Diagnostic Neuroimaging in Neuro-Ophthalmology

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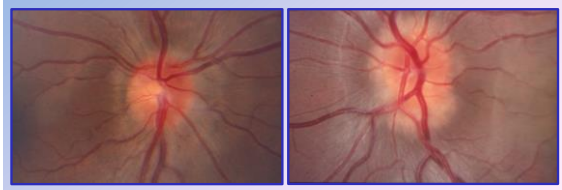
American Society of Neuroimaging
38th Annual Meeting

DISCLOSURES

Nothing to disclose!



Papilledema | **Pseudopapilledema: buried ONHD**

Aim of Today's Lecture

1. **Focus on N-Oph dz where neuroimaging recently advanced our understanding of underlying pathophysiology, diagnosis and treatment**
2. **Emphasize, how imaging helps N-Oph and Neuro-Oph helps imaging in differential diagnosis**

- **We will discuss:**
- Pseudotumor Cerebri Syndrome (PTCS)
- Intracranial hypotension
- Leptomeningeal disease
- Optic neuritis (ON)

PTC syndrome: Diagnostic criterias, Recent revision

1. **Dandy** WE. Intracranial pressure without brain tumor: diagnosis and treatment. Ann Surg **1937**;106:492–513.
2. Smith JL. Whence pseudotumor cerebri? J Clin Neuroophthalmol **1985**;5:55–56.
3. Friedman DI, Jacobson DM. Diagnostic criteria for idiopathic intracranial hypertension. Neurology **2002**;59:1492–1495.
4. **Friedman** DI et al. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology. **2013** Sep 24;81(13):1159-65.

Definitions

Table 1 Pseudotumor cerebri syndrome

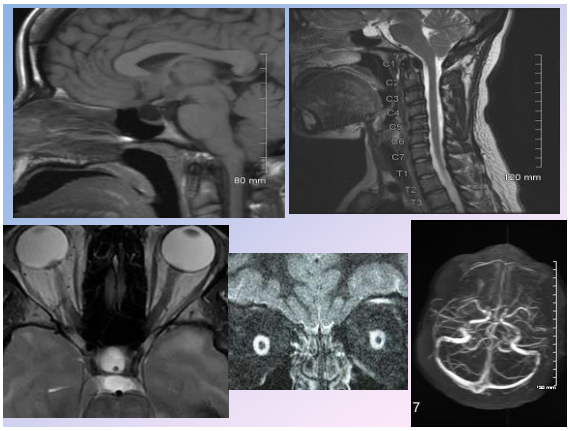
Primary pseudotumor cerebri	
Idiopathic intracranial hypertension	
Includes patients with obesity, recent weight gain, polycystic ovarian syndrome, and thin children	
Secondary pseudotumor cerebri	
Cerebral venous abnormalities	
Cerebral venous sinus thrombosis	
Bilateral jugular vein thrombosis or surgical ligation	
Middle ear or mastoid infection	
Increased right heart pressure	
Superior vena cava syndrome	R
Arteriovenous fistulas	I
Decreased CSF absorption from previous intracranial infection or subarachnoid hemorrhage	S
Hypercoagulable states	K
Medications and exposures	
Antibiotics	
Tetracycline, minocycline, doxycycline, nalidixic acid, sulfa drugs	
Vitamin A and retinoids	F
Hypervitaminosis A, isotretinoin, all-trans retinoic acid for promyelocytic leukemia, excessive liver ingestion	A
Hormones	C
Human growth hormone, thyroxine (in children), leuprorelin acetate, levonorgestrel (Norplant system), anabolic steroids	T
Withdrawal from chronic corticosteroids	O
Lithium	R
Chlordecone	S
Medical conditions	
Endocrine disorders	
Addison disease	
Hypoparathyroidism	
Hypercapnia	
Sleep apnea	
Pickwickian syndrome	
Anemia	
Renal failure	
Turner syndrome	
Down syndrome	

Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Friedman DI, Liu GT, Digre KB. Neurology. 2013 Sep 24;81(13):1159-65.

