

**6 week old infant boy with
polyuria**

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Med-Peds Endo

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HPI

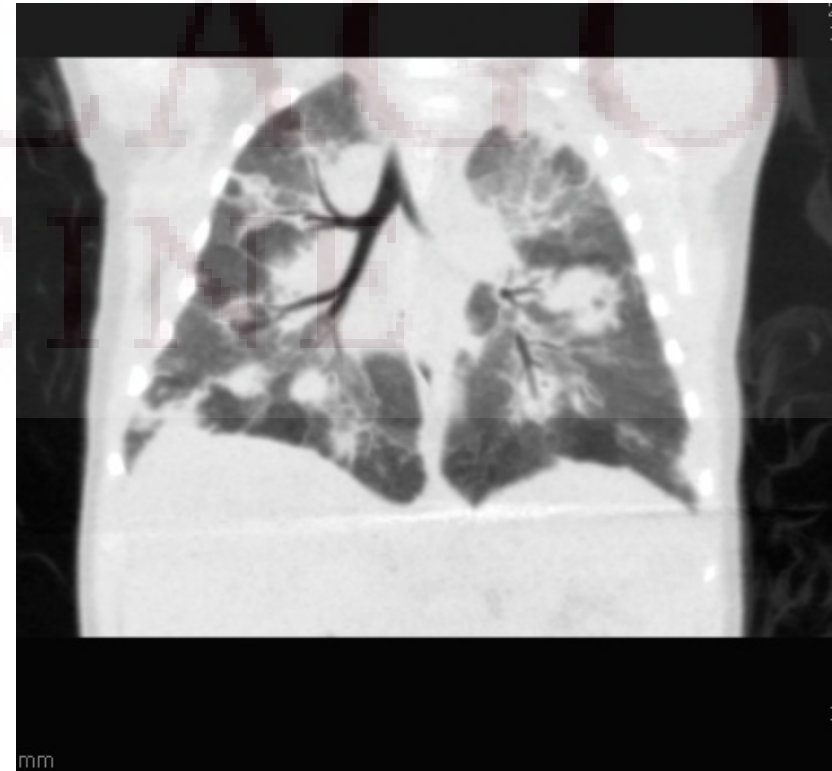
- 6 week old hispanic boy
- Full term, uncomplicated pregnancy
- Well until 3 weeks: irritability, difficulty breathing, poor feeding
URI sx – runny nose, cough
- Hospitalized x1wk – sepsis evaluation negative;
CXR suggestive of bilateral pneumonia
Received empiric abx: azithromycin + clindamycin



Re-Admission



- 1 week after discharge
- Increased work of breathing, persistent cough, difficulty feeding
- CPAP; CXR with bilateral infiltrates: CT
- HD#4 BAL and intubation
IV Abx: Azithro/Clinda
Amphotericin B (conventional)
- HD#7: consult Endo for polyuria for prior 1 day (11.7 mL/kg/hr) and Na rise from 135 to 146



Medical/Surgical History

PMH

- Pneumonia dx age 3wks
- Circumcision

Birth

- Full term, vaginal delivery
- 7lbs 2oz

Developmental

- Smile
- Tracking with eyes

Allergies: NKDA

Meds: Azithro

Clinda

Ampho B (conventional)

Versed

Morphine

Albuterol

Lasix x2 (HD#2, #5)



Family and Social History

Family


- Negative for diabetes or pituitary issues
- Negative for renal diseases
- No early neonatal death

Social

- Living with mother in apartment with mother's friend
- Father not involved
- Strong support from family's church

Physical Exam

Birth Wt 3.2 kg (27%)



