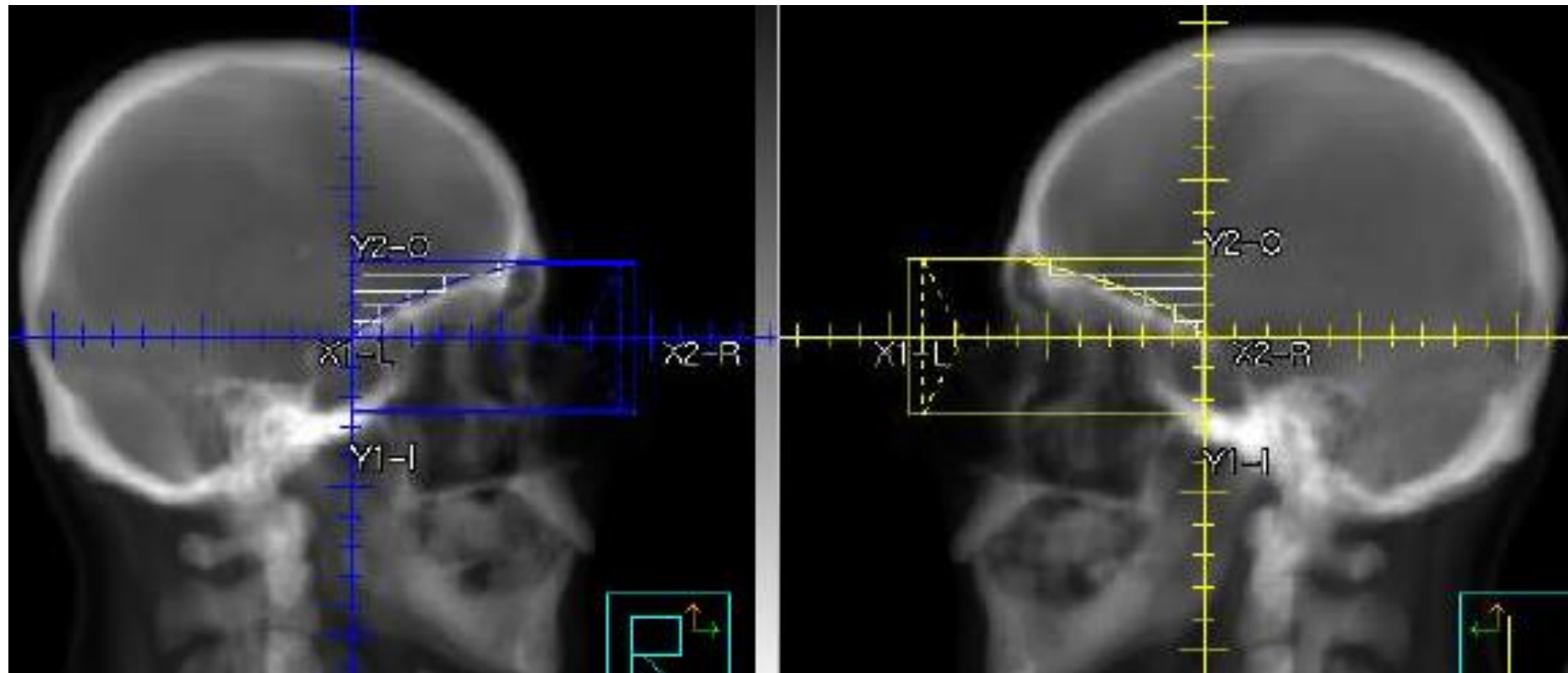
Case Management

- Patient with Stage IIE Orbital MALT with negative *C. psittaci* work up.
- Primary radiotherapy was recommended to bilateral orbits.
 - CT SIM: Facemask in neutral position with 2.5 mm slices
 - Prescribed 24 Gy at 2 Gy/fraction
 - Radiation delivered with opposed lateral 6 MV beams to cover both orbits
 - Beams half beam blocked posteriorly

