Case #4:
TB, Diabetes, Relapse and Recovery

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Stop TB Partnership of Tennessee

Objectives of this talk

- List risk factors for poor clinical response to standard anti-tuberculosis therapy and risk for relapse of TB disease.
- Define therapeutic measures which may accelerate clinical improvement of TB disease in patients with diabetes.

Case presentation – take 1

- 60 year old with a long standing smoking history and recent diagnosis of DM
  - 2 to 3 month history of not doing well
    - decreased energy level, malaise
    - weight loss
    - at some point developed subjective fevers
    - cough, not severe – no hemoptysis
    - denied night sweats
    - received a couple courses of antibiotics – “sinus infections”
  - Eventually these symptoms plus SOB and anorexia prompted his admission to the local hospital

Case presentation – take 1

- A little more history
  - About a month prior to this admission
    - evaluated at an ER with presyncopal episode
    - negative cardiac work-up
      - EKG, holter and cardiac enzymes [elevated glucose]
  - About 10 days prior to admission - f/u in PCP office
    - orthostatic?
    - HbA1C – 9.1 so metformin started
    - symptoms: chilling, fever, slight cough -> sinus infection
  - Admission time
    - pt: SOB, unable to eat fam: confusion, forgetful
    - glucoses were elevated

Case presentation – take 1

- The patient is admitted with the aforementioned symptoms
  - glucose control
  - work-up of the mental status changes
- He has an abnormal CXR -> prompts a CT chest
  - multiple bilateral PE's [among other things]
  - doppler U/S – bilateral lower extremity DVTs
  - he is also felt to have pneumonia
  - treated with anticoagulants and antibiotics
- With little improvement, more fever -> transferred to a hospital in Chattanooga

Case presentation – take 1

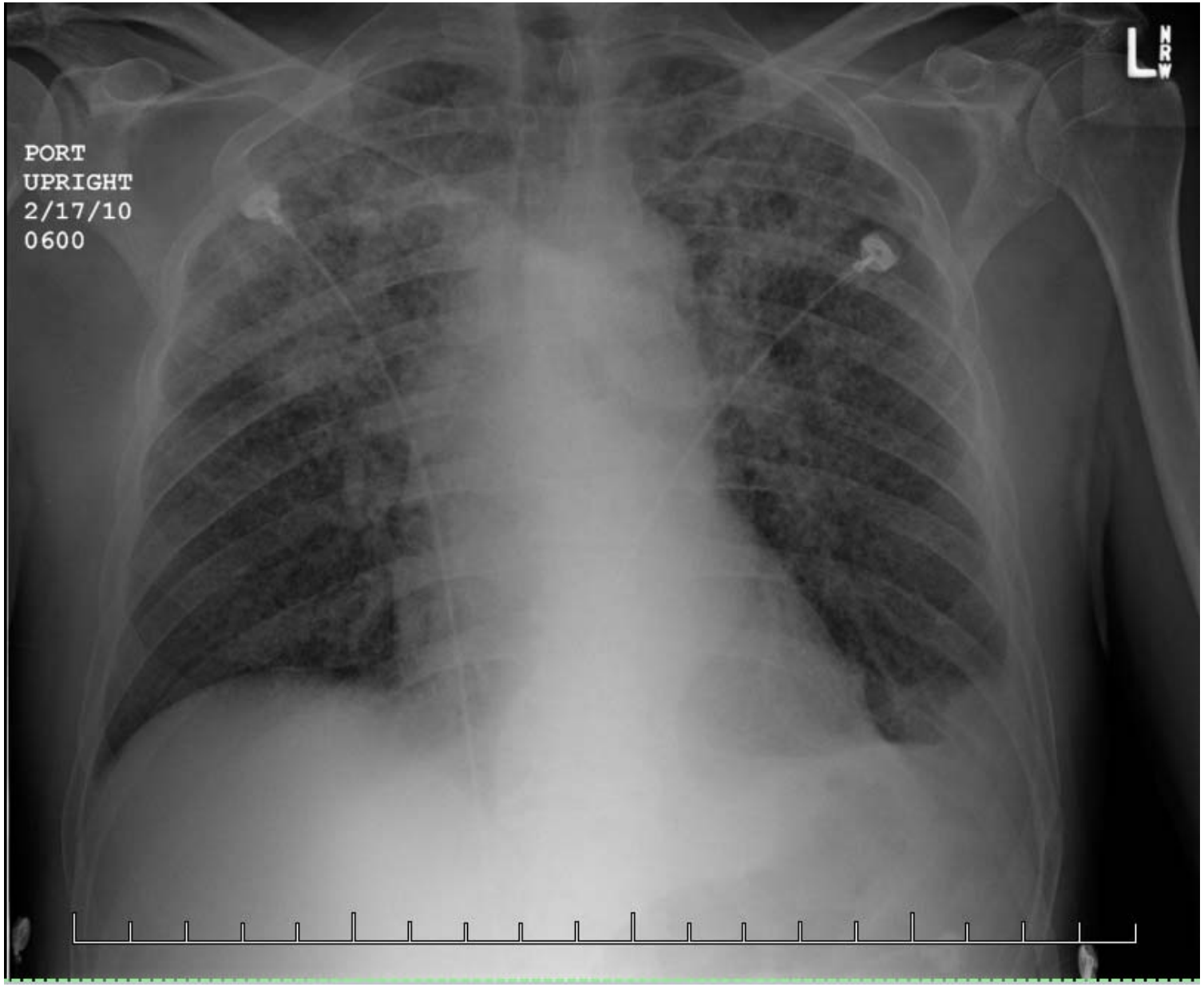
- PMH
  - knee surgery 10 yrs ago complicated by a peri op DVT
  - recent diagnosis of NIDDM
  - allergies – streptomycin [?rxn]
  - no known TB exposure
- Social history
  - lives alone, widower
  - works as a mail carrier for 24 years
  - EtOH – a few drinks (beer) on the weekends, occ. Bar
  - 15-20 year smoking history (cutting back last 8 mo)
  - no travel history – lived in the area all his life

