Goals

• Update knowledge pertaining to two general pediatric topics
• Understand recent changes in diagnostic testing
Objectives

• Examine the presentations and diagnostic evaluations of two patients
• Discuss diagnostic and treatment challenges of each condition
Case 1

- 12 month old FT biracial female with poor weight gain and DD presents to PCP for 12 month WCC
- Mother concerned about stools: still having 5-6/day, appear “cottage cheese-like”
- Dietary hx reveals mostly milk and juice consumption, wide variety of solid foods, no avoidance of certain foods
- No recent travel, city water source, no pets
Case 1

• Pt has life-long hx of FTT, tracking <3rd % for weight, 25th% for ht/HC
• Mild global DD
  – Currently no words, not yet pulling to stand
• Multiple sick visits for AOM, CAP, bronchiolitis
Case 1

• SHx
  – + maternal GC/Ch infection and smoking during pregnancy
  – Lives with married parents, 2 sibs
  – + tobacco smoke exposure
  – No pets

• FHx 3 yo sib with RAD
Case 1

- PE: Add growth chart
  - AF, vitals WNL
  - Petite, thin extremities, pleasant
  - Dev: no words but + vocalizations, sits independently, primitive pincer, engages with examiner
Case 1

• Abdomen without HSM, no T/R/G
• Neuro intact, non-focal, normal tone/strength
• Remainder of exam unremarkable
Case 1
Next Steps?

• Audience response
Case 1

- Screening labs
  - CBC WBC normal, Hb 11.2, MCV 70
  - AST 465, ALT 653, APhos 246, TB nl
  - TFTs normal

- HIV, RPR, Hepatitis panel negative

- Abdominal US normal

- Endocrinology referral
Case 1

- At 20 months, admitted for ongoing symptoms and social complexity
- Wt now at 2nd%, Length 3rd%, HC 25th%
- PE notable for thin extremities, gross motor/speech delay
- Feeding evaluation showed appropriate oral skills and caloric intake of 120 kcal/kg/day with no emesis
- 5-7 large BMs/day, “greasy” per RN staff
Case 1

- BMP normal
- WBC 8.4, Hb 10.6, Hct 32, Plus 244, MCV 66
- AST 206, ALT 263, APhos 216, GGT 12, TB <0.1
- Alb 3.9, coag panel normal
- TFTs normal
- CRP 0.5
Case 1

- GI consult obtained:
  - Total bile acids 7.4
  - Spot fecal fat 3g (24%)
  - Fecal elastase <50
  - ANA + 1:40 speckled
  - Anti-smooth muscle and anti-LKM Abs negative
  - Total IgG 2100, IgM 196, IgA 185
  - Tissue trans-glutaminase 12
  - α-1 anti-trypsin 171
  - Ceruloplasmin 31
  - Plasma amino acids, urine organic acids normal
  - Giardia, cryptosporidia negative
Case 1

- Audience response: Ddx
Case 1

- Ddx
  - Cystic fibrosis
  - Antibody-negative autoimmune hepatitis
  - Defect in bile acid synthesis
  - Metabolic disorder
- Ruled out: celiac, Wilsons, \( \alpha \)-1AT
Case 1

- Sweat chloride normal
- Panc enzyme supplementation initiated, pt began to gain weight and have formed stools
- Subsequent CBCs showing neutropenia, leading to suspicion for Schwachman-Diamond syndrome
Malabsorption

• Typically characterized by malodorous greasy stools, poor weight gain/growth, chronic diarrhea, abd pain/distention, anemia

• >10 g/kg/d stool volume in infants/toddlers, >200 g/d in older children

• >3 loose or watery BMs/day

• Not all have chronic diarrhea!
Malabsorption

- Severe:
  - Vit A def: hyperkeratosis, night blindness
  - Vit B12/folate def: neuropathy, megaloblasts
  - Vit D def: osteomalacia, rickets
  - Vit E def: ataxia, ocular palsy, hemolytic anemia
  - Vit K def: bruising, bleeding, petechiae
  - Protein loss: edema, decreased muscle mass, infection
# Malabsorption: Etiologies

