Obesity-related Comorbidities: Idiopathic Intracranial Hypertension and Nonalcoholic Fatty Liver Disease

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Disclosures

No, the speakers have not had a financial relationship with an ineligible company within the past 24 months.

Learning Objectives:

- Define Idiopathic Intracranial Hypertension and Nonalcoholic Fatty Liver Disease and review current diagnostic criteria
- Understand the role of the PCP in diagnosis and management of IIH and NAFL
- Understand best practice for referral to specialist

Idiopathic Intracranial Hypertension

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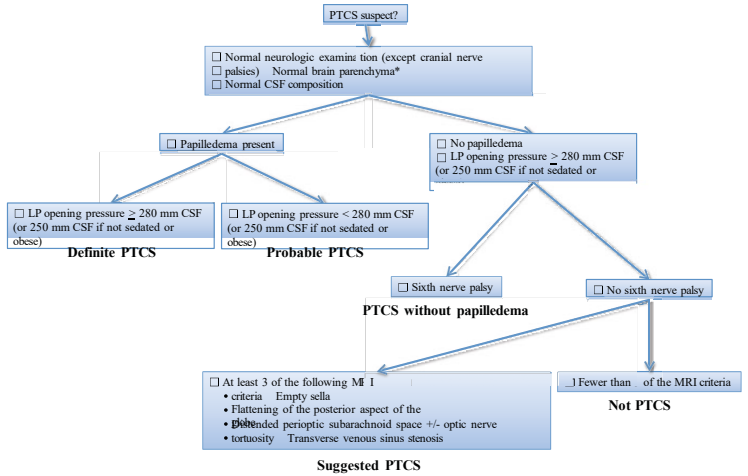
Definition & Diagnostic criteria

- Formerly known as Pseudotumor cerebri or benign intracranial hypertension
- Modified Dandy criteria:
  - Awake and alert patient
  - s/s of increased ICP
  - Absence of focal findings on exam with the exception of possible CN 6th palsy
  - Normal diagnostic studies except for elevated OP
  - No other etiology for increased ICP



*As seen on contrast-enhanced MRI neuro-imaging for typical patients (female and obese), plus MR-venography for atypical patients (male or non- obese female); or contrast-enhanced CT if MRI is not obtainable.

Fig. 1 Flowchart based on the recent diagnostic criteria for PTCS.[3] CSF, cerebrospinal fluid; CT, computed tomography; LP, lumbar puncture; MRI, magnetic resonance imaging; PTCS, pseudotumor cerebri syndrome.

280 mmH_2O in children is considered elevated; although greater than 250 mmH_2O is considered elevated in those not sedated during the lumbar puncture and nonobese children.[5] CSF composition should be normal, with necessary CSF analyses including cell count, cytology, and concentrations of glucose and protein.

Thus, in the presence of papilledema, key diagnostic requirements include (1) normal brain parenchyma on neuroimaging with contrast-enhanced MRI or CT, (2) normal venous imaging with MRI- or CT-venography in select cases, and (3) normal CSF composition on lumbar puncture. As outlined in recently revised diagnostic criteria for PTCS,[6] with elevated ICP, a diagnosis of definite PTCS can be made; if a normal ICP is measured, a diagnosis of probable PTCS can be made (►Fig. 1).

In the absence of papilledema, key diagnostic requirements include (1) normal brain parenchyma on neuroimaging with contrast-enhanced MRI or CT and (2) elevated ICP and normal CSF composition on lumbar puncture. With these features, in the added presence of unilateral or bilateral sixth nerve palsy, the diagnosis of definite PTCS can be made[3]; however, without a sixth nerve palsy, the diagnosis of suggested PTCS can be made if key neuroimaging features are observed (►Fig. 1). These neuroimaging features include distension of the perioptic subarachnoid space with or without optic nerve tortuosity, flattening of the posterior aspect of the globe, an empty sella, and transverse venous sinus stenosis.[3] As a group, the required neuroimaging features are highly suggestive of PTCS.[6] Symptom changes after a lumbar puncture and headache characteristics are not diagnostic of PTCS under the revised criteria.

Classification of Pediatric PTCS

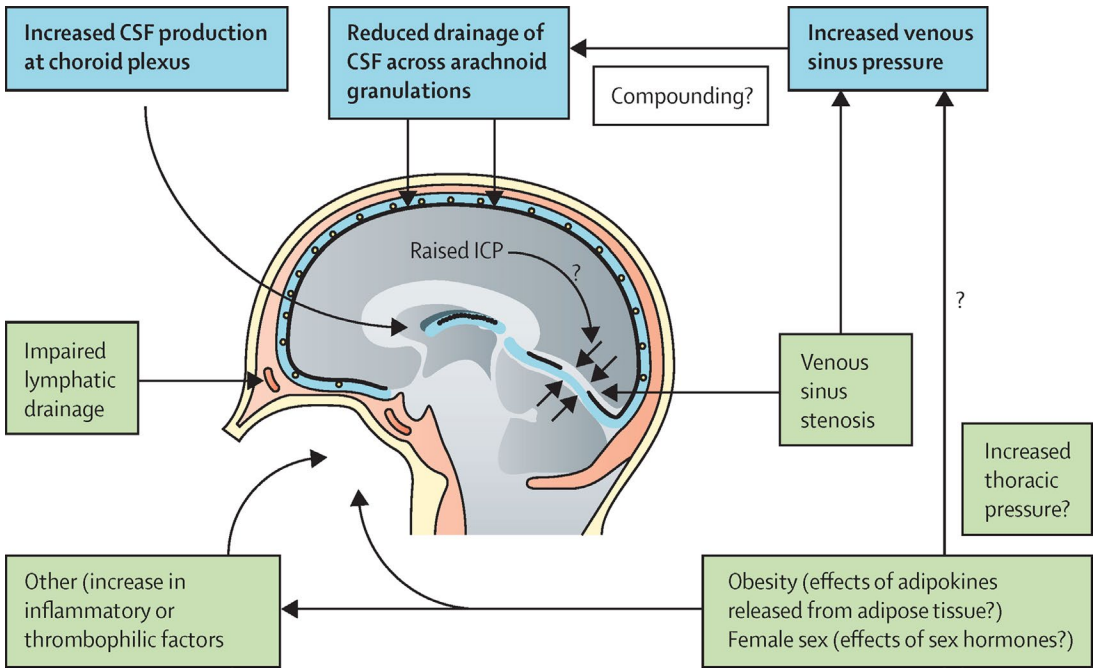
PTCS is classified as either primary or secondary (►Table 1). Primary PTCS is also referred to as idiopathic intracranial hypertension.[3] In the adult population, the typical patient with primary PTCS is a female of reproductive age who is overweight and/or has a history of recent weight gain. Primary PTCS is certainly seen in the pediatric population, although its epidemiology is complex and characterized by a multifaceted relationship between obesity, pubertal status, and sex. Adolescents with PTCS are more frequently obese and female, suggesting that the risk factors for developing PTCS in this age group may be similar to those in adults.[7] On the other hand, young, prepubertal children are less likely to be obese, are equally male and female, and may present without symptoms of headache or visual blurring.[8,9] Ongoing studies are examining the relative influence of sex, age, and key pubertal stages on the epidemiology of pediatric PTCS.[10] These observations highlight the need for vigilance by the medical provider, not only for overweight and obese children but also for young, thin children who may present with atypical or no symptoms.