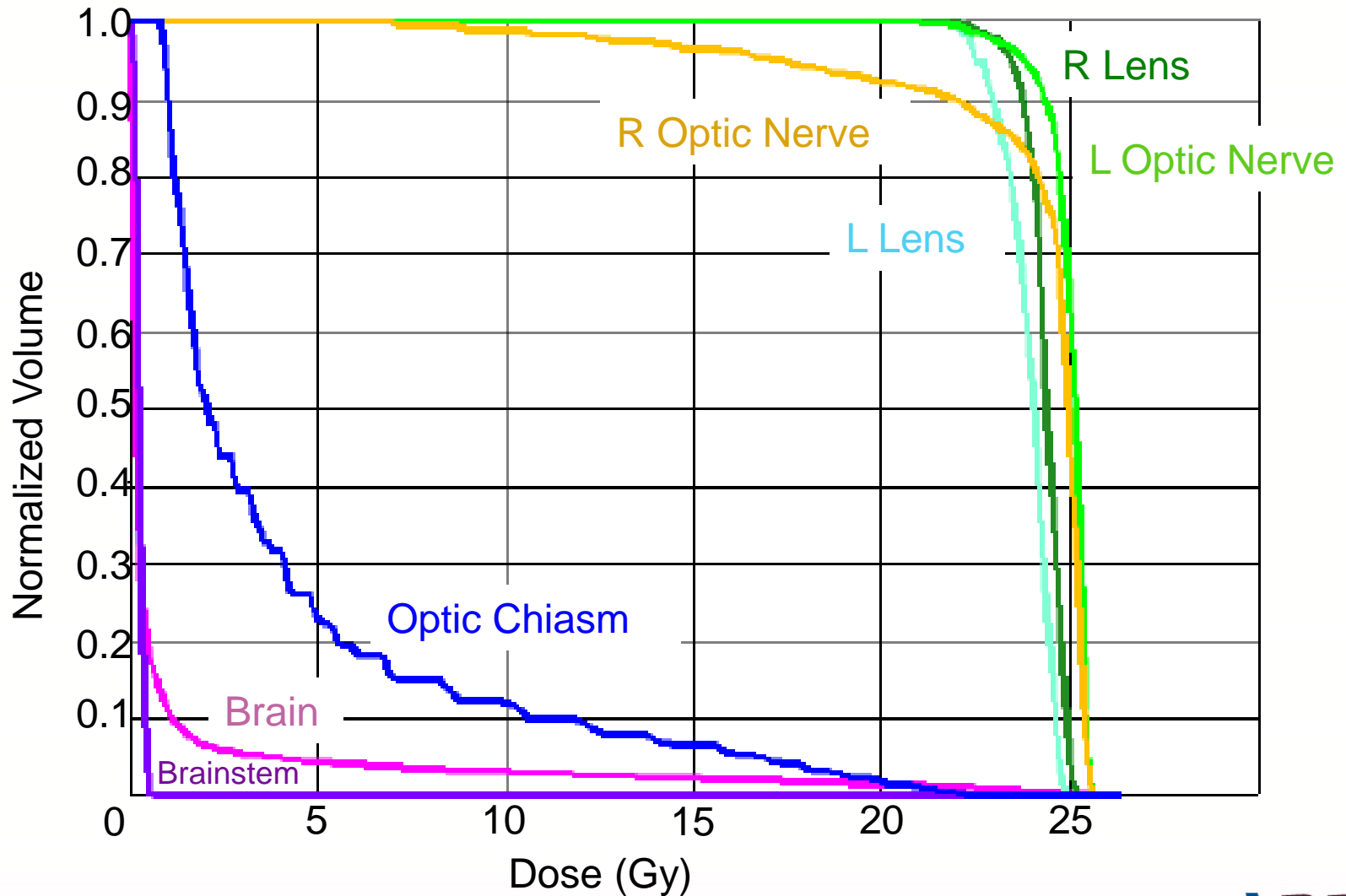
Radiation Therapy: Bilateral Orbits



Radiation Therapy: Bilateral Orbits



Dose Volume Histogram OAR



Prognosis

- 85-100% local control rate with radiotherapy
- Distant failure rates vary from 20 -50% usually involving other MALT tissues with indolent behavior and prolonged survival
- Primary Site correlates with risk for systemic involvement:
 - Conjunctival (lowest risk)
 - Eyelid (Highest risk)

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Side Effects of Treatment

- Acute toxicity:
 - Conjunctival reactions (erythema/irritation)
- Long-term complications (~50% of patients):
 - Cataract formation (30-50%)
 - Xerophthalmia (20-40%)
- RT doses >36 Gy associated with significant more toxicity
 - Ischemic retinopathy
 - Corneal ulceration
 - Optic atrophy
 - Neovascular glaucoma
 - Risk of vision loss

References

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