Table 2 Diagnostic criteria for pseudotumor cerebri syndrome

1. Required for diagnosis of pseudotumor cerebri syndrome[a]
A. Papilledema
B. Normal neurologic examination except for cranial nerve abnormalities
C. Neuroimaging: Normal brain parenchyma without evidence of hydrocephalus, mass, or structural lesion and no abnormal meningeal enhancement on MRI, with and without gadolinium, for typical patients (female and obese), and MRI, with and without gadolinium, and magnetic resonance venography for others; if MRI is unavailable or contraindicated, contrast-enhanced CT may be used
D. Normal CSF composition
E. Elevated lumbar puncture opening pressure (≥250 mm CSF in adults and ≥280 mm CSF in children [250 mm CSF if the child is not sedated and not obese]) in a properly performed lumbar puncture
2. Diagnosis of pseudotumor cerebri syndrome without papilledema
In the absence of papilledema, a diagnosis of pseudotumor cerebri syndrome can be made if B-E from above are satisfied, and in addition the patient has a unilateral or bilateral abducens nerve palsy
In the absence of papilledema or sixth nerve palsy, a diagnosis of pseudotumor cerebri syndrome can be suggested but not made if B-E from above are satisfied, and in addition at least 3 of the following neuroimaging criteria are satisfied:
i. Empty sella
ii. Flattening of the posterior aspect of the globe
iii. Distention of the perioptic subarachnoid space with or without a tortuous optic nerve
iv. Transverse venous sinus stenosis

[a] A diagnosis of pseudotumor cerebri syndrome is definite if the patient fulfills criteria A-E. The diagnosis is considered probable if criteria A-D are met but the measured CSF pressure is lower than specified for a definite diagnosis.



Other neuroimaging findings in PTCS

- **Primary spontaneous cerebrospinal fluid leaks** and idiopathic intracranial hypertension Pérez MA et al. Newman NJ. J Neuroophthalmol. 2013 Dec;33(4):330-7.
- **Meningoceles** in idiopathic intracranial hypertension. Bialer OY, Rueda MP, Bruce BB, Newman NJ et a. Am J Roentgenol.2014Mar;202(3):608-13.
- **MRI findings** of elevated intracranial pressure in cerebral **venous thrombosis versus** idiopathic intracranial hypertension with **transverse sinus stenosis.** Ridha MA et al. Neuroophthalmology. 2013 Feb 1;37(1):1-6.

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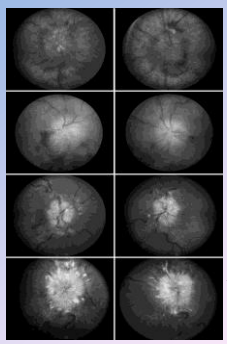
Fulminant idiopathic intracranial hypertension

OD



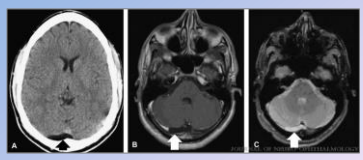
OS

Fundus photos of 4 patients

Thambisetty M et al. Neurology 2007;68:229-232

AMERICAN ACADEMY OF NEUROLOGY

PTCS associated with giant arachnoid granulation



A. CT reveals a hypodense filling defect at the origin of the right transverse sinus adjacent to the torcular, with involvement of the proximal left transverse sinus (arrow). B. T1 axial MRI shows the hypodense filling defect (arrow) at the origin of the right transverse sinus, corresponding to the CT image. C. T2 axial MRI shows a hyperintense signal (arrow) corresponding to the filling defect. CT, computed tomography; MRI, magnetic resonance imaging.

Rosenberg, Kevin I.; Banik, Rudrani
Journal of Neuro-Ophthalmology. 33(4):417-419, December 2013.
doi: 10.1097/WNO.0b013e3182a5943b

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Therapy: Guided by Neuroimaging Findings & Symptoms

- Cerebrospinal fluid diversion procedures in the treatment of patients with idiopathic intracranial hypertension. Malik A, Golnik K. Int Ophthalmol Clin.
- Optic Nerve Sheath Decompression: A Surgical Technique With Minimal Operative Complications. Moreau A, Lao KC, Farris BK. J Neuroophthalmol. 2013
- Stenting of the Transverse Sinuses in Idiopathic Intracranial Hypertension Ahmed, Rebekah; Friedman, Deborah I.; Halmagyi, G. Michael Journal of Neuro-Ophthalmology. 31(4):374-380, December 2011.
- Increasing intraocular pressure as treatment for papilledema. Fleischman D, Berdahl JP, Fautsch MP, Chesnutt DA, Allingham RR. Exp Eye Res. 2013

