

Clinical Problem Solving

Case 1

- 46 yo Caucasian man admitted with pneumonia 3 days ago
- During morning rounds he is found unresponsive
- Admitted with sudden onset fever, chills, chest pain, shortness of breath and cough
- Found to have RLL pneumonia

Case 1

- Social history:
 - Alcohol, 1-2 six packs a day, vodka 3-5 x week
- PMHx and FHx unremarkable, no meds
- On admission fever and increased breath sounds in R
- BCx growing α hemolytic Streptococcus at 24 hours
- WBC showed leukocytosis, other labs normal
- On day 2 feeling better, fever trending down, on ceftriaxone and azithromycin

Case 1

- On day 3:
 - Intern walks to see patient in morning and does not wake up after being called
- Exam
 - Somnolent, can be awoken but falls asleep easily
 - Otherwise unchanged, moves 4 extremities, no focal signs, withdraws to pain, reflexes normal, no nystagmus, no asterixis

Case 1

- Head CT normal
- CBC normal
- Na 137, K 3.6, Cl 104, HCO₃ 24, BUN 14, Cr 1, glucose 110, calcium 8.1, gap 9
- LFTs normal
- NH₄ normal
- UA showed 1+ ketones, otherwise negative
- EKG normal sinus rhythm

Case 1

- Another MD works in the room and feels a “funny odor”
- Nurses report no visitors
- Measured osmolality is: 325
- Calculated osmolality is: 285
- Ethanol level: 0

Case 1



Case 1

- Isopropyl alcohol: 82 mg/dL
- Nurse reports that 2 hand sanitizer containers were found empty that morning
- Managed conservatively and started improving later that day

Isopropyl alcohol (IPA) intoxication

- IPA is inexpensive and readily available
- Children
 - Use of rubbing alcohol for fever
 - Accidental ingestion
- Alcoholics
 - Cheap
 - Easy to find (rubbing alcohol, hand sanitizer)
- Suicide attempts

Common sources of IPA

Product	% IPA
Antifreeze	40-55
Frost remover	25-100
Liquid detergent	0-12
Disinfectant cleaners	6-15
Glass window cleaner	0-25
Jewelry cleaner	10-15
Rubbing alcohol	70
Stain spot remover	10-30

IPA toxicity

- Severe toxicity is rare but may be fatal
- Fruity or sweet odor can be mistaken with ethanol intoxication or DKA
- Gastritis, hematemesis
- Central nervous system depression
- Respiratory depression
- Myocardial depression, hypotension and shock
- Presence of acetone in the breath (fruity odor) and urine, in the absence of glycosuria or hyperglycemia, and without acidosis, suggest IPA intoxication

Laboratory findings

- Increased osmolal gap (measured – calculated)
 - Methanol, ethylene glycol, ethanol
 - IPA
- Anion gap acidosis
 - Primary alcohols are metabolized to aldehydes and then to carboxylic acids elevating the anion gap
 - Secondary alcohols (IPA) are oxidized to ketones but under normal physiology are not metabolized to acids
- Increased ketones

Differences in alcohol intoxications

	Methanol	ETOH	IPA	Ethylene Glycol
Characteristic odor	Yes	Yes	Yes	No
Metabolic acidosis	Severe	Mild	No	Severe
Ketones	Ketobutyric	Acetoacetic	Hydroxybutyrate	Acetone
Anion gap	Large	Moderate	Slight	Large
Osmolar gap	Yes	Yes	Yes	Yes
Elevation of serum creatinine	No	Yes	Yes	No
Hypoglycemia	No	Yes	Yes	No
Metabolites	Formic acid	Hydroxybutyric	Acetone	Glycolic acid, oxalic acid
Other findings	Blindness	Acetoacetic acids	Gastritis hematemesis	Crystalluria