Case presentation – take 1

- Family hx
  - History of thrombotic problems; father with lung cancer
- Physical exam
  - 60 yo looks older than stated age – disheveled and unshaven
  - Tm 102/Tc 99.3 BP 138/92 P 88 R 22 (sat 98%) 82kg (180)
  - HEENT oral cavity clear; edentulous
  - lungs clear, no crackles, wheezes or rub
  - heart RRR with soft systolic murmur LLSB
  - abdomen benign
  - extremities venous stasis changes in the LLE, no cellulitis and no significant edema

Case presentation – take 1

- Lab data on presentation
  - WBC 11.2 Hgb 12.3 plt 186
  - BMP ok Cr 1.1 LFT normal except AST 60 alk phos 171
  - alb 2.2 with prealbumin of 4.3
- Echocardiogram
  - normal LV function EF 60% - dilated LA MVP with mod MR
- Doppler ultrasound legs
  - extensive clot in both lower extremities
- Head CT
  - no gross abnormality



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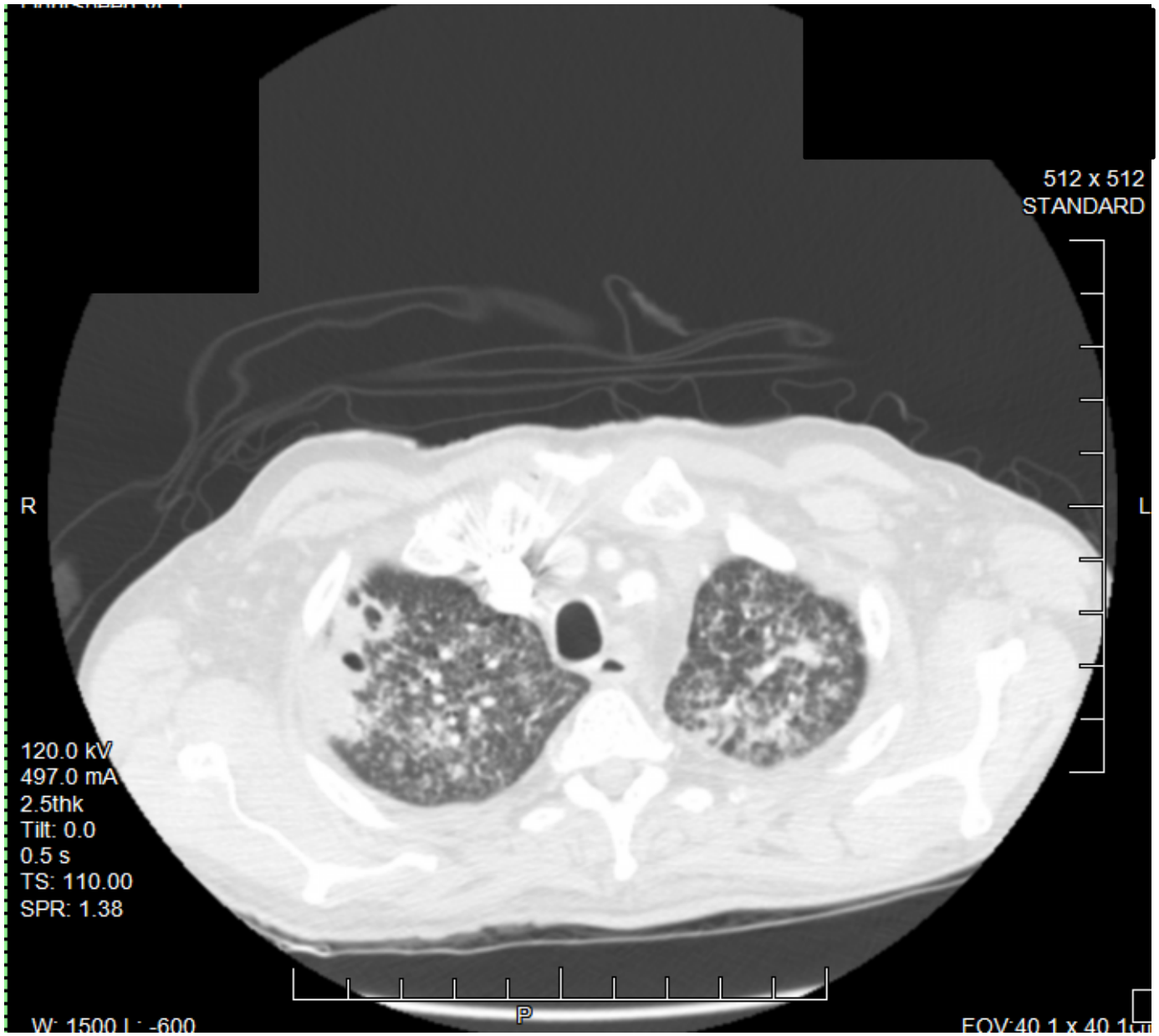