36.5 C, HR 157, BP 72/42, RR 44, Wt 3.9kg (5%), Lgth 54.4cm (20%)

Gen: Sleeping/sedated

Head/Face: no dysmorphia, PERRLA, anterior fontanelle flat

Nose: intubated, NG tube

Mouth: mucosa moist

Neck: no thyromegaly, no acanthosis

Resp: +crackles bilaterally

CV: RRR no m/r/g

Abd: Soft, scaphoid, non-tender, no masses

GU: Normal male genitalia, testes descended, circ

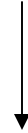
Ext: cap refill <2sec

Neuro: no focal neurologic signs

Derm: pustular/papular rash on face

Fluid and Sodium Data

consult



Hosp Day	#1	#2	#3	#4	#5	#6		#7
Na	135				137	141	146	141
Ins	270	345	365	507	628	794		
Outs	155	245	170	149	415	1090		
Net	+115	+100	+195	+358	+213	-295		
mL/kg/hr	1.7	2.6	1.8	1.6	4.5	11.6		
Urine SG	1.007			1.014			1.006	1.008
Sosm						293	304	288
Uosm							283	
Una							124	

Meds

Lasix

Ampho B

Lasix



Other Labs

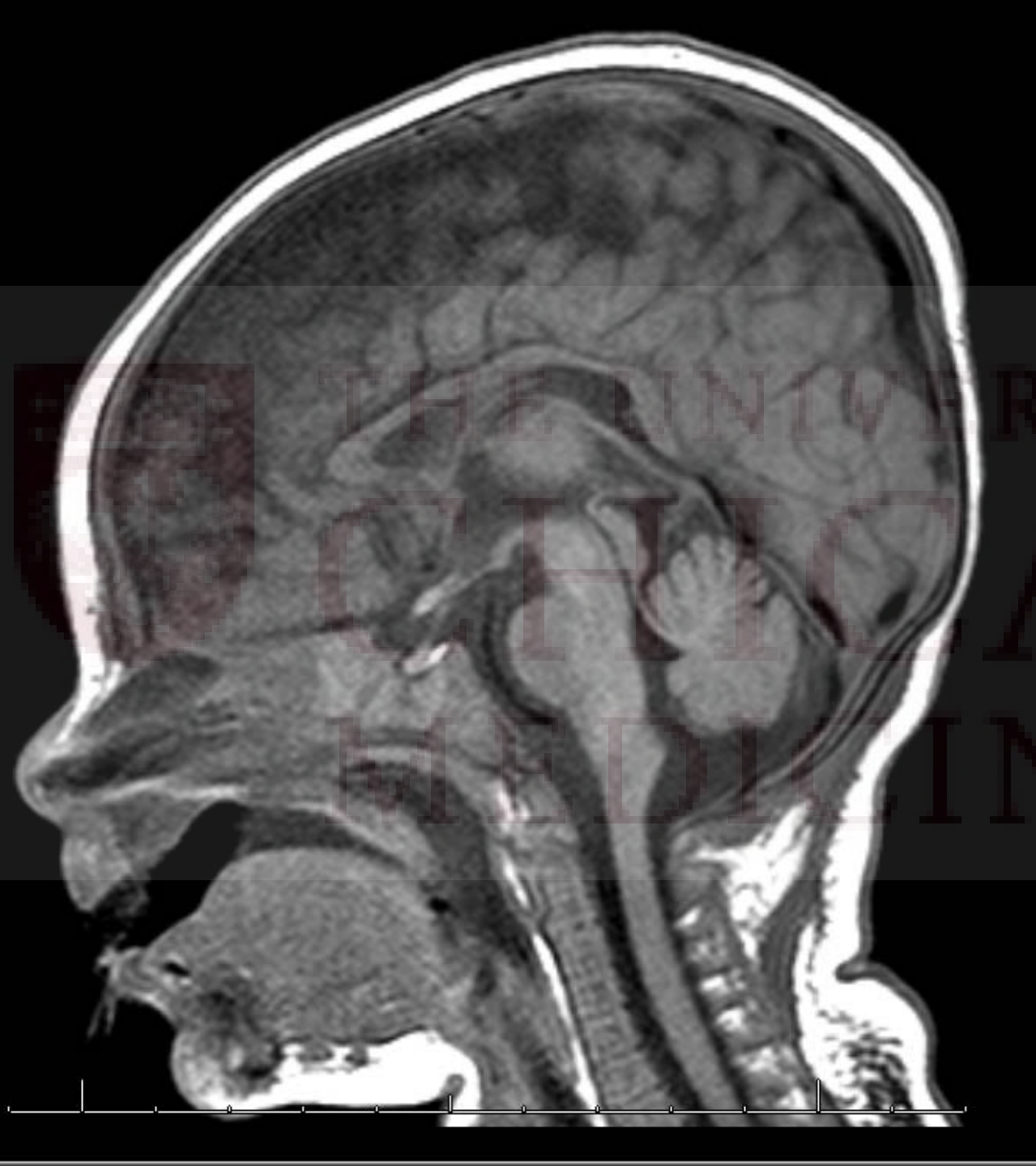
BASIC & COMPREH...		
Glucose, Ser/Pl...	!▲	121 !▲
Sodium		141
Potassium, Ser/...		4.0
Chloride	!▲	106
Carbon Dioxide		27
BUN		8
Creatinine		0.4 !▼
GFR Estimate (C...		<i>Result not calc...</i>
Calcium	!▼	9.2
Inorganic Phosp...		3.8
Magnesium		2.0
Total Protein		