Increased plasma osmolal gap

Differential diagnosis of an elevated plasma osmolal gap

With anion gap metabolic acidosis

Ethylene glycol ingestion

Methanol ingestion

End-stage chronic kidney disease (GFR <10 mL/min) without regular dialysis

Diabetic ketoacidosis

Alcoholic ketoacidosis

Lactic acidosis

Formaldehyde ingestion

Paraldehyde ingestion

Without metabolic acidosis

Ethanol or isopropyl alcohol ingestion

Diethyl ether ingestion

Infusion of nonconductive glycine, sorbitol, or mannitol solutions

Severe hyperproteinemia

Severe hyperlipidemia

Management of IPA intoxication

- Rapid intestinal absorption, limited value of charcoal and lavage
- No role for alcohol dehydrogenase inhibitors, metabolite (acetone) is less toxic than IPA
- If awake and hemodynamically stable, supportive care with intravenous fluids is sufficient
- Hemodialysis indicated If comatose, respiratory depression, severe hypotension requiring pressors, or with serum IPA levels > 400 mg/dL

Case 2

- 45 yo Caucasian woman, brought by EMS after passing out
- Seen 1 day prior by relatives, no issues
- Family came to visit, she opened the door and she looked confused
- She went to the restroom and passed out
- EMS called, brought to ER

Case 2

- In ER intubated for airway protection, confused
- Temp 101.6, RR 36, BP 88/50, HR 98
- Lungs: bilateral wheezes and rales