Secondary PTCS refers to a clinical diagnosis of PTCS attributable to one or more of a variety of identifiable causes, including venous sinus thrombosis, medications, and medical conditions other than obesity alone. Some of the most

Epidemiology

- Incidence in the US can be variable, but incidence is higher in geographic areas where there is a higher prevalence of obesity
- Most common in women
  - Notably increased in women with BMI >30
  - One study found that greater levels of weight gain associated with increased risk of IIH although an increased risk also present in women with BMI < 30 who had moderate weight gain → therefore it is an important question to ask your patients in who you might suspect IIH
- In children, incidence is ~ 0.71 per 100,000
  - To 4.18 per 100000 in adolescent males and 10.7 per 100000 in adolescent females with increased BMI respectively
  - Trends show that with in older teens and adolescents, most with IIH were overweight or obese

Pathophysiology



- Poorly understood
- Blockage of CSF absorption at level of arachnoid villi
- Exacerbated by cerebral venous HTN secondary to transverse venous sinus stenosis

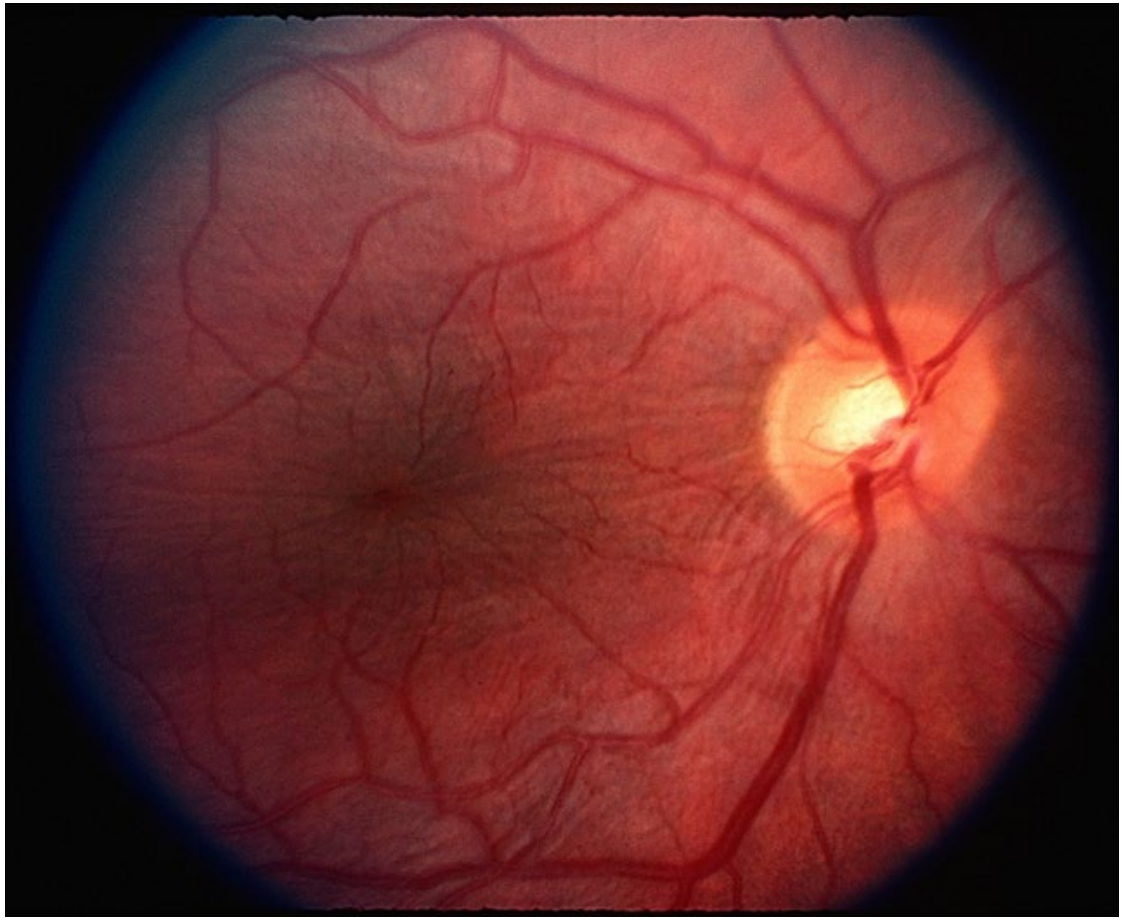
Symptoms- most common

- Headache 94%
  - Holocephalic
  - Aggravated by Valsalva-like maneuvers
  - Worse when supine
  - N/V
  - Can sometimes mimic TTH and migraines

Symptoms- visual

- TVOs occur in 68% of patients
  - ? Due to transient ischemia of the edematous optic nerve head
  - Can occur many times per day
  - Partial or complete vision loss
  - Also aggravated by Valsalva-like maneuvers or postural changes
  - Associated with higher grades of papilledema
- Other less specific visual changes have been reported
  - Blurred vision
  - Metamorphopsia (distortion of vision due to retinal folds)
  - Blind spot (but usually not noticed)
    - Can present as irreversible by the time it is realized
  - Photopsia (shimmering lights with colored center)
- Diplopia
- Retrobulbar pain or retrobulbar pain on eye movement

Retinol folds

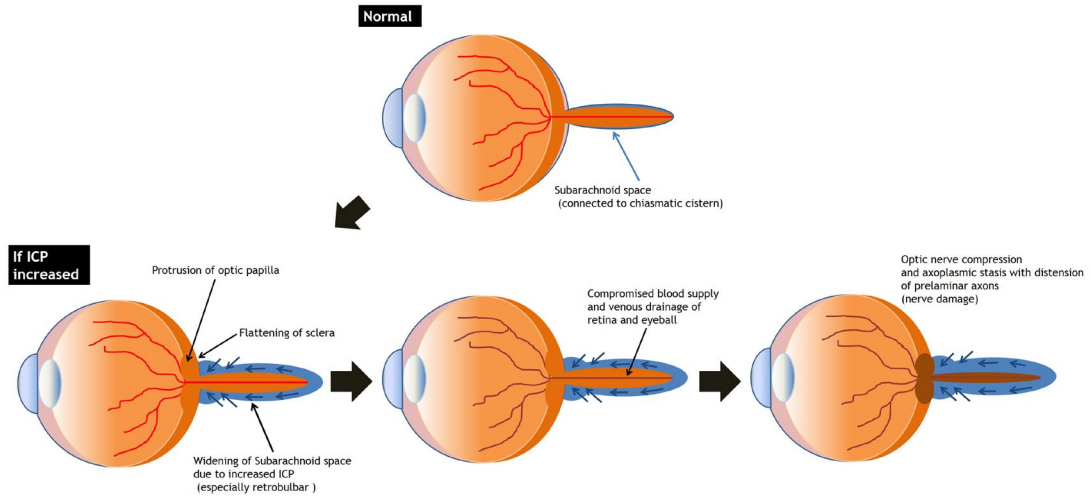


Symptoms- other

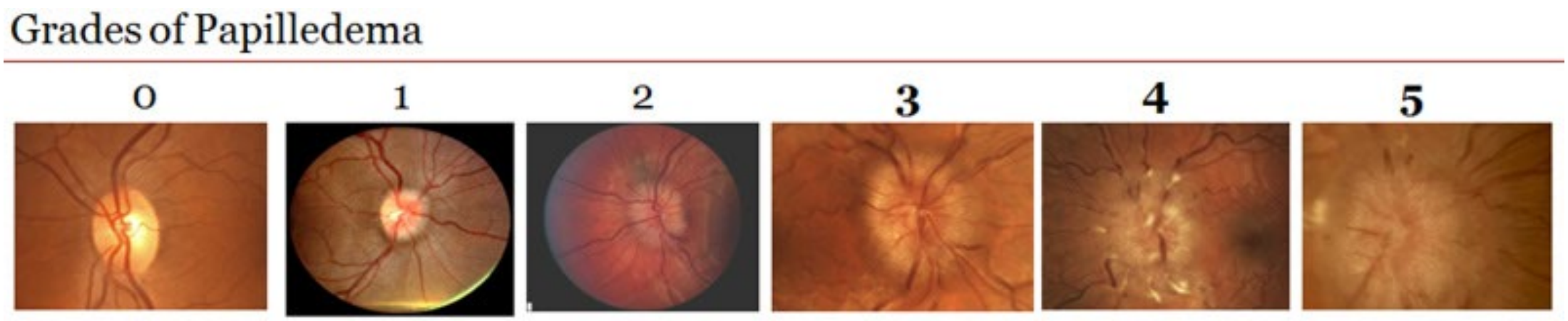
- Pulsatile tinnitus in ~50-60% of patients
  - Patients are usually not aware of this
  - Can be unilateral or bilateral
  - Buzzing or “heart beating in ear”
- Facial weakness
- Asymptomatic