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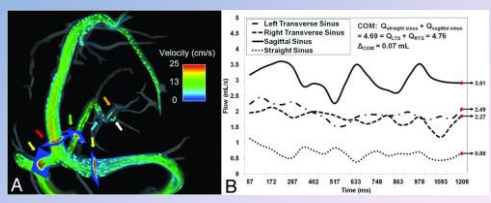
Example of flow visualization for COM



Schrauben E et al. AJNR Am J Neuroradiol 2014;35:999-1006

AJNR AMERICAN JOURNAL OF NEURORADIOLOGY

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Case of 47 y/o WM

- WITH RECENT RIGHT UPPER ROOT CANAL
- NEXT DAY DEVELOPS SEVERE H/A WHILE DRIVING X 8 HOURS
- H/A IS AT BASE OF SKULL WITH FEELING OF OFF BALANCE WHEN MOVING HEAD SIDE-TO-SIDE; BLURRED VISION with sudden head motion OU
- NO PMH; NO FH OF MIGRAINE; NO TRAUMA

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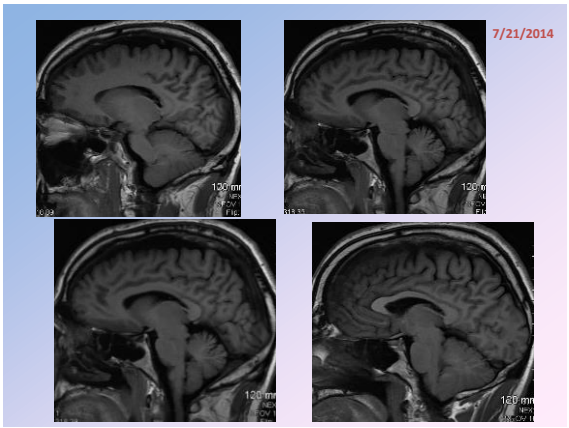

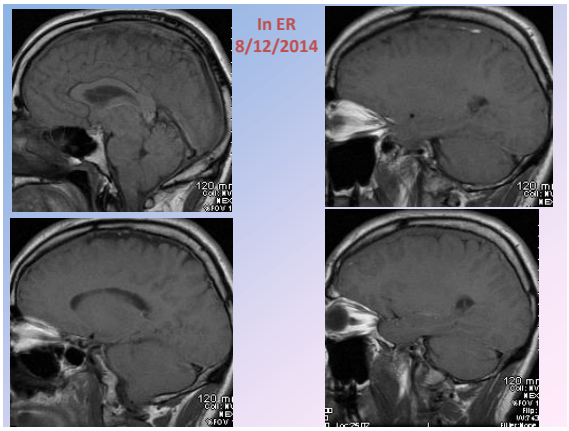

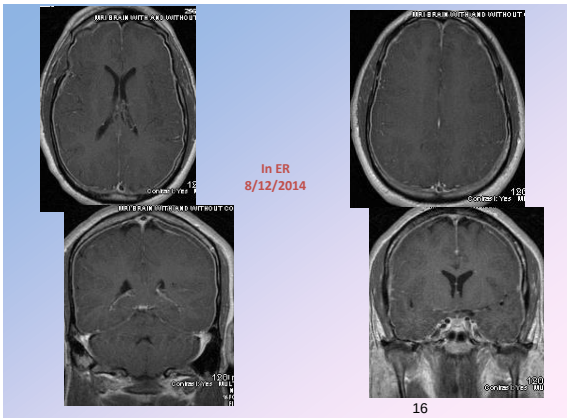

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Diagnosis?

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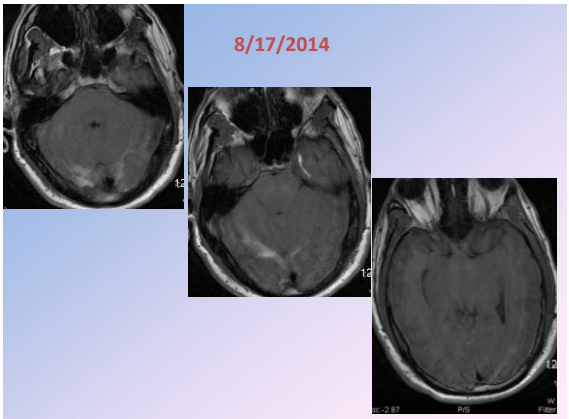