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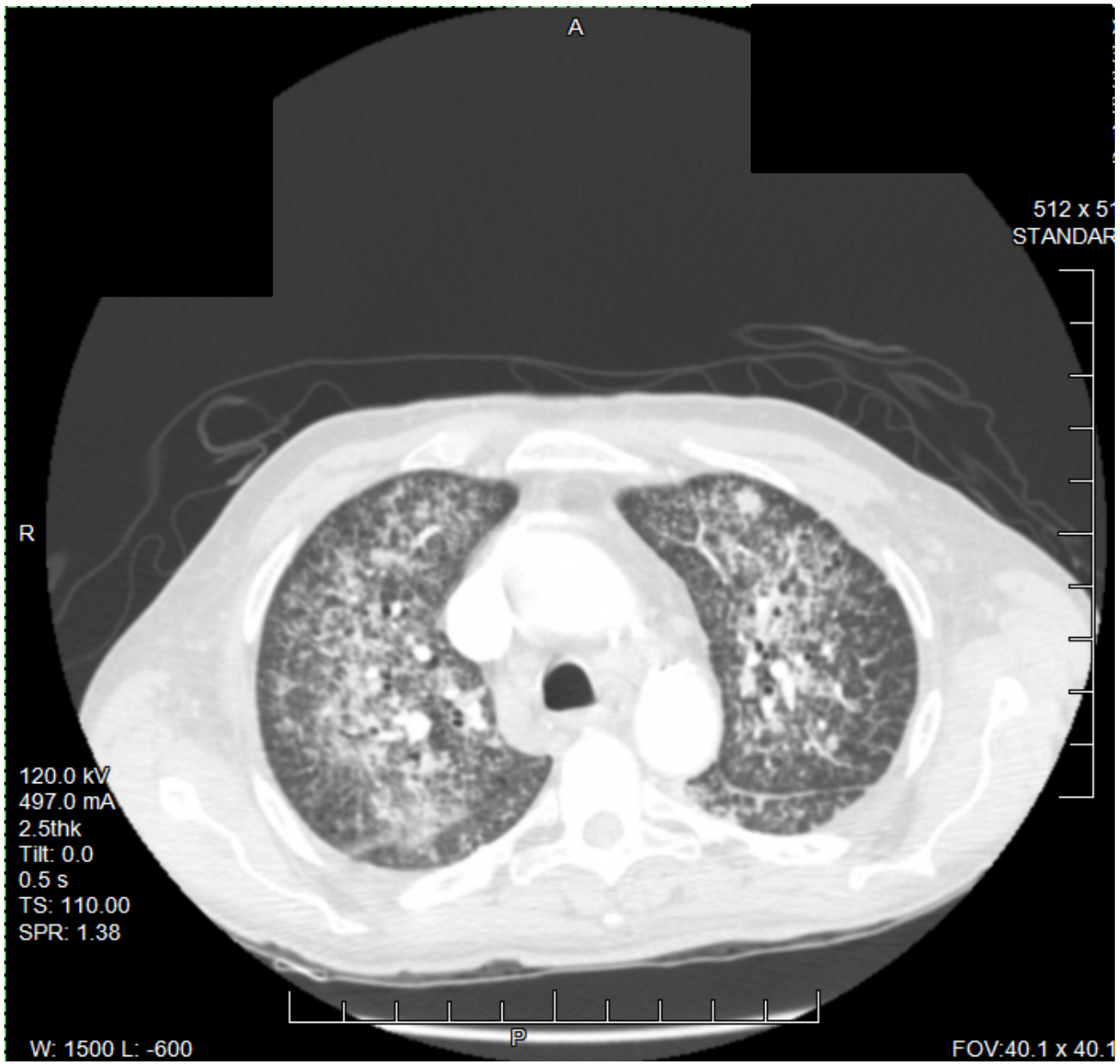

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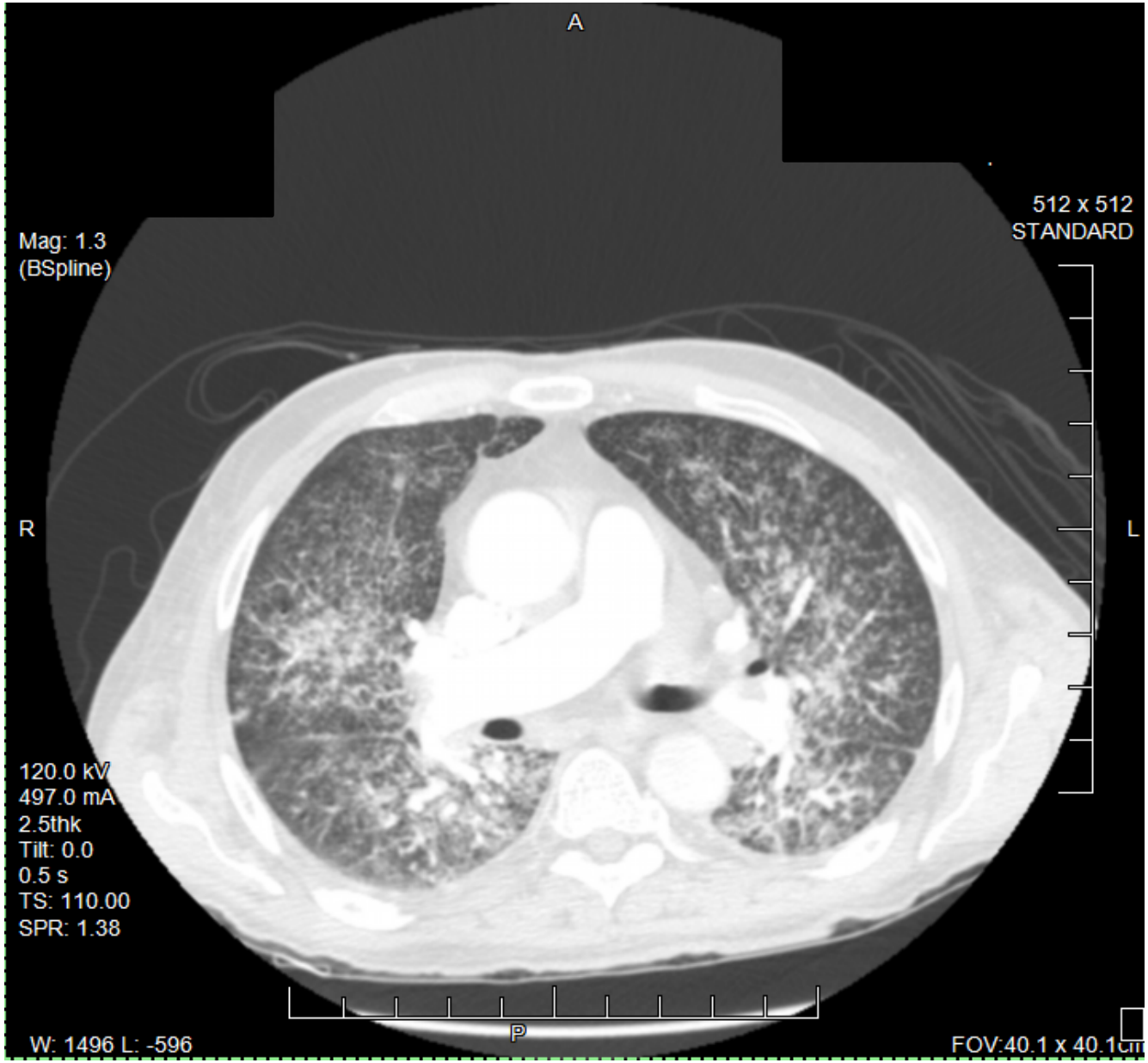