Signs- most common

- Papilledema 100%
  - Usually bilateral and concentric
  - Correlated to threat of vision loss
  - If untreated then can be irreversible and lead to optic atrophy
  - Due to axoplasmic flow stasis secondary to increased ICP → edema to retinal fibers

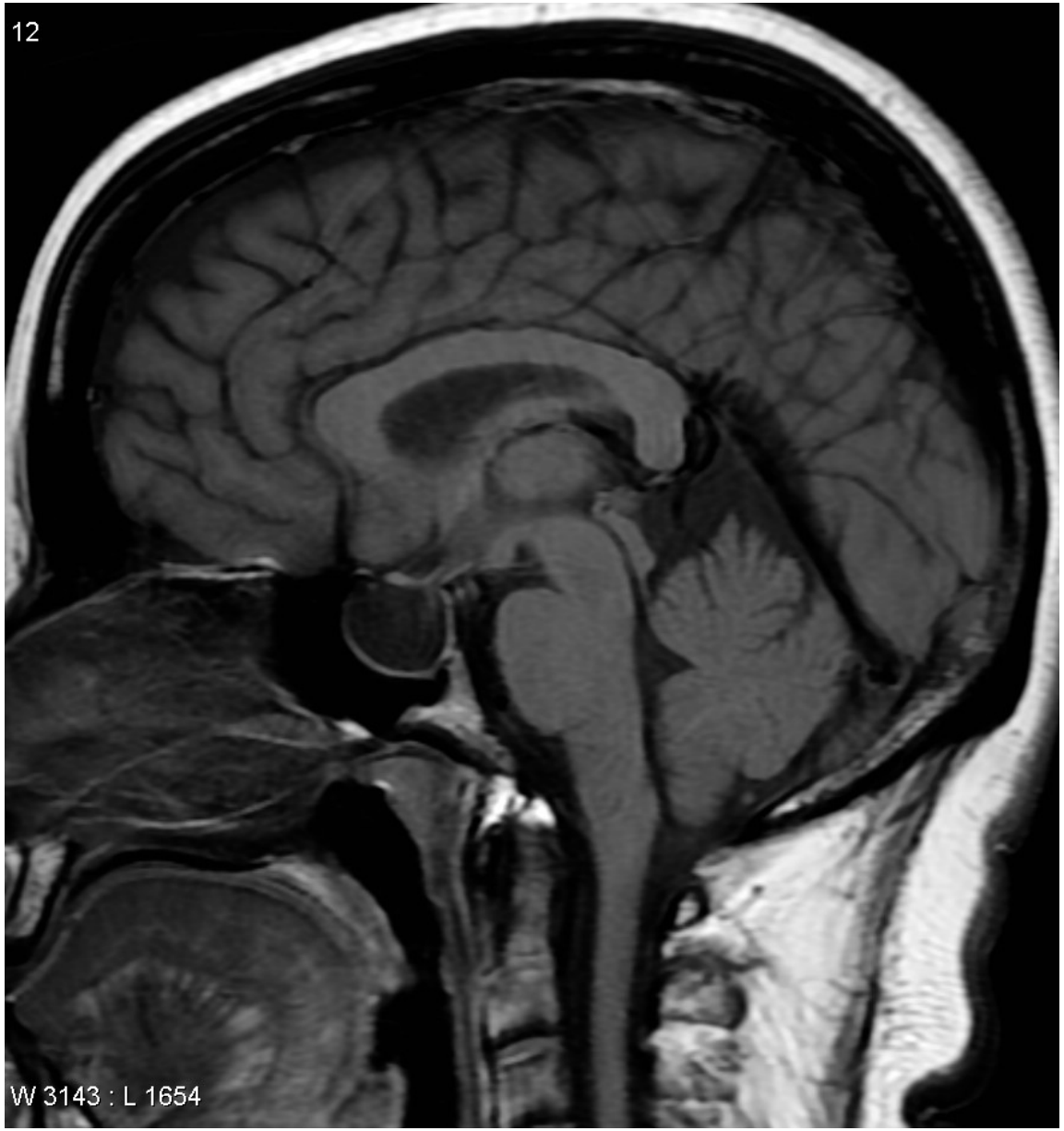


Grades of papilledema

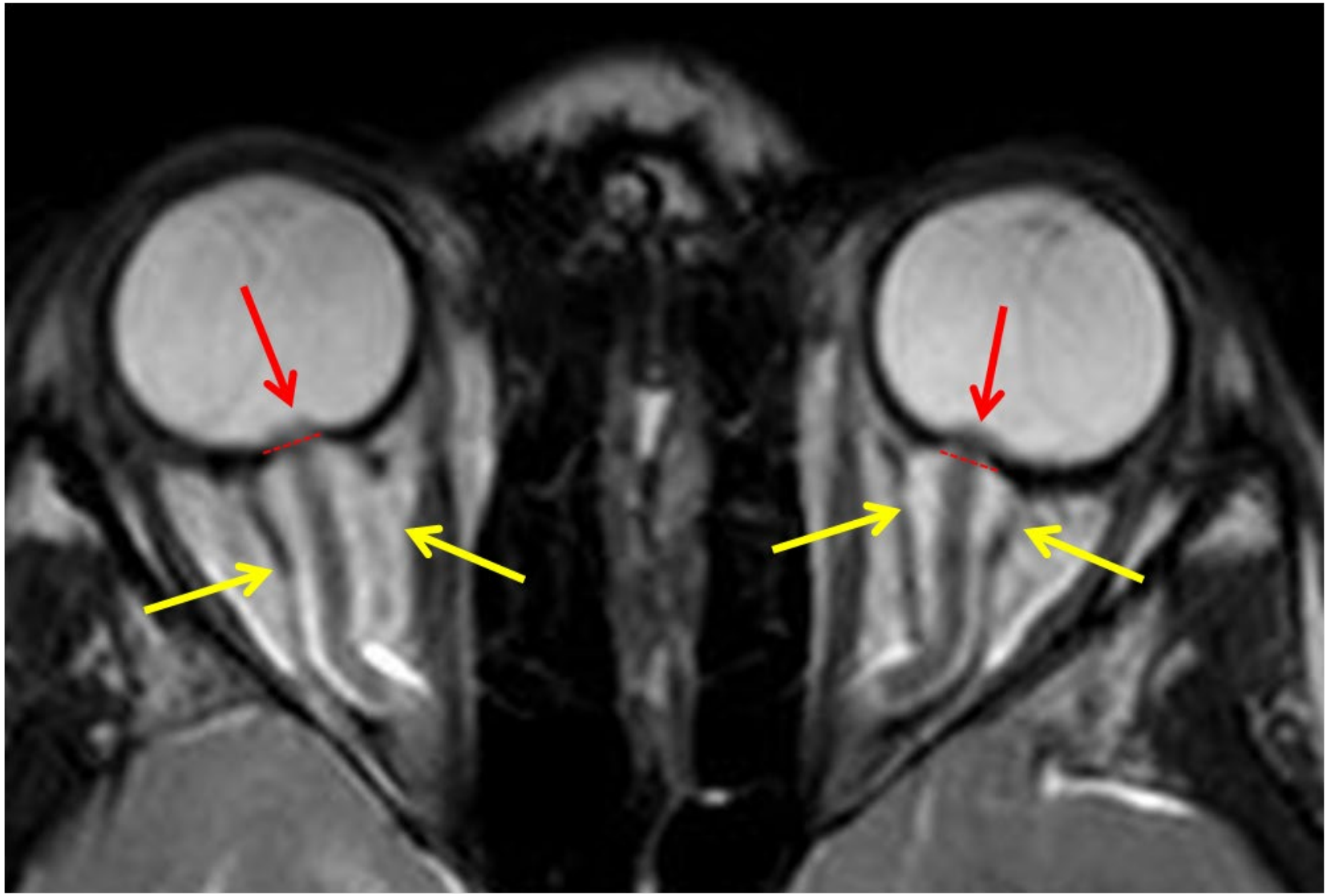


Neuroimaging

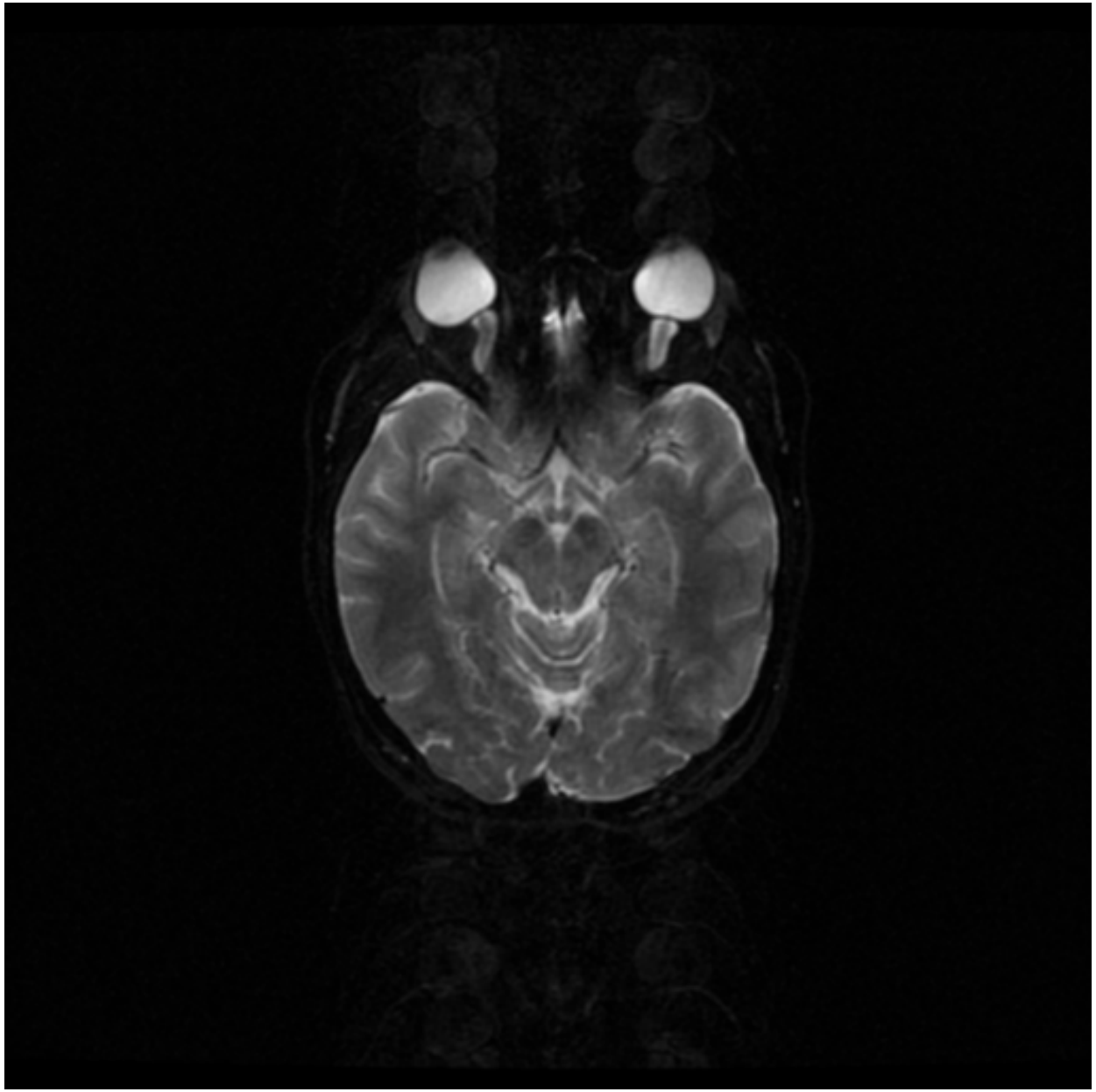
- MRI brain w/wo contrast → can be normal
  - Empty sella turcica (can also be incidental) or partially empty sella (70%)
  - Dilation (45%) and increased tortuosity (40%) of optic nerve sheaths
    - Sometimes can see enhancement of optic discs (50%)
  - Posterior globe flattening (80%)
  - Acquired cerebella tonsillar descent below level of FM
- MRV if high suspicion for CSVT
  - Especially for atypical or fulminant presentation



Case courtesy of Frank Gaillard, Radiopaedia.org, rID: 5661



Case courtesy of Dalia Ibrahim, Radiopaedia.org, rID: 29638



Case courtesy of Frank Gaillard, Radiopaedia.org, rID: 42782

Reference chart detailing differential

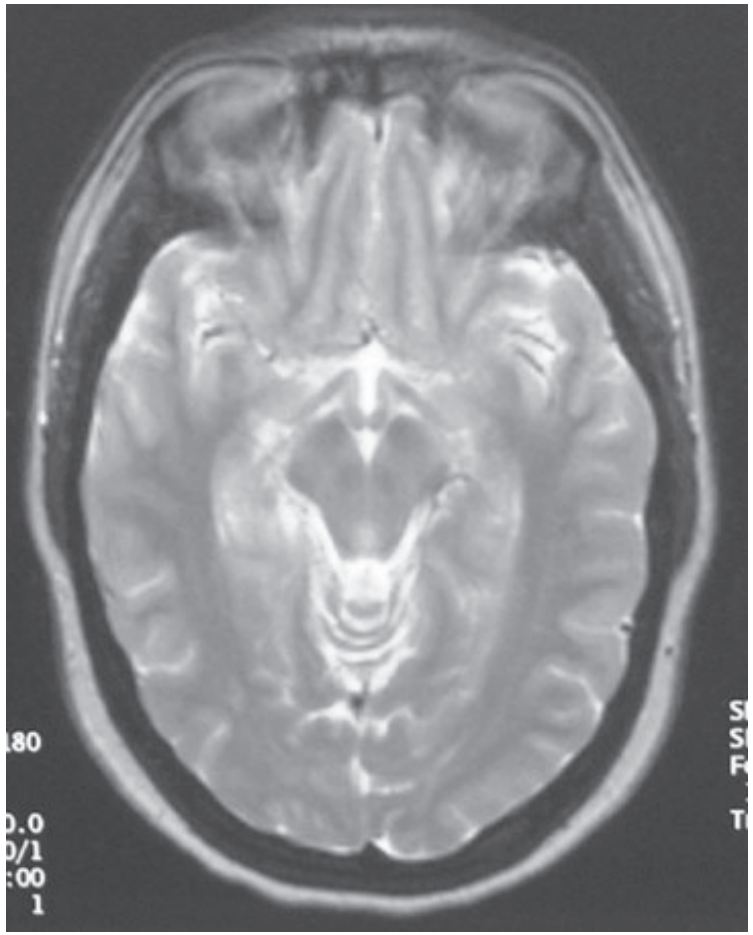
Table 1 Pseudotumor cerebri syndrome

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
Arteriovenous fistulas
Decreased CSF absorption from previous intracranial infection or subarachnoid hemorrhage
Hypercoagulable states
Medications and exposures
Antibiotics
Tetracycline, minocycline, doxycycline, nalidixic acid, sulfa drugs
Vitamin A and retinoids
Hypervitaminosis A, isotretinoin, all-trans retinoic acid for promyelocytic leukemia, excessive liver ingestion
Hormones
Human growth hormone, thyroxine (in children), leuprorelin acetate, levonorgestrel (Norplant system), anabolic steroids
Withdrawal from chronic corticosteroids
Lithium
Chlordecone
Medical conditions
Endocrine disorders
Addison disease
Hypoparathyroidism
Hypercapnia
Sleep apnea
Pickwickian syndrome
Anemia
Renal failure
Turner syndrome
Down syndrome

Serial LPs Without Serial Imaging in Idiopathic Intracranial Hypertension: A Lesson Learned

Headache April 2008

- 30yo female diagnosed with IIH (OP 42) and treated with serial lumbar punctures for 4 years prior to her final diagnosis of a anaplastic ependymoma
- Necessary to continue to monitor for secondary causes in all IIH pts not responding to tx



Who gets an LP?