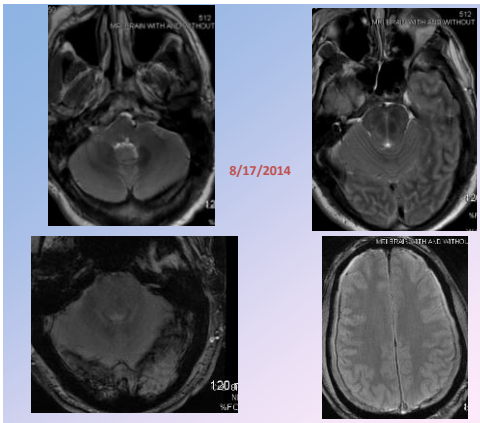

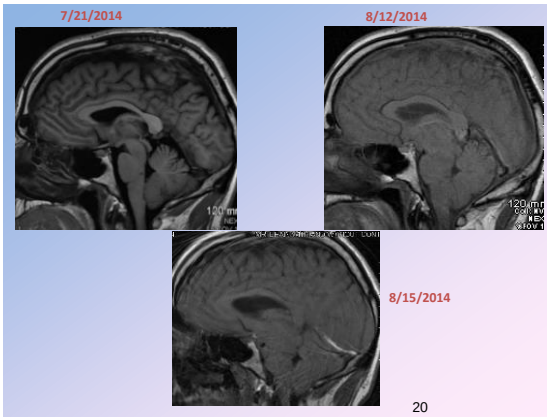

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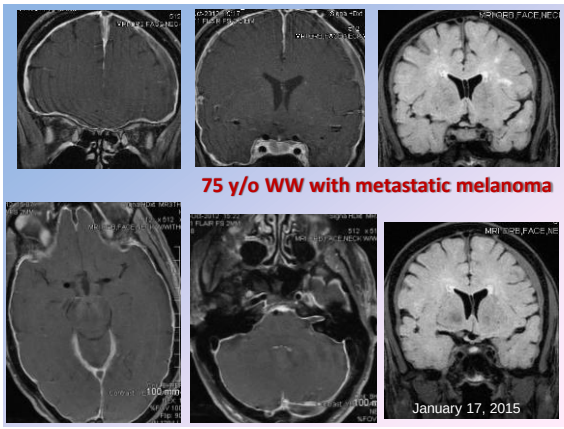
DDx of meningeal enhancement

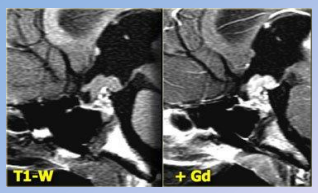
1. Chemical "meningitis" (chemotherapeutics, heavy metals)
2. Granulomatous infiltration (sarcoid, tb)
3. Inflammation (RAs, eosinophilic granuloma)
4. Infection (viral, bacterial, fungal)
5. Neoplastic "meningitis" (carcinomatous, hem)
6. Subarachnoid haemorrhage
7. Trauma, intracranial surgery
8. Venous thrombosis



Neuro-ophthalmologic Complications in the Patient with Cancer

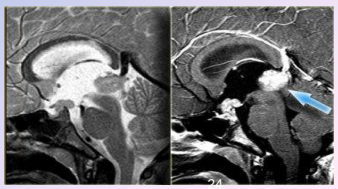
- Tumor cells reach the subarachnoid space either **through the blood, by growing** along nerve & vascular sheaths, or by migration from a tumor adjacent to CSF (parenchymal, bony lesions in the skull or spine)
- Katz et al. reported **not only ONS** coverage with tumor cells but neoplastic invasion **along the Virchow-Robin spaces** (mesenchymal septae) resulting in demyelination, and axonal beading and degradation of the optic nerve itself.

Germinoma



- 80-90% along IIIrd ventricle
- 5-10% basal ggl
- Bifocal germinoma: pineal + suprasellar

- DWI restriction: high cellularity
- Intense homogeneous Gad+
- ± CSF seeding,
- ± brain invasion



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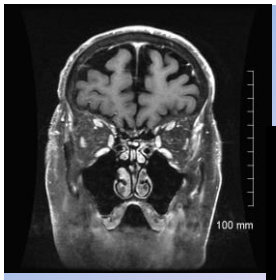
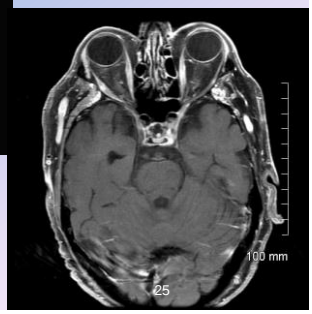