AVP level sent same day – pending
(later came back undetectable)
(concurrent Na by blood gas: 136)

Assessment and Recs

Diabetes Insipidus (central vs. nephrogenic) partial

- Medication induced? Amphotericin B
- Aspergillus-related?
- Congenital? – AVP-R or AQP mutations (nephrogenic)
Prepro-AVP or mitochond 4p16 deletion (central)
- Replace free water losses with hypotonic fluid
- Change Ampho B to alternative formulation
- Continue to monitor Na/I&O's daily
- DDAVP trial or Diuretics/NSAID if recurrence/persistence
- MRI of brain/pit (PICU team already pursuing)



MRI of Brain/Pituitary

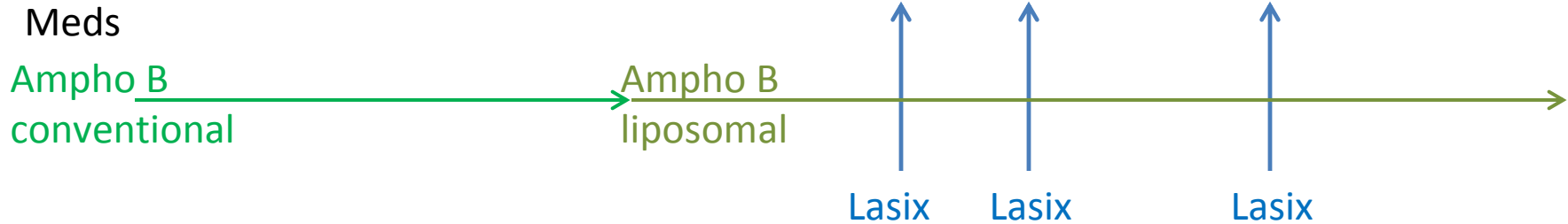
Normal

Fluid and Sodium Data

consult



Hosp Day	#6		#7	#8	#9	#10	#11	#12	#13	#14	#15
Na	141	146	141	136	137	135	137	134	136	134	135
Ins	794		986	753	599	783	688	758	684	471	441
Outs	1090		678	525	532	989	930	628	725	205	263
Net	-295		+308	+227	+67	-205	-242	+130	-41	+265	+176
mL/kg/hr	11.6		6.2	5.5	5.5	10.4	9.8	6.2	7.5	2.2	2.8
Urine SG		1.006	1.008								
Sosm	293	304	288								
Uosm		283									
Una		124									



Clinical Questions

- 1) How do you define polyuria in children?
- 2) What is the mechanism of amphotericin B causing nephrogenic DI – is there a role for changing the formulation?
- 3) Can Aspergillus cause DI and/or pituitary disease?

Polyuria in Children



- Polyuria

urine output >5 mL/kg/hour (Saborio – Costa Rica, PedsinRev 2000)

>2 L/m²/day (Bichet – Montreal, Uptodate 2012)