<table>
<thead>
<tr>
<th></th>
<th>Congenital</th>
<th>Acquired</th>
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</table>
| Carb  | • CF/SDS (↓ amylase)  
• Gluc-Glact txp def  
• Sucrase-isomaltase  
• Microvillus inc dz  
• Lactase def                                                                                                                                  | • Mucosal BB damage                                                                                                                   |
| Protein| • CF/SDS (↓ protease)  
• Enterokinase                                                                                                                                                                                                                              | • Nonspecific                                                                                                                            |
| Lipid | • CF/SDS (↓ lipase)  
• Primary bile acid malabsorption  
• Prim intest lymphangectasia                                                                                                                 | • Secondary to liver/GB/pancreatic dz  
• Secondary intest lymphangectasia                                                                                                           |
Malabsorption: Screening

• Blood
  – CBC: leukocytosis, neutropenia, anemia, thrombocytosis
  – CMP, LFTs
  – ESR
  – TTG and total IgA

• Stool
  – WBC, occult blood, calprotectin: inflammation
  – O&P, Giardia antigen, C diff antigen
  – Elastase: pancreatic insufficiency
  – Stool pH, reducing subs: carb malabsorption
  – α-1AT: protein loss
Malabsorption: Stool Studies

- Spot Fecal Fat
- Calprotectin
- Elastase
SDS

- Autosomal recessive disorder caused by mutations in the SBDS gene
- Triad
  - Exocrine pancreatic dysfunction
  - Bony metaphyseal dysostosis
  - Degrees of BM dysfunction (neutropenia)
- Up to 1/3 with MDS or AML
- Multifactorial immune dysfunction
Case 2
Case 2

- 8 yo 👦🏼 with PMH ADHD presenting with spell of altered mental status witnessed by mother at home.
- 2 hours after unwitnessed fall onto linoleum floor, mother found him lying supine on the floor with legs in the air, crying and agitated.
- Mother also noted that his body felt limp.
- ROS + one episode NBNB emesis; - fever, URI, diarrhea, known ingestions/exposures.
Case 2: History

- PMH and PSH otherwise negative
- No medications, allergies
- SH 2nd grade, doing well, many close friends, denies drug exposure, married parents, father active military, mother student
- FH unremarkable
Case 2: PE

- Vitals AF, HR 125, otherwise normal
- Growth parameters 25th %
- Gen alert, mildly anxious, conversive and appropriate
- Neuro notable for mild amnesia to event, mild anxiety, slightly increased tone in UE bilaterally (? cooperation/anxiety) but otherwise entirely intact
- Remainder normal with no signs of trauma
Case 2: Additional Information?

- Word cloud
Case 2: Labs/Studies

- Head CT normal
- CBC normal
- CMP normal
- Urine drug screen negative
- Serum drug screen negative
Case 2: Continuation

• One week later, patient represented to ED with maternal concerns for intermittent agitation and arm stiffening
• New concern for hallucinations and periodic unresponsiveness
• PE now remarkable for agitation/combativeness, no verbalization, bilateral UE hypertension
Case 2: Labs/studies

• CBC, CMP again unremarkable
• Rapid RSV, influenza negative
• EKG NSR with questionable LVH
Case 2: Progression

• While in ED, patient noted to have GT/C seizure for which he was given IV lorazepam
• Transferred to Duke
Differential Dx?

• Word cloud ddx
Case 2: Further Evaluation

- Very broad diagnostic evaluation ensued, most of which was uninformative
- CSF autoimmune encephalopathy panel returned positive for anti-N-methyl-D-aspartate receptor and glutamic acid decarboxylase antibodies
Autoimmune Encephalitis

- Relatively new group of diseases characterized by acute onset neurologic and psychiatric symptoms
- Mediated by auto-antibodies that irreversibly bind to neuronal cell surface/synaptic proteins
- Best characterized is anti-NMDA receptor group
## AE Features