- History of chronic headache that is not associated with typical migraine features including photo/phonophobia, N/V
- Frequent photopsias or TVOs
- Headaches worst when lying flat
- Not responsive to 1-2 preventative meds

CSF evaluations

- 90th percentile for all patients in the reference population, was 28 cm of water.
- The threshold for an abnormally reduced pressure in the 10th percentile was 11.5 cm of water.
- Sedation plays a minor role
  - With minimal or no sedation < 25 cm H2O is normal
- Diagnosis:
  - >/= 25 in adults
  - >/= 28 in children

Ophthalmic investigations

- Formal perimetry
- Helpful to rule out pseudopapilledema
  - Fundus autoflorescence
  - Ultrasonography
- Optical coherence tomography
  - Helps qualify severity of papilledema

Medical Therapies

- Weight loss (if indicated)
  - 6-10% of initial body weight
  - Long term goal
- CAIs
  - Acetazolamide
    - Associated with stat significant improvement in papilledema grade, sxs, and QOL
    - Consider rapid up-titration
    - Important to review SEs:
      - Paresthesias
      - Dysgeusia
      - N/V
      - Diarrhea
    - Monitoring: MA, hypokalemia
    - Txt failure seen in male sex, higher papilledema grade, dec VA at presentation, > 30 TVOs/month
  - Thought to descrease CSF production
  - Also have a mild diuretic effect

Medical Therapies (cont)

- TPM
  - For primary HA disorders
  - Weak CAI
  - Can help with weight loss but concern for anorexia
  - Can use with Diamox as a combo
- Adjunctive: furosemide
- Steroids

Surgical Therapies

- Usually needed for fulminant presentations
  - Makes the case for good ophth evaluation
- Three most common txts:
  - CSF shunting
    - VP > LP; high complication rate → not first line
  - ONSF
    - t/c when vision threatened
    - Creates fistula between SA space and orbital cavity
    - Complications such as persistent VL due to trauma to ON, tonic pupil, diplopia
  - Transverse venous sinus stenting
    - In pts who have transverse venous sinus stenosis with pressure gradients > 8 mm Hg
    - Should reduce cerebral venous HTN

Summary of what to do

- Weight loss is very important
- Withdrawal of offending agent if present
- Do not do repeat LP's
- Acetazolamide – use long acting sequels when possible
  - start at 10-25mg/kg or 125 -250mg BID if <10yo
    - Suspension 125/5 compounded at most pharmacies
    - Goal sx improvement or 100mg/kg or 1gram max
  - Start at 250 -500mg BID if >10yo
    - Goal sx improvement or 2g max
- Topamax if borderline pressures (20-35cm) at 5mg/kg or 100mg per day
  - Carbonic anhydrase inhibition, HA control, and wt loss
- Repeat ophtho exam 2wks after starting diamox

Prognosis

- Cessation of symptoms in 70% of IIH patients within 3 months of medical treatment
- Recovery from headache and TVO in 84% and 78%, respectively, after 2 months
- Up to a quarter of IIH patients experience a more protracted course of symptoms
- Median time needed on diamox is 13mos
- 40% have relapse within 6yr

Another case

- A 27-year-old woman was diagnosed with IIH at age 22 when she developed blurred vision, diplopia, and headaches. Her examination revealed visual acuities of 20/30 in both eyes, marked blind spot enlargement on perimetry, mild bilateral abduction deficits, and bilateral Frisén grade 4 papilledema. Imaging and LP confirmed the diagnosis. She was treated with acetazolamide and weight loss. Her symptoms and examination abnormalities resolved and the acetazolamide was discontinued after a year.

- Three months ago, she developed similar headaches, transient obscurations of vision, and blurred vision. Examination showed visual acuities of 20/25 in both eyes with blind spot enlargement on perimetry. Ocular motility was full and there was no active disc edema but the disc margins were mildly elevated and gliotic.
- Thoughts?

- Imaging showed a partially empty sella and distention of the perioptic subarachnoid space. LP opening pressure was 300 mm CSF. She reports a 15-pound weight gain over the past year. Papilledema may not be present in recurrent PTCS because of gliotic changes in the nerve fiber layer or subtle optic atrophy. Based on her symptoms and other findings, this patient has recurrent PTCS.

One more…

- A 16-year-old girl has a 9-month history of constant, global aching headaches associated with mild nausea, photophobia, and phonophobia. There are no episodes of transient visual loss or pulsatile tinnitus. She takes naproxen 3 days weekly for her headaches but is on no other medications.
- Examination reveals a BMI of 33 kg/m2, normal visual acuity, diffuse constriction of the visual fields on kinetic perimetry without physiologic expansion using a larger test target, full ocular motility, and normal optic discs bilaterally.
- What would you do?

- Her MRI is normal. Lumbar puncture reveals an opening pressure of 270 mm CSF with normal CSF contents. PTCS is a suspected cause of chronic daily headache in an obese female patient. However, this patient has no papilledema or other symptoms or signs of PTCS and the visual field constriction is not organic (“functional” visual field loss). The elevated LP opening pressure is neither specific nor diagnostic in this setting. She does not have PTCS.

Nonalcoholic Fatty Liver

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Disclosures

Name	Role	Disclosure	Resolution
Rohit Kohli	Chair	Research Grant Site Principal Investigator for Raptor & Shire Pharmaceuticals Speaker Bureau for Alexion, and Scientific and Medical Advisory Bd. Member for Takeda	Restricted to best available evidence and ACCME content validation statement
Stephanie H. Abrams	Faculty	Nothing to disclose	N/A
Marialena Mouzaki	Faculty	Nothing to disclose	N/A
Pushpa Sathya	Faculty	Nothing to disclose	N/A
Jeffrey B. Schwimmer	Faculty	Nothing to disclose	N/A
Shikha S. Sundaram	Faculty	Nothing to disclose	N/A
Miriam Vos	Faculty	Nothing to disclose	N/A
Stavra A. Xanthankos	Faculty	Stock in Proctor& Gamble, Merck and Pfizer and is a research Grant Site Principal Investigator for Raptor Pharmaceuticals	Restricted to best available evidence and ACCME content validation statement
Elizabeth Yu	Faculty	Nothing to disclose	N/A
Richard Weimer	Faculty	Nothing to disclose	N/A

NAFLD Umbrella

- Includes any fatty infiltration of the liver >5% by imaging or histology
  - No significant alcohol intake
  - No genetic disease
  - No medications causing steatosis
- This includes all of the following
  - Bland steatosis (NAFL) 66%
  - Steatohepatitis (NASH) 10-15%
  - NAFLD with fibrosis or cirrhosis (3%)

NAFLD- Prevalence in Children

- Prevalence of NAFLD parallels obesity - 2.7 fold since 1980s
- Most common cause of pediatric liver disease; varies by age, gender, race, ethnicity and BMI
- Increased prevalence of NAFLD with certain risk factors
  - Insulin resistance, T2DM, OSA, hypopituitarism, obesity
- Prevalence depends on method use (ALT, imaging, biopsy)

Welsh JA, et al. *J Pediatr* 2013;162(3):496-500e1. Wiegand S, et al. *Int J Obes* 2010;34 910):1468-74. Malespin M, et al. *J Clin Gastroentero*l 2015;49(4):345-9.