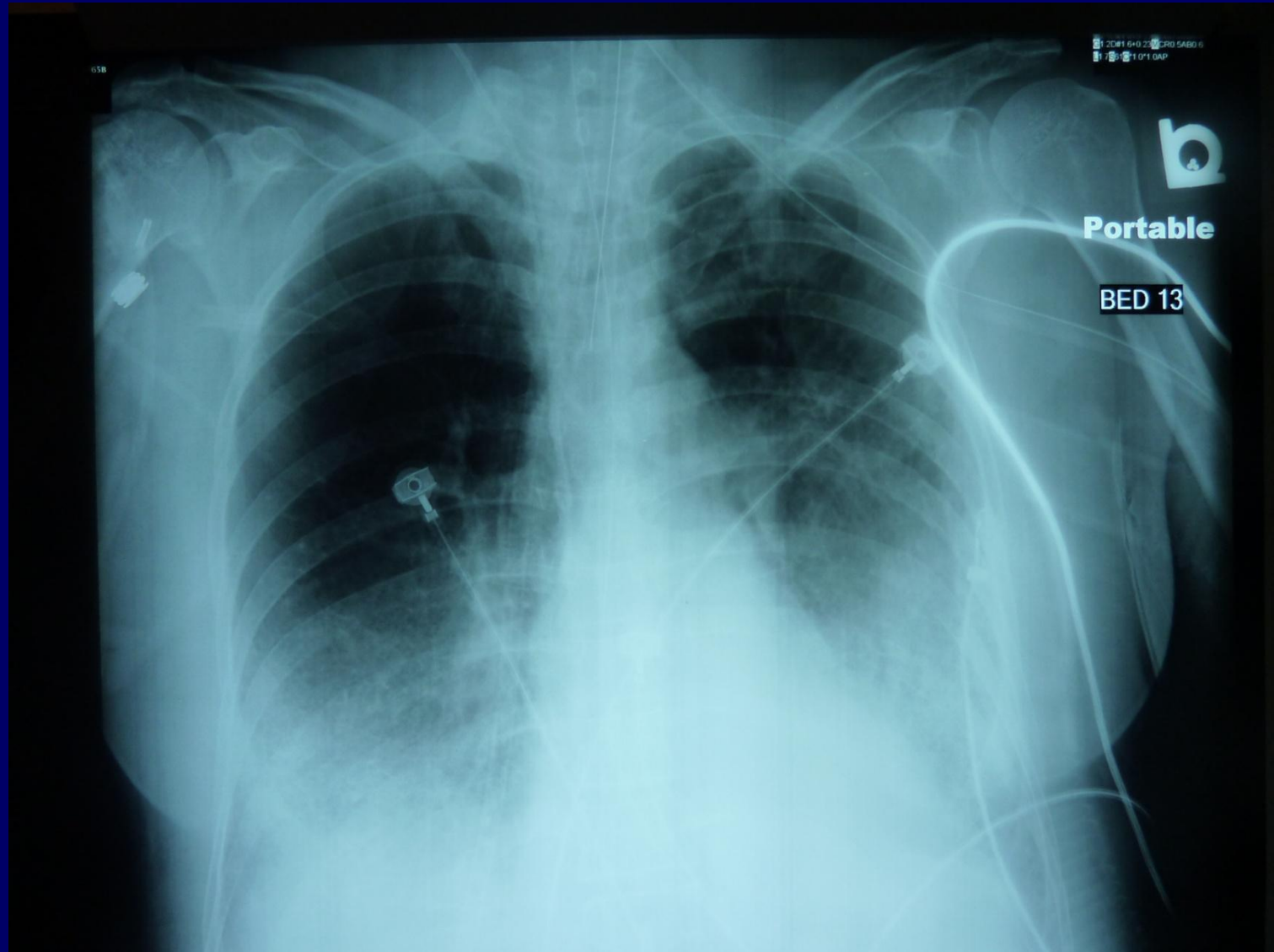
Case 2

- Social history:
 - Alcoholic
 - Tobacco
- Past medical history:
 - Perforated peptic ulcer
 - COPD
 - Hypothyroidism
 - Depression
- Meds:
 - Levothyroxine
 - Citalopram
 - Buspirone
 - Gabapentin
 - Tramadol
 - Esomeprazole

Labs

- WBC 24K (60 P, 25 L)
- Hct 34%
- Plt 162K
- UDS negative
- Na 135, K 3.5, Cl 106, HCO₃ 16, BUN 7, Cr 0.9, glucose 136, gap 13
- ABG: 7.38 / 25 / 58
- No significant osmolar gap
- EKG NSR

CXR



Labs

- ABG after intubation:
 - 7.12 / 46 / 55
- Gap increased

Labs

- Salicylate level 81 mg/dL
 - Therapeutic level <30
 - Toxic level > 40

Salicylate intoxication

- ASA is rapidly converted to salicylic acid in the body
- Also seen after ingestion of topical products that contain salicylic acid (wart removal, ointments)
- Fatal intoxication can occur after the ingestion of 10 to 30 g by adults and as little as 3 g by children
- Peak levels may be delayed for hours, as a result of pylorospasm, bezoar formation, or ingestion of enteric-coated formulations

Salicylate intoxication

- Tinnitus, vertigo
- Fever
 - Uncouples oxidative phosphorylation in the mitochondria generating heat
- Increased respiratory rate
 - Stimulation of medullary respiratory center
- Nausea, vomiting, diarrhea
- Altered mental status
- Noncardiac pulmonary edema
- Hypotension

Salicylate intoxication

- Acid-base abnormalities
 - Respiratory alkalosis, which may also increase lactate production to keep pCO₂ close to normal
 - Gap metabolic acidosis, due to accumulation of organic acids, including lactic acid and ketoacids
 - Metabolic alkalosis from vomiting
- Leukocytosis
- Prolonged PT

Sepsis “features” seen in salicylate toxicity

Fever

Leukocytosis, leftward shift in differential cell count

Hypotension, reduced SVR

Acid-base disturbance (respiratory alkalosis, metabolic acidosis, increased anion gap)

Organ system failure

ARDS

Acute renal failure

Encephalopathy

DIC

“Pseudosepsis” in salicylate toxicity

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Systemic features					
Temperature (maximal), °C	39.2	39.8	38.6	38.8	40.0
White blood cell count (fraction bands), × 10 ⁹ /L	22.7 (0.17)	25.7 (0.23)	11.2 (0.7)	28.8 (0.15)	8.9 (0.37)
Organ system involvement					
ARDS	+	+	+	+	-
Acute renal failure	+	+	-	-	-
			(onset day 3)	(onset day 3)	(onset day 4)
DIC	-	-	-	-	-
	(onset day 3)	(onset day 4)	(onset day 3)	(onset day 3)	(onset day 4)
Encephalopathy	Confusion, coma	Confusion, coma, seizure	Moderate confusion	Marked confusion	Mild confusion
Hemodynamics[†]					
Mean arterial pressure, mm Hg	52	68	83	63	55
Cardiac output, L/min	7.9	7.0	8.5	8.1	5.1
SVR, dynes·cm ⁻⁵ (normal, 900 to 1,400 dynes·cm ⁻⁵)	607	512	770	464	658

Salicylate intoxication

- Supportive, GI decontamination with charcoal
- Fluids, glucose if AMS
- Increase pH with bicarbonate, urine pH 7.5-8, serum (7.5-7.59)
- Hemodialysis: AMS, pulmonary edema, levels > 100 mg/dL, significant renal failure
- Intubation should in general be avoided if at all possible, if done assure appropriate high minute ventilation