Squamous cell carcinoma
Perineural spread



- Cardiac transplantation on immunosuppressants
- CN V, VI followed by complete ophthalmoplegia;
- LR atrophy

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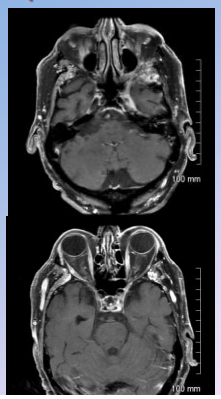
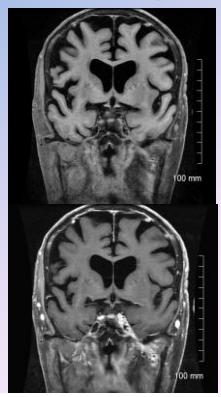
Squamous cell carcinoma Perineural spread





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MRI in Optic Neuritis
MS vs. NMO

- Abnormal optic nerve enhancement in 94% of affected nerves (Kupersmith et al.)
- ON hyperintensity on FLAIR in 82-100 %
- Abnl. signal length >17.5 mm and canalicular location a/w poor or slow recovery from ON even if treated with steroids
- Simultaneous ON OU in a monocularly symptomatic patient or chiasmal enhancement should warrant careful evaluation for NMO!

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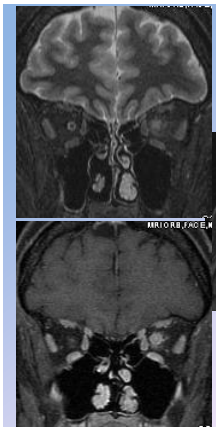
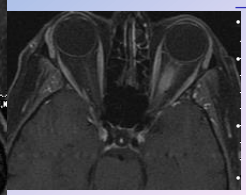


40 Y WF pain on EOM x 1 wk, abrupt onset ↓ VA: CF 1' OS



Enhancement

- may persist up to **4 mo**
- **non-specific** marker of breakdown of BBB
- intraorbital & canalicular segment
- **Lesion length > 17.5 mm** – poorer prog.

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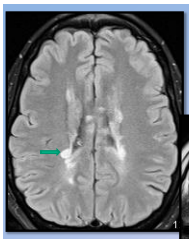
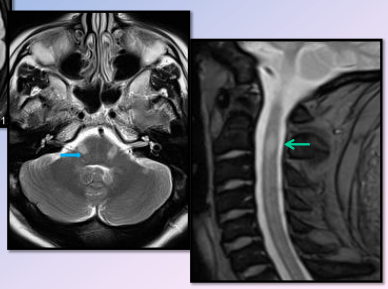


1 year later facial and upper extremity numbness, bilaterally



Demyelinating plaques

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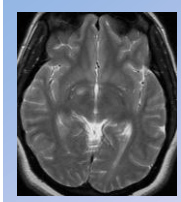
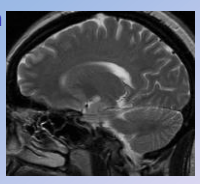
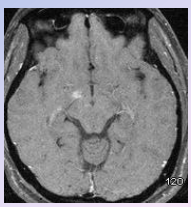
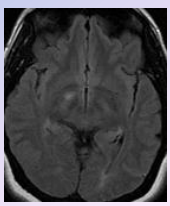
Optic tract lesion
First sign of MS









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MRI & Eye as Predictors of MS

- MRI: best predictor of present and future **risk of CDMS** *not* for diagnosis in 5-yr: 16 vs 51%; in 10-yr 22 vs 56% if no vs 1 or > brain lesion(s); in 15-yr 25 vs 72%
- After ON highest risk of developing MS: **in 5 yrs**; If baseline **MRI-** then ↑risk if preceding viral syn.
- If no eye pain or NLP or severe disc edema or peripapillary hem. or macular exudates *then* **No MS**
- Revised McDonald criteria: Dx of MS with MRI can be made at initial presentation

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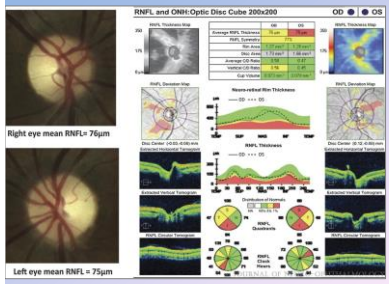
Optical Coherence Tomography (OCT)

32 y/o ♀ with RRMS x 3 yrs & ON OS x 1 yr



Presented with ON OS **1 year earlier**. She had no history of ON OD. Fundus: optic disc pallor OU. SD-OCT demonstrates RNFL thinning in both eyes, suggesting prior subclinical optic nerve damage in OD and optic nerve damage in OS secondary to known ON.