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Case presentation – take 1

- Early interventions
  - BS antibiotics: vancomycin, ceftriaxone, azithromycin
  - anticoagulation – heparin -> anticipated bronch
  - IVC filter

  Pulmonologist: wt loss, clotting, mediastinal nodes → cancer
- ID consultation
  - PPD, check HIV, antigens for histo, blasto, crypto and ANA
  - check sputa for AFB, in agreement for bronch if sputa neg
- Some early data
  - PPD, HIV, ANA, crypto ag all negative; no sputum produced

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Case presentation – take 1

- Clinical course:
  - Rapidly progressive down hill course
    - lethargy → obtundation
    - remained highly febrile
    - respiration labored and ineffective
    - worsening chest x-ray
  - Resulted in emergent unit transfer
    - intubation
    - pressor support
    - broader antibiotics
    - urgent bronchoscopy

  3 bronchial washings were sent and all 3 with numerous AFB and was immediately started on 4 drug MTB therapy

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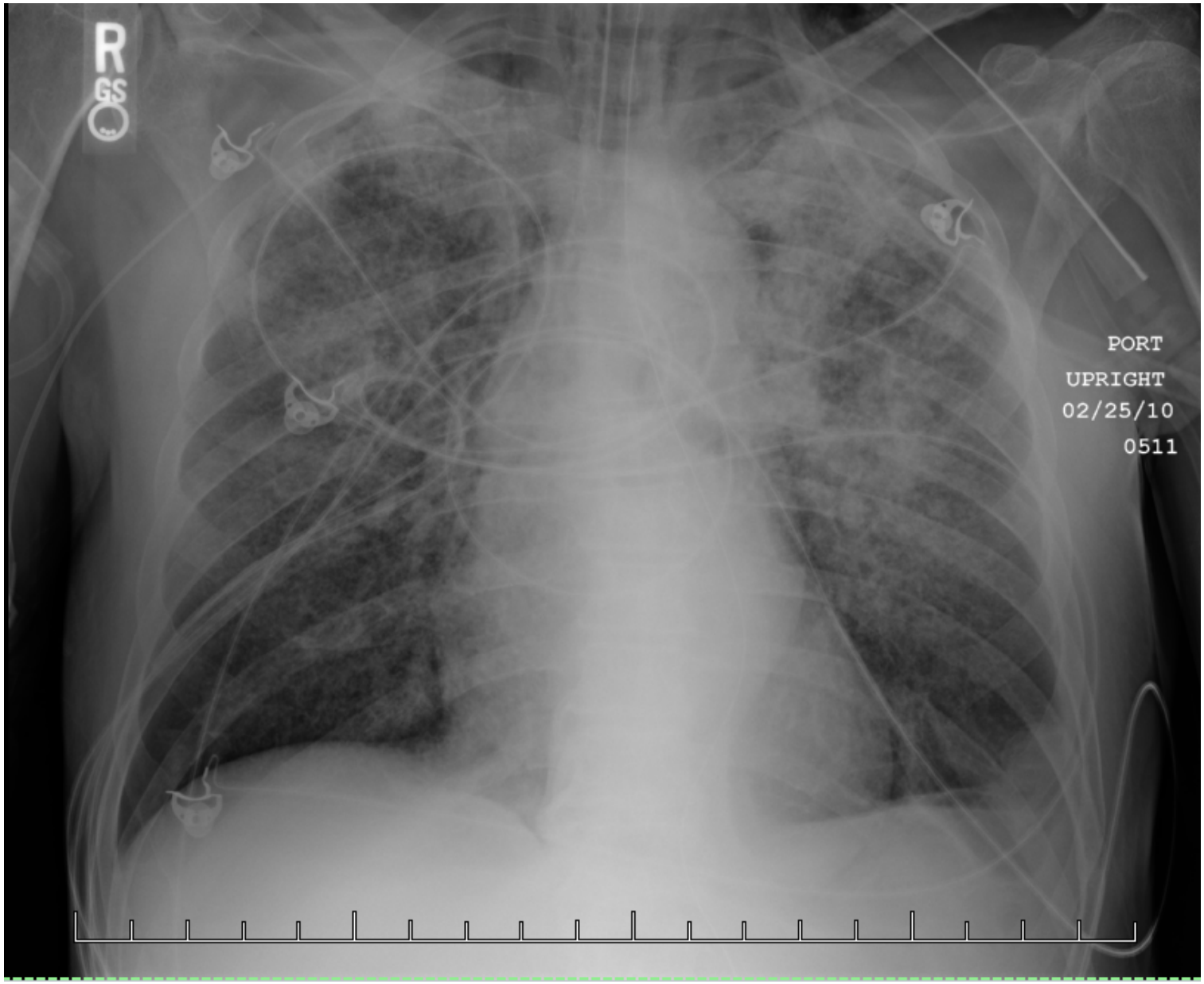