Case 3

- 65 year old Caucasian man comes to clinic with rash in the face
- Present for the last 2 years
- On the cheeks and forehead
- No itching or pain, no drainage
- Paid no attention to it for a year
- Saw primary care physician, diagnosed with rosacea, failed to respond to topical creams

Case 3

- Also complains of shortness of breath for the last month
- Worse with activity, 2 flights of stairs
- Mild intermittent chest tightness not associated with activity, 10-40 minutes for a few weeks
- No fevers or chills
- No weight loss

Case 3

- ROS
 - A couple of months of fatigue, dry cough, leg edema, otherwise negative
- PMH
 - HTN for 40 years, type II DM for 10 years, gout, hypothyroidism
- Meds
 - Allopurinol, colchicine, glimepiride, sitagliptan, valsartan, levothyroxine, simvastatin
- SH
 - Lives in AL, retired. No tobacco or ETOH, no drugs

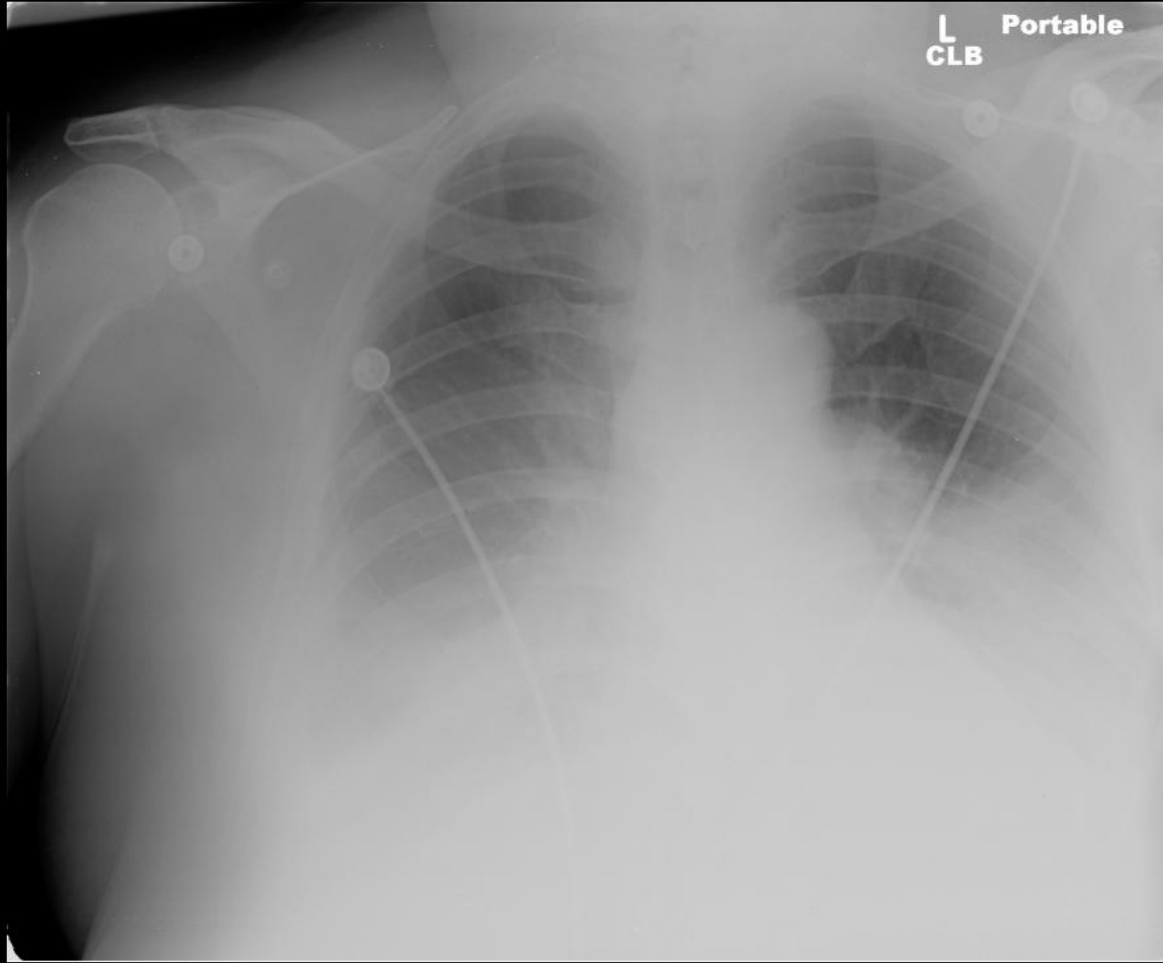
Case 3

- AF, HR 96, RR 22, BP 137/55, sats 94% RA
- HEENT and neck normal, unable to assess JVP
- Lymph, CV, Abd normal
- Resp: decreased breath sounds in both bases, L > R, dullness to percussion
- Ext: pitting edema to mid calf bilateral, pale nail beds
- Neuro: normal
- Skin:.....





CXR



Labs

- WBC 10.3K, Hb 11.9, plt 138K
- ALB 2.7, Na 141, K 3.9, Cl 102, HCO₃ 31, BUN 18, Cr 1.2, Ca 8.5, glucose 225
- PT 12.9, PTT 23
- Trop I <0.01
- Alk phos 50, AST 28, ALT 16, TB 1
- UA 1+ LE, no protein, no blood, no cells
- EKG old changes, nonspecific

Hospital course

- Admitted to cardiology
- MIBI showed fixed and reversible defect in the inferior and lateral wall of left lateral ventricle
- On diuretics he failed to improve and creatinine increased to 2
- Echo normal EF, thickened MV and AV
- Thoracentesis
 - LDH 183 (serum 227), TP 3.9 (serum 6.1), alb 2.1 (serum 2.7), 9075 cells, 81% lymphs

Hospital course

- Flow cytometry
 - Monoclonal lymphoid population with kappa light chains
- IgA 167, IgG 1080, IgM 1330
- SPEP: paraprotein present, IgM