<table>
<thead>
<tr>
<th>Neurologic</th>
<th>Psychiatric</th>
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<tbody>
<tr>
<td>Prodrome (HA, fever, viral)</td>
<td>Anxiety</td>
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<tr>
<td>Memory deficit</td>
<td>Agitation</td>
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<tr>
<td>Abnormal Behavior/Cognition</td>
<td>Bizarre behaviors</td>
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<tr>
<td>Speech Disorder</td>
<td>Hallucinations</td>
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<tr>
<td>Dyskinesias</td>
<td>Delusions</td>
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<tr>
<td>Autonomic dysfunction</td>
<td>Disorganized thinking</td>
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<tr>
<td>Seizures</td>
<td></td>
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<tr>
<td>Central hypoventilation</td>
<td></td>
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<tr>
<td>Cerebellar ataxia/hemiparesis</td>
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</tr>
<tr>
<td>Category</td>
<td>Conditions</td>
</tr>
<tr>
<td>------------------------</td>
<td>-------------------------------------------------</td>
</tr>
<tr>
<td>Infectious</td>
<td>EBV, VZV, HHV-6, CMV, HIV, HSV, entero, arbo, Bartonella, other bacterial, Lyme/spirochetes, fungal, TB</td>
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<tr>
<td>Toxic-Metabolic</td>
<td>Drugs, CO, IEM/mitochondrial</td>
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<tr>
<td>Demyelinating/inflammatory</td>
<td>MS, NMO, ADEM, neurosarcoidoisis</td>
</tr>
<tr>
<td>Rheumatologic/Vascular</td>
<td>Lupus cerebritis, Hashiromotos, Sjogrens, Bechets, CNS vasculitis</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>Schizophrenia, Psychosis, Bipolar, Conversion</td>
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# AE Diagnosis

## Diagnostic criteria for anti-NMDA receptor encephalitis

<table>
<thead>
<tr>
<th>Probable anti-NMDA receptor encephalitis*</th>
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<tbody>
<tr>
<td>All three criteria must be met:</td>
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<tr>
<td>1. Rapid onset (&lt;3 months) of at least four of the six following major groups of symptoms: ¶</td>
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<tr>
<td>- Abnormal (psychiatric) behavior or cognitive dysfunction</td>
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<td>- Speech dysfunction</td>
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<tr>
<td>- Seizures</td>
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<tr>
<td>- Movement disorder, dyskinesias, or rigidity/abnormal postures</td>
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<tr>
<td>- Decreased level of consciousness</td>
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<td>- Autonomic dysfunction or central hypoventilation</td>
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<tr>
<td>2. At least one of the following laboratory results:</td>
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<td>- Abnormal EEG (focal or diffuse slow or disorganized activity, epileptic activity, or extreme delta brush)</td>
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<td>- CSF with pleocytosis or oligoclonal bands</td>
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<tr>
<td>3. Reasonable exclusion of other disorders</td>
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<table>
<thead>
<tr>
<th>Definite anti-NMDA receptor encephalitis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. IgG anti-GluN1 antibodies(^{A}) in the presence of one or more of the six major groups of symptoms, after reasonable exclusion of other disorders</td>
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</table>

AE Diagnosis: Additional Studies

- **Brain MRI**
  - signal hyperintensities on FLAIR or T2-weighted images in affected brain regions (e.g., medial temporal lobes and/or brainstem); subcortical regions and the cerebellum are sometimes affected

- **EEG**
  - “extreme delta brush” characteristic for anti-NMDAR

- **Chest/abd/gonadal imaging** to eval for tumor
AE: Treatment

• Immune suppression and antibody clearance
  – High-dose corticosteroids
  – IVIG
  – Immunomodulators
  – Plasmaphoresis

• 85% make full recovery, 15% relapse
AE: Complications

- Agitated catatonia
  - benzodiazepines
- Delerium/hallucinations
  - avoid antipsychotics!
- Dyskinesia
  - trihexyphenidyl
- Seizures
  - depakote, lacosamine
- Insomnia
  - clonidinle, trazodone, temazepam, melatonin, hydroxyzine
- Dysautonomia
- Orofacial dyskinesia
- Weight loss
- Vomiting
- Constipation
- Transaminitis
- Urinary retention
- Deconditioning
AE: Multidisciplinary Treatment

- Neurology
- PT/OT/ST
- GI
- Nursing
- Quality of Life
- Psychiatry
- Surgery
- Social Work
- Rheumatology
- Hospitalists
- Nutrition
- Family
- Patient
Case 2: Resolution

• Ultimately hospitalized for 78 days
• Treated with 5 day burst high-dose IV corticosteroids and IVIG
  – Repeated corticosteroid dosing q1-2 wks
  – Repeated IVIG x 3
• Rituximab given HD#7
• Slow, gradual improvement
References

• Ammoury RF and Croffie JM. Malabsorptive Disorders of Childhood. *Pediatrics in Review* 2010;31;407