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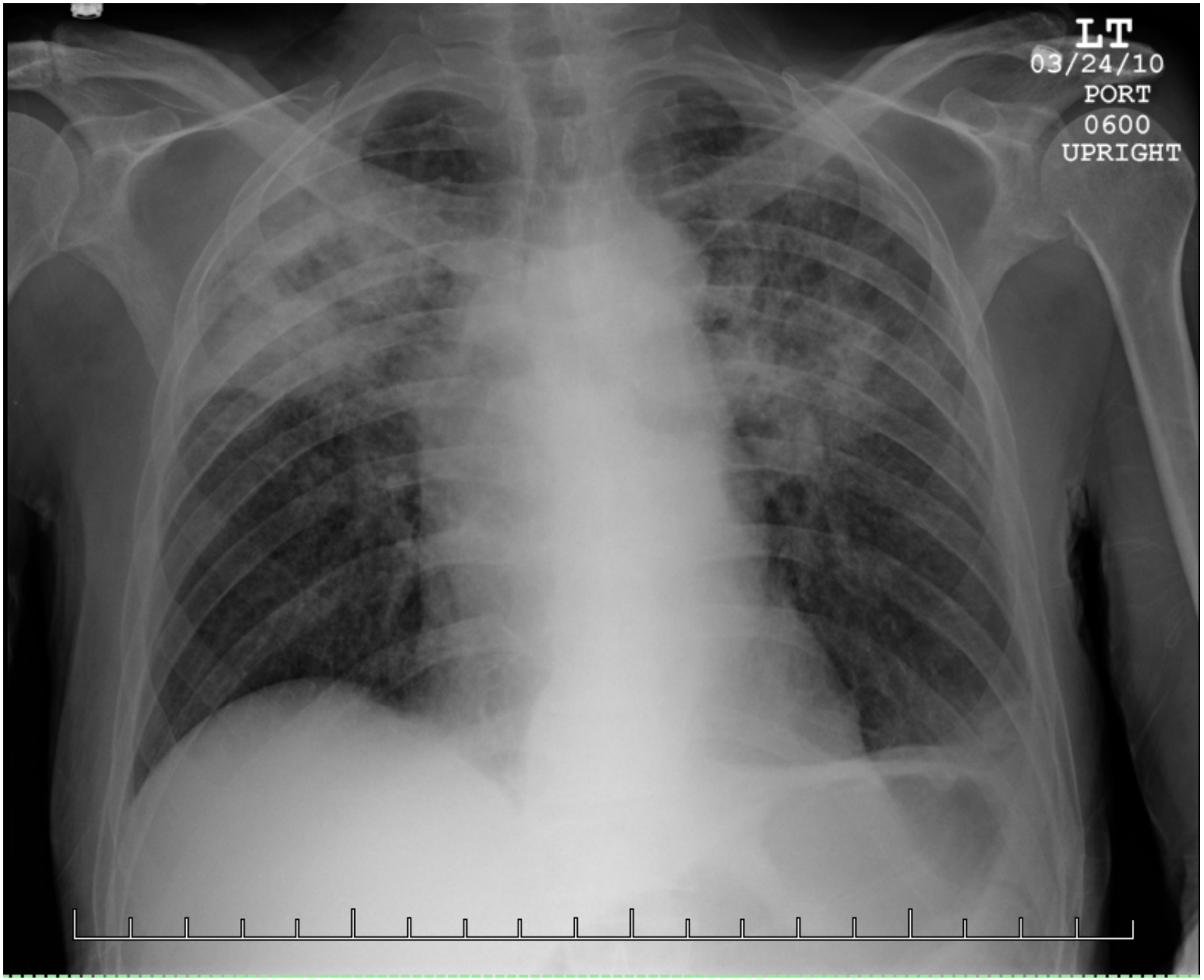
Case presentation – take 1

- His course was far from smooth
  - spent about 10 days on the ventilator
  - once extubated was on bi-pap for 7 days
  - developed AKI [Cr 0.8 → 2.8 – with hypernatremia]
  - mental status was down for quite some time
  - nutrition was difficult – NG tube, considered PEG
  - developed a HA pneumonia with pseudomonas
  - marked decrease in exercise capacity
  - elevated lipase and alk phos → possible GB disease

He was discharged on hospital day 55



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Case presentation – take 1

- The patient was followed in the SE region thru the completion of his therapy
  - he converted his sputa within 2 mo of initiating therapy
    - he received just over 6 months of therapy
    - much of the therapy was 5 days per week (5 months)
  - marked clinical improvement [wheelchair → walking in]
  - appropriate weight gain 154 → 185 [voracious appetite]
  - chest x-ray showed extensive scaring in the upper lobes
  - final follow-up film was about 8 months from diagnosis
  - plan was to follow him as needed thereafter