Should Optical Coherence Tomography Be Used to Manage Patients With Multiple Sclerosis?

Costello, Fiona; Van Stavern, Gregory P.

Journal of Neuro-Ophthalmology. 32(4):363-371, December 2012.

doi: 10.1097/WNO.0b013e318261f7e7

Wolters Kluwer | Lippincott Williams & Wilkins

Where OCT & MRI meets: Pathophysiology

- Focal demyelinated plaques: varying levels of inflammation, gliosis, neurodegeneration
- Evidence: **permanent disability** correlates best with ↓CNS neurons & axons not demyelination**!**
  Infer from OCT: structural info of retina & ON
- **Thinning of RNFL** & **↓ MV** found in MS pts, both with & wout distinct episodes of ON suggesting ongoing neuronal & axonal loss
- OCT: *Macular thinning predominant phenotype*

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Neuromyelitis optica Devic's disease NMO spectrum disorders

- Severe inflammation & necrosis of ONs & spinal cord (<5 yrs 50% is blind in 1 or both eyes or need walking aid)
- Non-caucasian, mean age: 40 yrs, ♀:♂=9:1
- 80% +Anti-NMO-IgG serum Abs
- A/w other autoimmune dz: celiac, MG & systemic infection: hepatitis, Lyme, syphilis, TB
- Poor visual recovery≈ **bilat. ON (NMO-),** LETM, intereye RNFL asymm.>15μm (>3 mths of ON)
- On low immunosupp: Ocular toxo, CMV retinitis (important DDx of visual loss in NMO)
- Beta-IFN for MS considered harmful in NMO!

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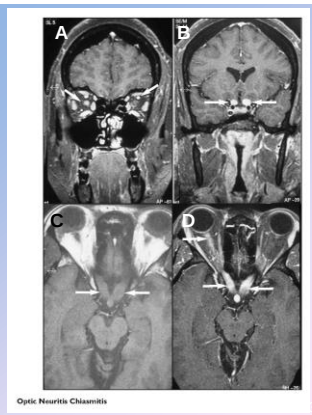

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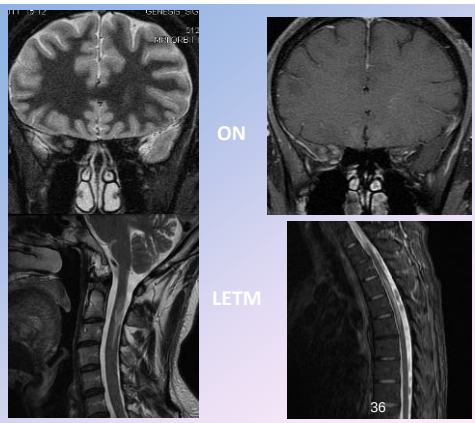

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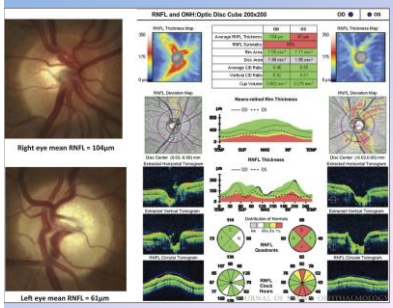
30-year-old man with NMO & prior left ON



Manifests significant optic disc pallor in OS and marked intereye asymmetry (43 μm) of the mean RNFL thickness, reflecting significant optic nerve damage in OS. His VA was 20/20 OD, and 20/100 OS, with a left RAPD, a dense central scotoma in the left visual field, and absent color vision in OS

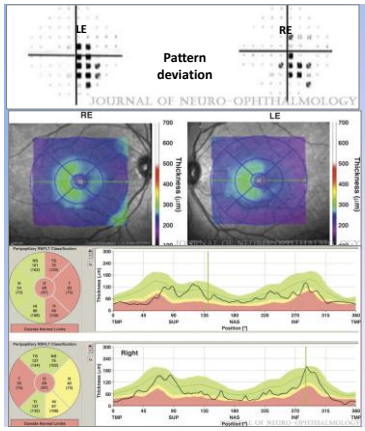
In eyes with ON both TD- & SD-OCT showed **thinner** RNFL in NMO **vs** RR MS

Costello, Fiona; Van Stavern, Gregory P.