Epidemiology

- NAFLD prevalence varies by age and BMI
  - 2-4 yrs = <1%
  - 15-19 = 17%
  - Obese children measured by ALT = 29-38%

Welsh JA, et al. *J Pediatr* 2013;162(3):496-500e1. Rehm JL, et al. *J Pediatr*. 2014 Aug;165(2):319-325.e1

Louthan MV, et al. *J Pediatr Gastroenterol Nutr* 2005;41(4):426-9.
Patton HM, et al. *J Pediatr Gastroenterol Nutr* 2006;43:413-427.

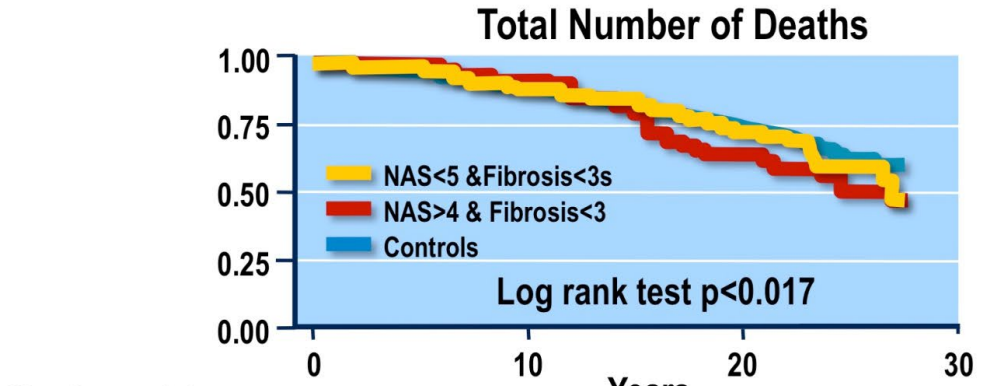
High Risk Features

- Prevalence varies by race/ethnicity
  - Hispanic children have 4-fold increased risk compared with non-Hispanic adolescents (PNPLA3 gene) (12%)
  - Similar in Asians (10%) and Caucasians (8%)
  - NAFLD is relatively rare in black adolescents (1-2%)
- Typically associated with central obesity, insulin resistance, and dyslipidemia (low HDL, high TG)
- Risk factors for severe disease include insulin resistance, diabetes, OSA, & panhypopituitarism, ALT>80, high AST and GGT

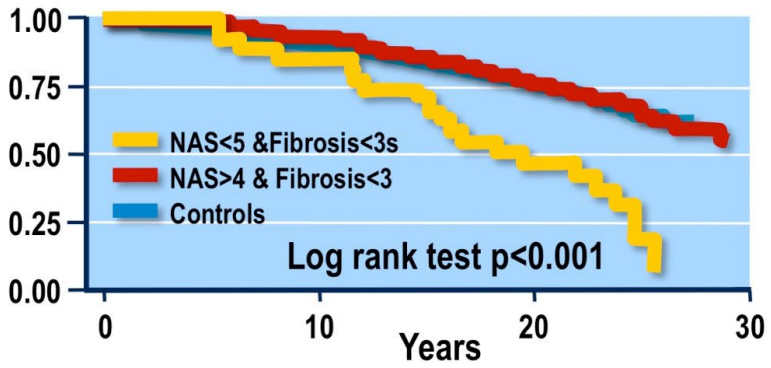
Valenti L, et al. *Hepatol* 2010;52:1274-1280.
Louthan MV, et al. *J Pediatr Gastroenterol Nutr* 2005;41(4):426-9.
Newton KP, et al. *JAMA Pediatr* 2016;170:e161971. Schwimmer JB, et al. *Aliment Pharmacol Ther* 2013;38:1267-77.

Fibrosis and Increased Mortality

- No increase in mortality with NAS 5-8
- No increase in mortality with fibrosis stage 0-2
- Fibrosis stage 3-4, irrespective of NAS with increased mortality (HR 3.3)



Number at risk				
NAS<5 & Fibrosis<3	76	70	61	16
NAS>4 & Fibrosis<3	57	53	39	12
Controls	2286	2085	1818	387



Number at risk				
Fibrosis<3	198	184	156	28
Fibrosis>2	25	21	13	0
Controls	2286	2085	1818	387

Ekstedt M et al. *Hepatol* 2015;61(5):1547-54.
Holterman AX et al. *Obesity* 2013;21(3):591-7.

Pediatric NAFLD: An Aggressive Phenotype?

Comparison of severely obese adults vs. adolescents at bariatric surgery (BMI ≥40)

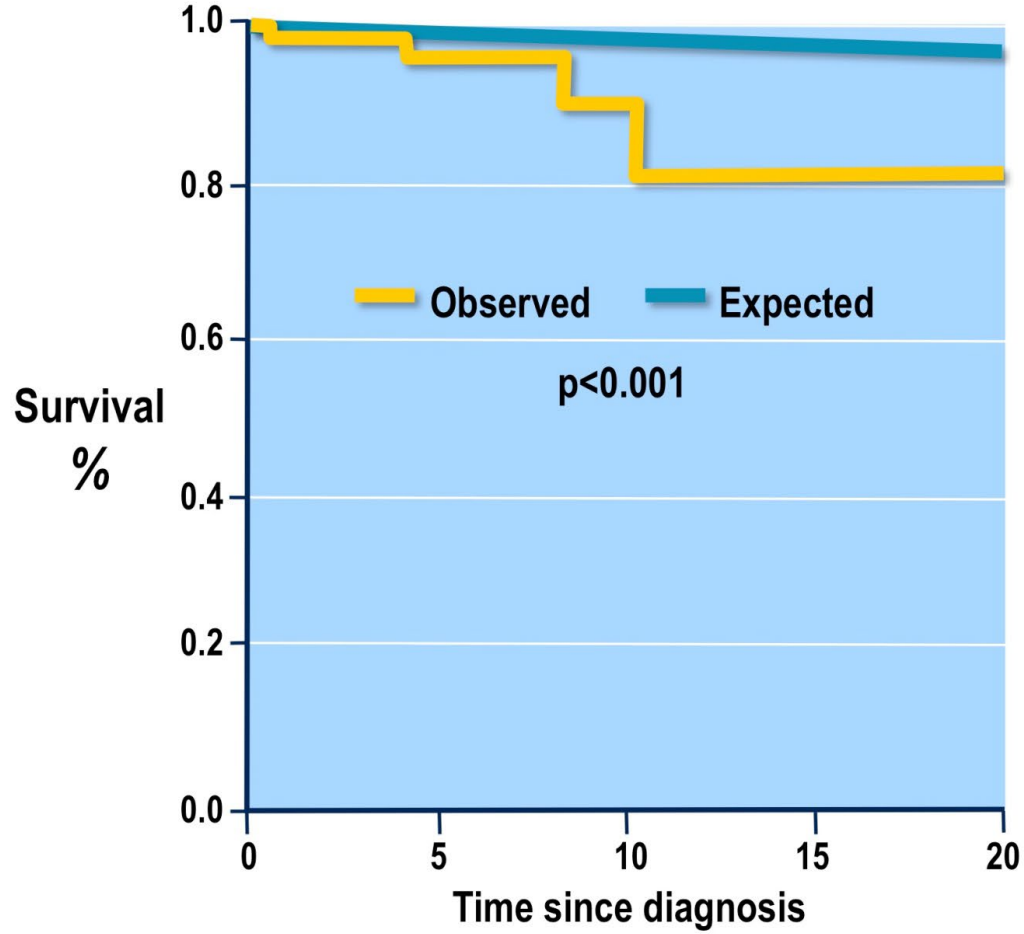
Histologic Feature	Severely obese adults (n=24)	Severely obese adolescents (n=24)	p value
Definitive NASH	25%	63%	0.009
Mean NAS	2.5	3.3	NS
Presence of fibrosis	29%	83%	0.002
Mean fibrosis score	0.4	1.3	0.002

Select adolescents with NAFLD have more advanced disease than comparable adults

Holterman AX et al. *Obesity* 2013;21(3):591-7.