- Viscosity 2.5 (<1.8)
- Bone marrow
 - Clonal B cell lymphoplasmacytic aggregates (20% of marrow), kappa light chain
- Diagnosed with Waldenstrom's macroglobulinemia

Waldenstrom's macroglobulinemia

- Syndrome of IgM monoclonal gammopathy and lymphoplasmacytic lymphoma in the bone marrow
- IgM macroglobulinemia not unique to WM
 - Also may be seen with MGUS, CLL, a number of lymphoma variants, primary amyloidosis
- 3 per million per year, median age at diagnosis is 64
- Much more common in Caucasians

Symptoms of WM

- Asymptomatic in up to 25%
- Non-specific
 - Weakness, fatigue, weight loss
- Related to infiltration of tissues
 - Anemia, lymphadenopathy, hepatosplenomegaly
- From monoclonal IgM
 - Hyperviscosity: blurred vision, headache, dizziness, confusion
 - Neuropathy: usually sensory, demyelinating

Less common manifestations of WM

- Recurrent infections from IgG deficiency
- Cryoglobulinemia
- Renal, GI, bone
- Lung
 - Pleural effusion, pulmonary infiltrates, mass
- Skin
 - Purpura, skin infiltration producing macular or papulonodular lesions, facial lesions

Skin lesions in WM



Lab findings in WM

- Anemia, neutropenia, thrombocytopenia, lymphocytosis, monocytosis
- Rouleaux formation in blood smear
- Bone marrow shows lymphoplasmacytic lymphoma
- SPEP/IFE reveals a monoclonal IgM
- Serum viscosity may be increased
- Diagnosis:
 - Monoclonal IgM + lymphoplasmocytic lymphoma

Differential diagnosis of rosacea

- Acne
- Seborrheic dermatitis
- Perioral or steroid dermatitis
- Carcinoid syndrome
- WM
- Demodex infection
- Systemic lupus erythematosus
- Cutaneous TB
- Sarcoidosis

Differential diagnosis of rosacea



Final messages

- Keep in mind the diff dx for increased osmolal gap
- Recognize differences in the presentation of the different alcohol intoxications
- Suspect ASA toxicity in the setting of respiratory alkalosis
- Alkalinize in salicylate toxicity, be careful with intubation
- Recognize manifestations of WM