Journal of Neuro-Ophthalmology. 32(4):363-371, December 2012.

doi: 10.1097/WNO.0b013e318261f7e7

VF-OCT–MRI–DTI tractography correlation



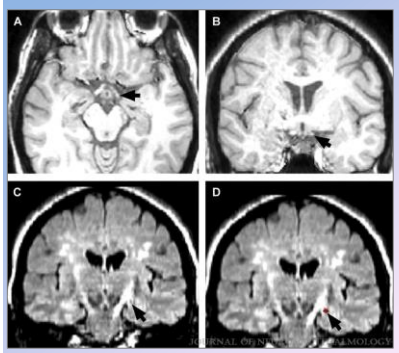
- Incongruous right HH
- OCT hemimacular thinning in a pattern consistent with a left retro-chiasmal injury
- OCT shows diffuse loss of RNFL in each eye, most marked temporally

Romero, Rebecca S.; Gutierrez, Ismael; Wang, Eugene; Reder, Anthony T.; Bhatti, M. Tariq; Bernard, Jacqueline T.; Javed, Adil

Journal of Neuro-Ophthalmology. 32(2):150-153, June 2012.

doi: 10.1097/WNO.0b013e318250468

MRI & DTI



Axial (A) and coronal (B) **T1** MRI demonstrates decreased size of the left optic tract (OT) (arrows). C. Coronal **FLAIR** MRI reveals an area of demyelination (arrow) in the vicinity of the left OT. D. **Diffusion tensor tractography** confirms the location of the left OT (red).

Romero, Rebecca S.; Gutierrez, Ismael; Wang, Eugene; Reder, Anthony T.; Bhatti, M. Tariq; Bernard, Jacqueline T.; Javed, Adil

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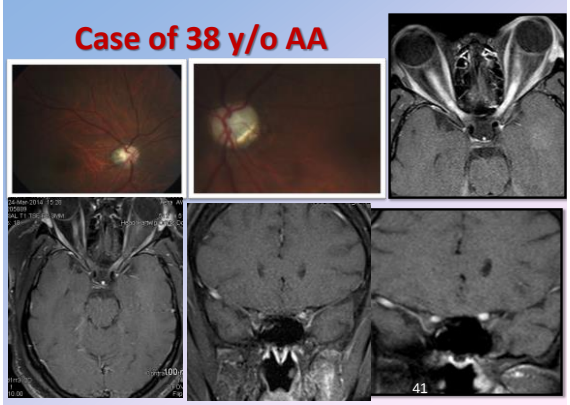
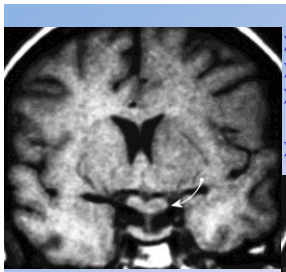
DDx of Optic Neuritis & abnl. MRI

- **Isolated inflammatory: MS, NMO, ADEM, AION, CRION, postvaccination ON, anti-myelin oligodendrocyte glycoprotein (MOG)-associated Diagnosis of exclusion, recurrent events, worsening with steroid withdrawal**
- **Systemic dz. associated eg. GCA, paraneoplastic, sarcoid, SLE, Wegener granulomatosis**
- **Infectious: B. h neuroretinitis, CMV, Lyme, mycosis, syphilis, TB, WNV)**

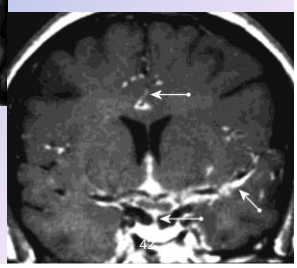
Case of 38 y/o AA



NEUROSARCOIDOSIS

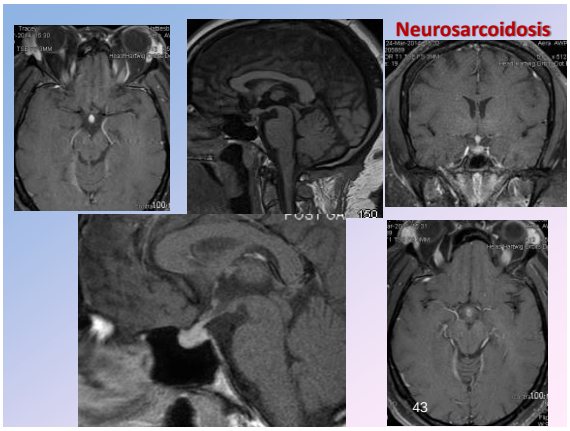


- abnl. CXR in >90% of NS
- WM small vessel vasculitis/angiitis
- Coats CNs/fill IAC