- Our patient on HD#6:

urine output 1090 mL = **11.6 mL/kg/hr**

0.24m² = **4.5 L/m²/day**

Drug induced DI

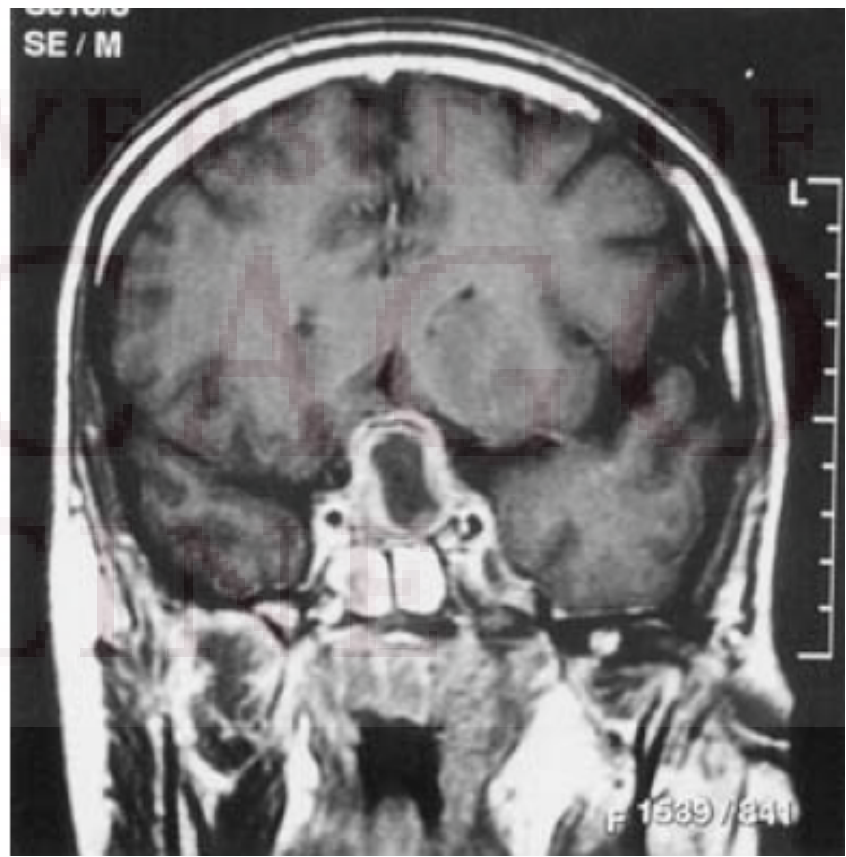
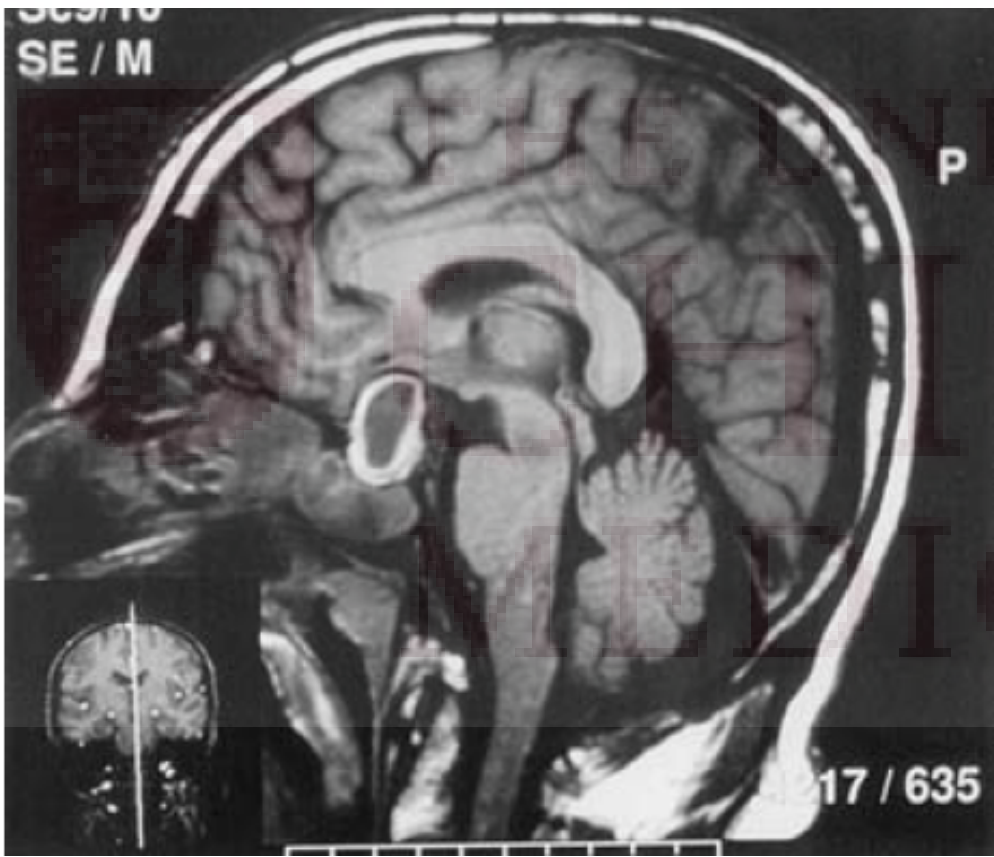
Table 5. Classification of Risk Factors According to Criteria Met for the Causal Association