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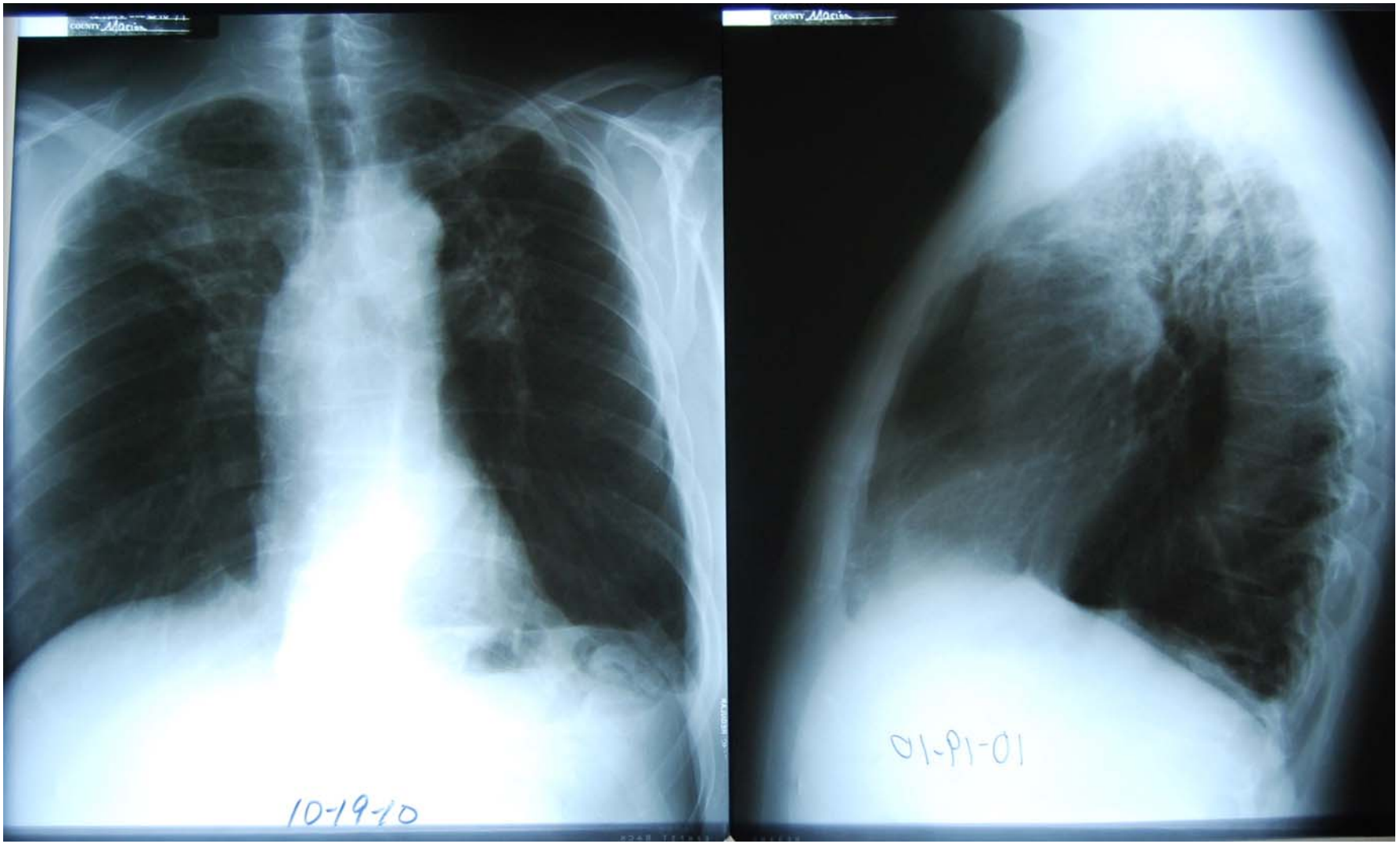
CXR October 2010



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Case presentation – here we go again

- Interim history
  - 4 years after we had last seen the patient
    - had shortness of breath and found to have significant CAD
    - underwent coronary bypass surgery
    - lost some weight around that time [to about 170 lbs]
  - states that he felt better after treatment of TB
    - regained weight and appetite
    - never gained all his strength back
    - not sure he is compliant with diabetic diet

Case presentation – here we go again

- About 10 months after bypass [5 yrs post TB Rx]
  - Pt presented with a 1 week history
    - intermittent chills
    - feeling feverish
    - sinus drainage
    - sore throat – right side of the throat, quite severe
    - anorexia with weight loss
    - decreased energy
    - hematuria
    - some shortness of breath – no real cough or sputum

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Case presentation – here we go again

- Past history
  - NIDDM
  - HTN
  - hyperlipidemia
  - CKD – baseline 1.4-1.8
  - AAA 4.5 cm – being observed
  - CHF – EF 40%
  - hx DVT and PE – s/p filter
  - CAD – s/p CABG
  - hx TB s/p treatment
  - hx knee surgery
  - BPH
  - hx cystitis

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Case presentation – here we go again

- Physical exam
  - chronically ill appearing in NAD
  - T 97.3 P 109 BP 136/82 R 20 100% sat on RA
  - HEENT dry mucus membranes, no pharyngeal erythema, no tonsillar exudate; no nodes
  - heart tachycardic without murmur or rub
  - lungs clear bilaterally
  - abd nondistended, non-tender normal bowel sounds
  - skin tenting noted to suggest dehydration

Case presentation – here we go again

- Data
  - Laboratory
    - CBC – WBC 10.0 H&H 16/45 plt 416
    - BMP Na 134 HCO3 16 BUN/Cr 92/4.45
    - troponin negative BNP 45
    - UA large blood and LE → 95 RBC >182 WBC - culture neg
  - Post void residual 95
  - EKG normal sinus with L anterior fasicular block