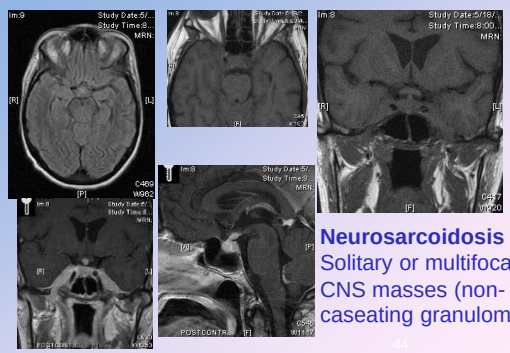


- Leptomeningeal dz of the base of the brain
- spreads along the Virchow-Robin spaces to form intraparenchymal masses

Neurosarcoidosis

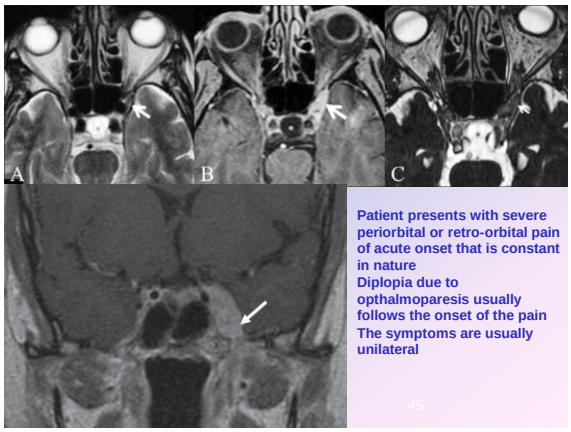


45 Y/O WOMAN WITH CONFUSION



Neurosarcoidosis
Solitary or multifocal CNS masses (non-caseating granulomas)

44



Patient presents with severe periorbital or retro-orbital pain of acute onset that is constant in nature
Diplopia due to opthalmoparesis usually follows the onset of the pain
The symptoms are usually unilateral

45

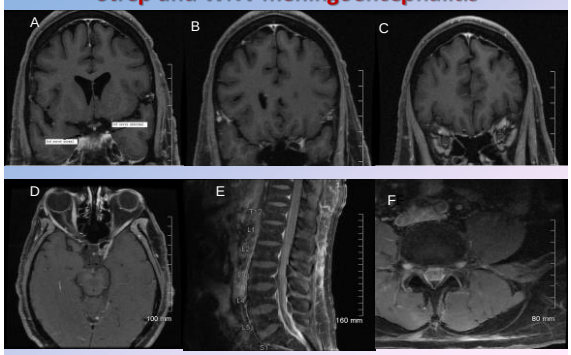
50 y/o WW

Eye pain worse with movement

46

Strep and WNV meningoencephalitis

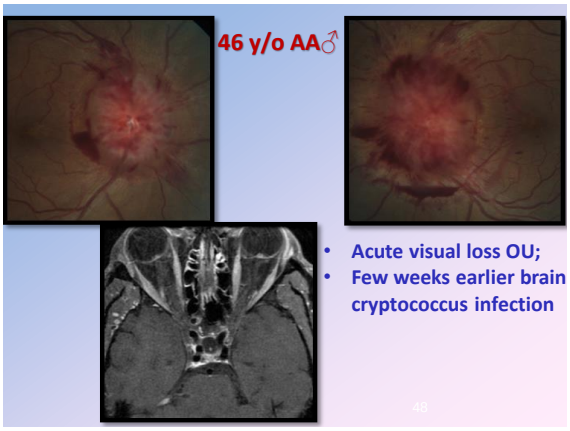
Szatmáry



Relapsing-remitting clinical course

47

46 y/o AA♂



- Acute visual loss OU;
- Few weeks earlier brain cryptococcus infection

48

Thank you!