Risk Factor		
Definite	Probable	Possible
Amphotericin B ²⁸	Colchicine ⁷⁴	Epirubicin ⁹²
Demeclocycline ^{77,78}	Contrast agents ^{93,94}	Hypergammaglobulinemia ^{82,83}
Dexamethasone ⁹⁵	Cyclophosphamide ⁷⁵	Hyperthyroidism ⁸⁷
Dopamine ⁹⁶	Cydofovir ⁹⁷	Hypokalemia ⁹⁸
Hypercalcemia ^{39,81}	Ethanol ¹⁰¹	Netilmicin ⁹⁹
Ifosfamide ¹⁰⁰	Foscarnet ⁸⁰	Polydipsia ^{17,18}
Lithium ^{56,8,59,62,102}	Indinavir ¹⁰⁴	
Ofloxacin ¹⁰³	Lobenzarit ⁸⁴	
Orlistat ¹⁰⁵	Mesalazine ¹⁰⁶	
	Methoxyflurane ^{86,107}	
	Pimozide ¹⁰⁸	
	Rifampin ⁸⁸	
	Streptozocin ^{89,109}	
	Tenofovir ^{90,91,110}	
	Triamterene-hydrochlorothiazide ⁷⁹	

Amphotericin B and DI

- Incidence of NDI with Ampho B uncommon
- Case reports
- Mechanism(s) not fully described
 - prostaglandin excess – degrade AQP channels
 - hypokalemia – defective adenylate cyclase
- 1 report of resolution with change to liposomal form (Spath-Schwalbe 1999)
- 3 reports of liposomal Ampho B causing NDI (Metzger 2009, Canada 2003, Araujo 1998)
- 2 reports lipid complex Ampho B causing DI (Metzger 2009, Hopp 2001)

Aspergillus and Pituitary Mass



Return to Our patient

- Remains in PICU
- Extubated to CPAP, clinically improving
- Transitioning off amphotericin B to voriconazole
- No recurrence of polyuria or hypernatremia
- Probable immunodeficiency: (CGD)
chronic granulomatous disease – impairment
in phagocyte oxidase mechanism

Take Home

- Polyuria in children is defined as urine output $> 5 \text{ mL/kg/hr}$ or $>2 \text{ L/m}^2\text{/day}$
- Amphotericin B is an uncommon, reversible cause of drug-induced nephrogenic DI; changing formulation to liposomal/lipid complex may improve this, though DI also shown with these formulations
- Aspergillus is a rare cause of pituitary abscess

References

- Saborio P, Tipton GA, Chan JC. Diabetes Insipidus. *Pediatr Rev.* 2000;21:122–9.
- Spath-Schwalbe et al. Successful use of liposomal amphotericin B in a case of amphotericin B-induced nephrogenic diabetes insipidus. *Clinical Infectious Diseases* 1999;28:680-1.
- Hopp et al. Amphotericin B-induced partial nephrogenic diabetes insipidus in a child 2001;16:594-597.
- Pinzer et al. Primary aspergillosis of the sphenoid sinus with pituitary invasion – a rare differential diagnosis of sellar lesions. *Acta Neurochirurgica* 2006;148:1085-1090.
- Iplikcioglu AC et al. Aspergillus pituitary abscess. *Acta Neurochirurgica* 2004; 146:521-524.