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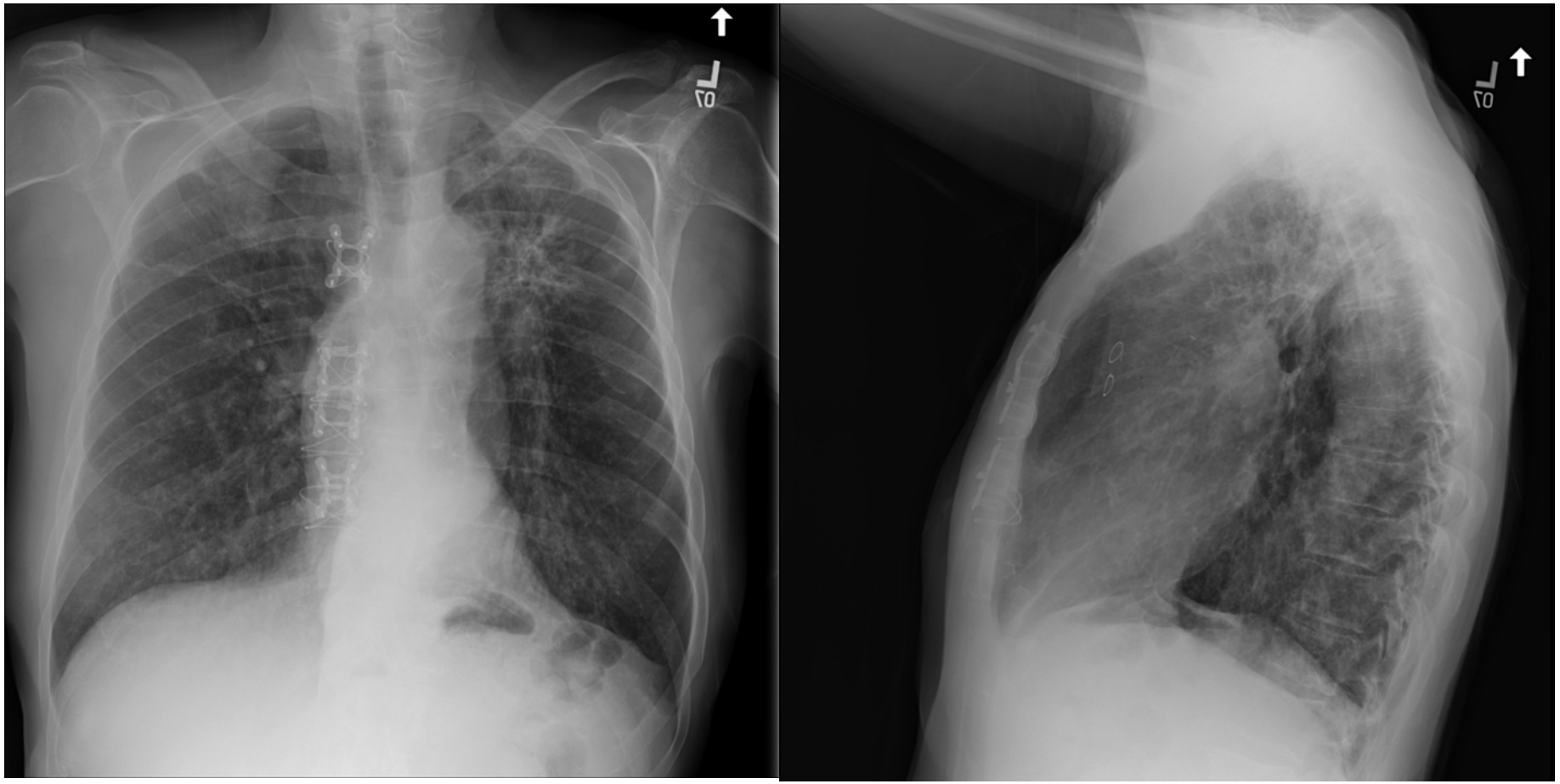
CXR



Case presentation – here we go again

- Interventions
  - IV fluids as the pt was felt to be dry
  - Renal ultrasound – bilateral hydronephrosis
  - CT chest – pts complaint of dyspnea
- Consultations
  - Pulmonary
  - Urology - CT of the abdomen to explain hydronephrosis

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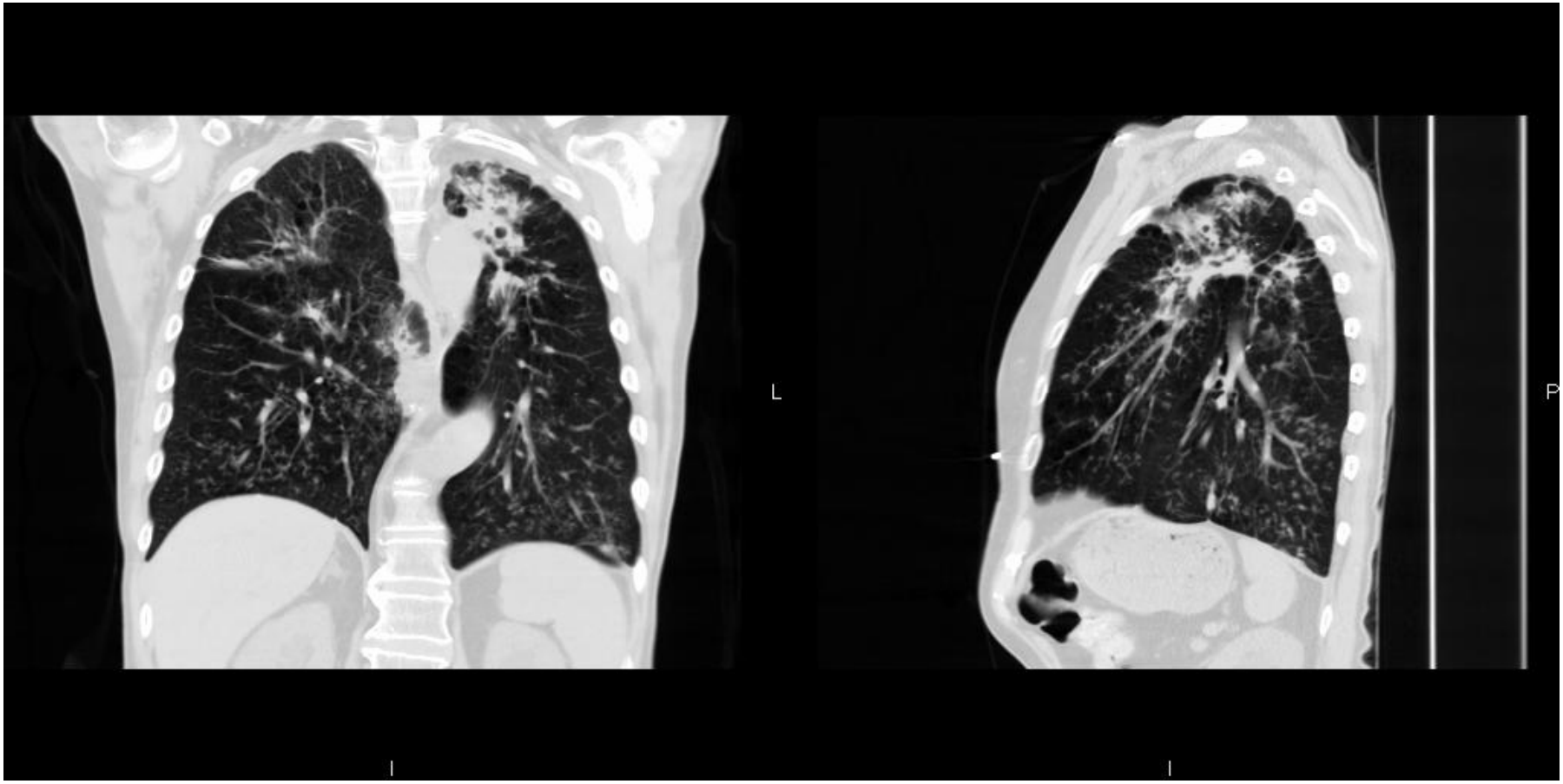
CT Chest