Increased Mortality in Pediatric NAFLD

- 66 children
  (mean age 13.9 years)
  - Mean follow up: 6.4 years (Range 0.05-20 years)
  - Total of 409 person years follow up
  - 4 events
    - 2 patients died, 2 liver transplant
    - Observed vs. expected survival - p<0.001



Feldstein AE et al. *Gut* 2009;58(11):1538-44.

Case Presentation

- 9 y/o obese (BMI 27.46, Z-score +2.26, 122% of the 95th percentile) hispanic female with abdominal pain, constipation, hyperinsulinemia, and hypertriglyceridemia referred from NEW Kids Clinic with AST 125, ALT 264.
- Nl albumin, alkaline phosphatase, bilirubin, GGT, but high protein 9.1.
- Additional workup included normal alpha-1 antitrypsin phenotype, ceruloplasmin, HBV, HCV, Total IgG, ANA, liver-kidney-microsomal Ab, tTG, PT/INR.
- Anti-actin Ab high at 34.
- Although NASH is primary concern even with a positive autoantibody, a liver biopsy was recommended.

Pathology

- Moderate inflammatory infiltrate with lymphocytes, plasma cells, eosinophils with interface hepatitis = autoimmune hepatitis
- Extensive macro- and micro-vesicular steatosis
- Mild periportal fibrosis
- Tissue copper <10 (normal)

Treatment

- MRCP to eval for primary sclerosing cholangitis is normal.
- Started on prednisone and azathioprine for autoimmune hepatitis but also educated about diet and exercise.
- Labs initially improved over 2 months: AST 47, ALT 94, Prot 8.1, but started to increase again with AST 341, ALT 504 1 yr post treatment with AZA levels in normal range.
- Unknown whether ongoing AIH or exacerbation of NASH with prednisone and no improvement in BMI so repeat liver biopsy performed.

Liver Biopsy #2

- Mild-moderate inflammatory infiltrate with lymphocytes, plasma cells, eosinophils with interface hepatitis.
- Diffuse macrovesicular steatosis
- Early bridging fibrosis
- (Worsening fibrosis otherwise no improvement)

Treatment

- Azathioprine switched to mycophenolate mofetil
- Weight management again emphasized
- Encouraged to participate in the NEW Kids program again

What are the Red Flags?

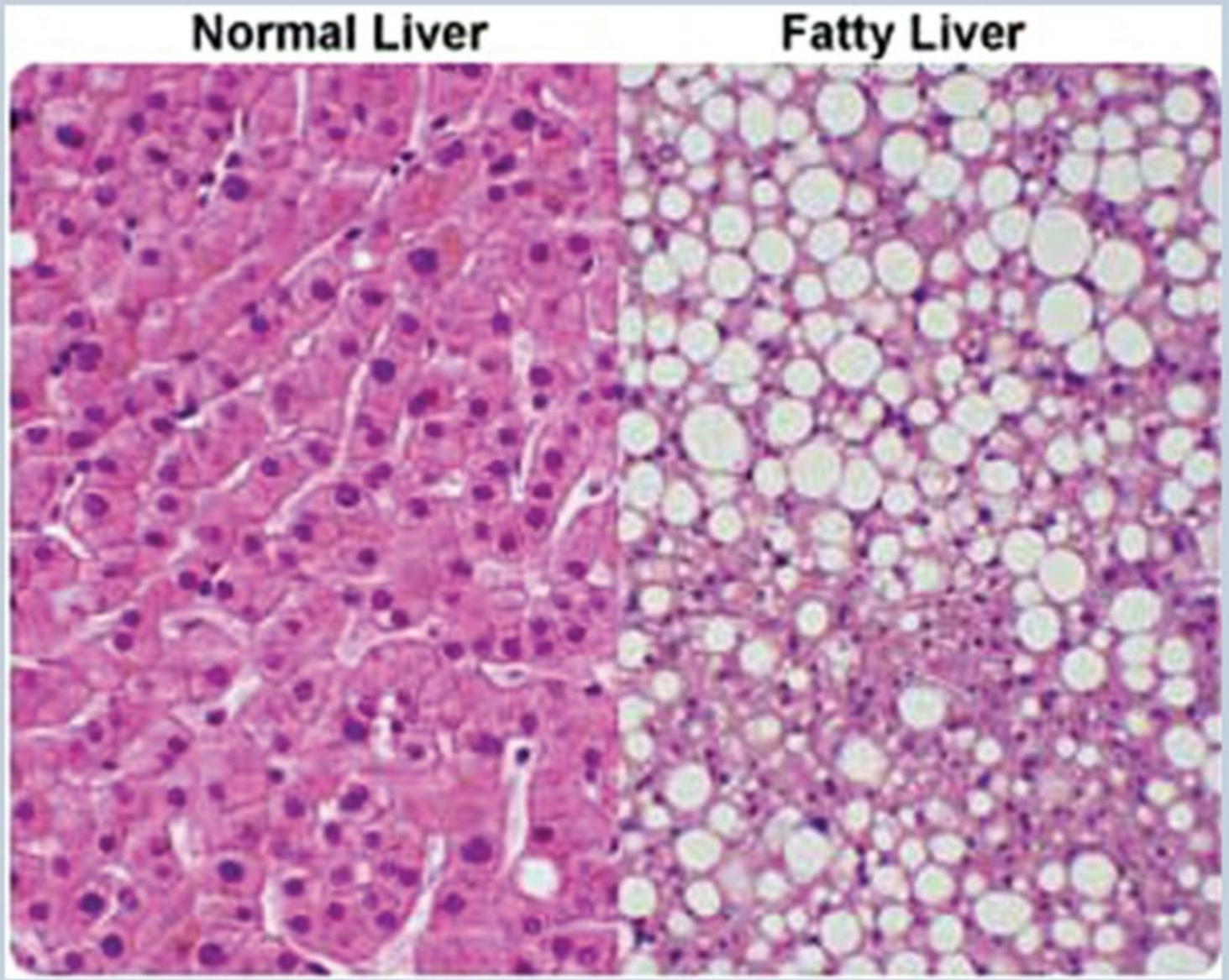
- Typical scenario for fatty liver disease
  - Obese, hispanic, insulin resistance, high TG
- Red flags
  - Female, ALT >80, insulin resistance, high TG, high protein, +autoantibody
- In routine pediatric visit with ALT only
  - Female, ALT>80

NASPGHAN Guidelines

- Recommendations for clinical practice, including screening, diagnosis, treatment, and public health considerations
- Based on formal review of world literature, other guidelines, and experience of expert committee
- Intended for pediatricians, pediatric gastroenterologists, hepatologists, endocrinologists, & preventive cardiologists

Definitions

- NAFL- Hepatic steatosis >5% without inflammation or hepatocyte ballooning +/- fibrosis
- NASH - Hepatic steatosis >5% with inflammation +/- hepatocyte ballooning +/- fibrosis
- NAFLD - Inclusive term indicating fatty infiltration of the liver without evidence of significant alcohol use, genetic/metabolic abnormality, malnutrition, or medication use that causes steatosis


Normal Liver
Fatty Liver

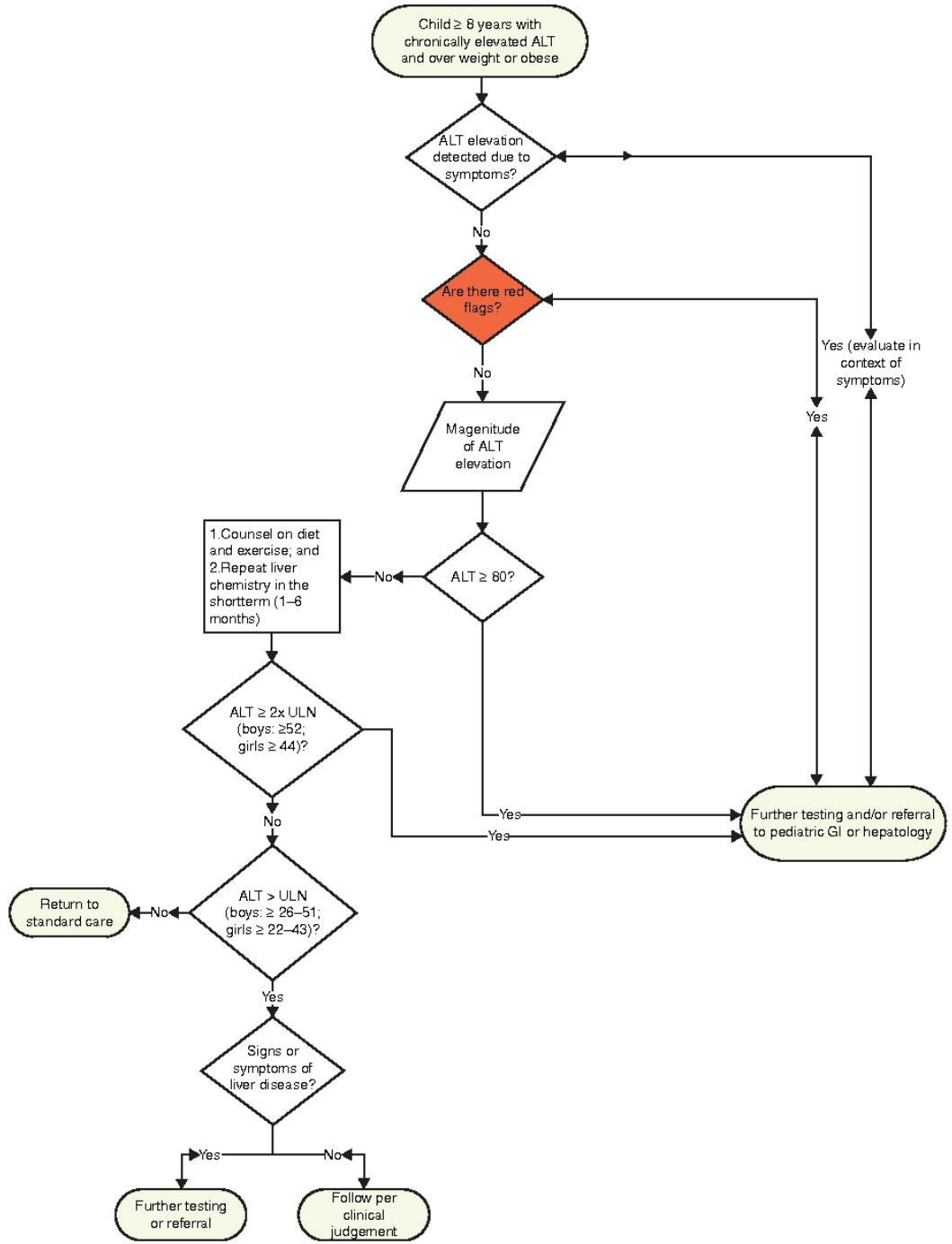
Future Implications

- NASH cirrhosis in the US has increased 6-fold in adults in the last decade
  - Now 2nd leading cause for liver transplant in adults
  - Fastest growing indication for liver transplant due to hepatocellular carcinoma
- Long-term outcomes in children with NASH are unknown but trends are worrisome

. 2015 Mar;148(3):547-55

Screening Recommendations

- Measure ALT in:
  - Obese children 9-11
  - Overweight children 9-11 with risk factors (insulin resistance, DM, central adiposity, OSA, FH NAFLD, dyslipidemia)
  - Consider earlier screening is severe obesity, panhypopit, FH
  - Consider screening siblings if risk factors present
- Repeat ALT in 2-3 years if initial ALT is normal & risk factors persist
- ALT elevated >3 months or ALT >80 warrants further evaluation


Child ≥ 8 years with chronically elevated ALT and over weight or obese
ALT elevation detected due to symptoms?
No
Are there red flags?
No
Yes (evaluate in context of symptoms)
Yes
Magenitude of ALT elevation
ALT ≥ 80?
No
1.Counsel on diet and exercise; and 2.Repeat liver chemistry in the shortterm (1–6 months)
ALT ≥ 2x ULN (boys: ≥52; girls ≥ 44)?
Yes
Yes
No
Further testing and/or referral to pediatric GI or hepatology
ALT > ULN (boys: ≥ 26–51; girls ≥ 22–43)?
No
Return to standard care
Yes
Signs or symptoms of liver disease?
Yes
No
Further testing or referral
Follow per clinical judgement

Evaluation

- Exclude other etiologies of steatosis or hepatitis
- Consider liver biopsy in those with high risk of NASH/fibrosis:
  - ALT >80, splenomegaly, AST/ALT>1, high GGT, DM, OSA, panhypopituitarism
- Consider US to evaluate for portal hypertension, gallbladder disease or masses. Not useful for NAFLD alone.

Lab Evaluation

- Autoimmune
  - Celiac screen, IgG, ANA, Smooth muscle (actin) Ab, Liver Kidney Microsomal (LKM) Ab
- Endocrine/Infectious
  - TSH, free T4, HCV Ab, HBs Ab, HBs Ag, HBc Ab
- Genetic
  - A1AT phenotype, Ceruloplasmin, +/- serum and urine Copper, lysosomal acid lipase

Treatment

- Lifestyle intervention for weight management
- Avoidance of added/free sugar to diet*
- Weight loss surgery
  - Not recommended for NAFLD alone
- No medication/supplement has been approved for NAFLD treatment

Medications

- Although there are no approved medications for NAFLD treatment, there are medications for obesity
- Glucagon-like peptide 1 receptor agonists (semaglutide, liraglutide) - Approved for treatment of diabetes or obesity in pts >12 yrs
  - Shown to cause weight loss (5-15%) via decreasing appetite and delaying gastric emptying in adults and adolescents
  - Decreased ALT/AST in obese teens & adults with T2DM and/or NASH
  - Resolution of NASH on biopsy in 40-60% (48 wks vs 72 wks) vs 9-17% in placebo in adults

Nevola R, et al. *Int J Mol Sci.* 2023; Jan 24(2):1703. Weghuber D, et al. *N Engl J Med* 2022; 387:2245-2257.
Armstrong MJ, et al. *Lancet*. 2016;387:679-690. Eguchi Y et al. *Hepatol Res*. 2015;45:269-278.

Clinical Care for NAFLD

- Screen at diagnosis and at least annually for
  - Diabetes, hypertension, dyslipidemia
- Visits at least annually, more frequent visits for wt mngt
- Consider repeat liver biopsy in 2-3 yrs or with new risk factors

Clinical Care Continued

- Avoid binge drinking, smoking, 2nd hand smoke
- Vaccinate against HAV and HBV
- Check labs before starting hepatotoxic meds
- Consider psychosocial issues and screen for depression/anxiety, poor sleep, bullying
- Assess snoring, daytime somnolence for OSA

Screening

- ALT - preferred first line screening tool
  - Normal cut off for adolescent girls = 22 mg/dL and boys = 26 mg/dL
  - ALT > 2x nl in overweight/obese children >10 yrs has sensitivity 88%, specificity 26%
- Imaging - No modality is recommended for screening due to 1) limited sensitivity/specificity (US), 2) cost (MRI), or 3) radiation exposure (CT)

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Thank you!

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