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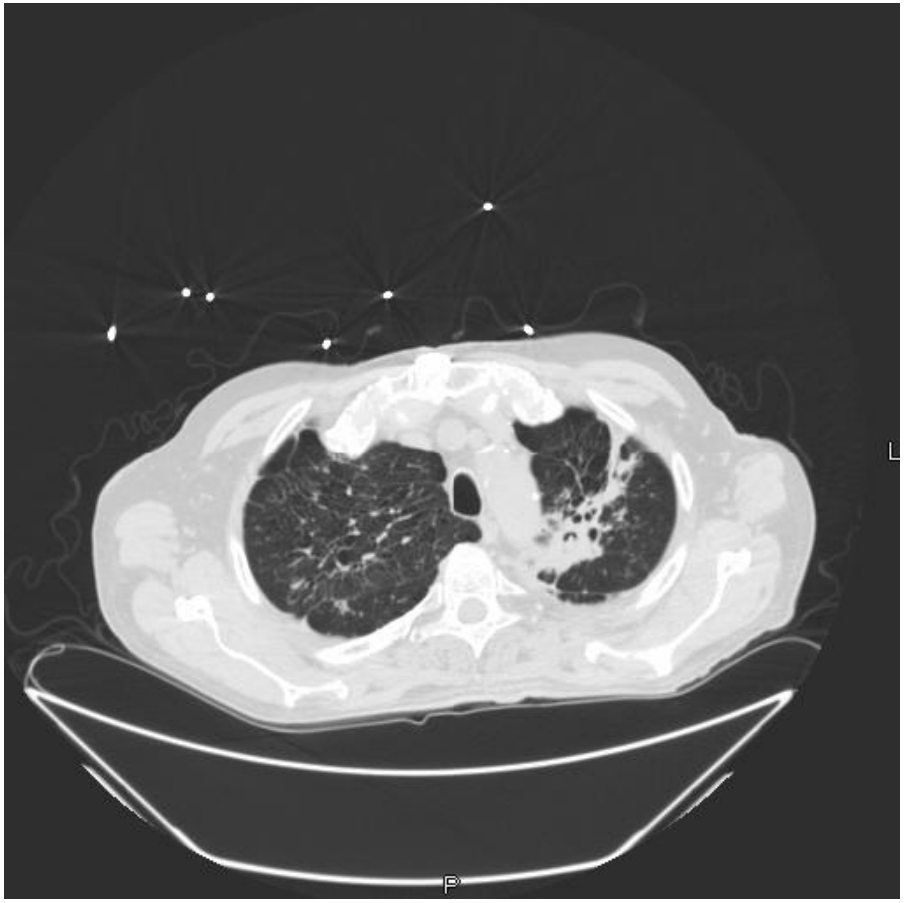
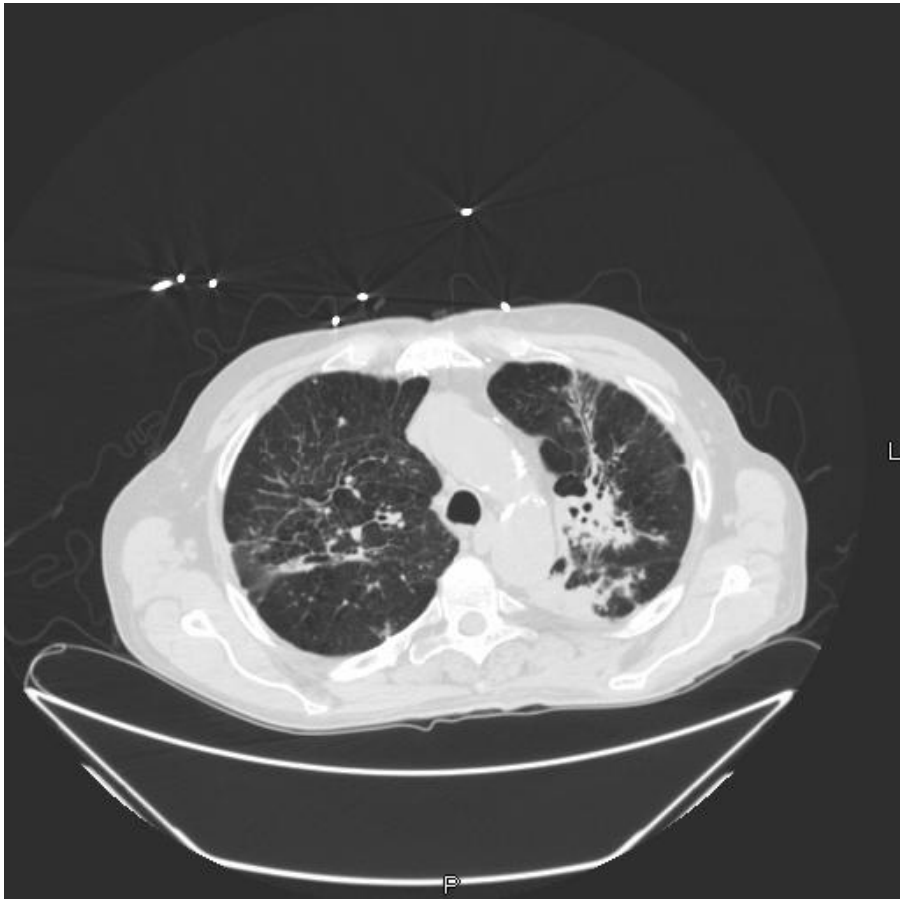
Chest CT





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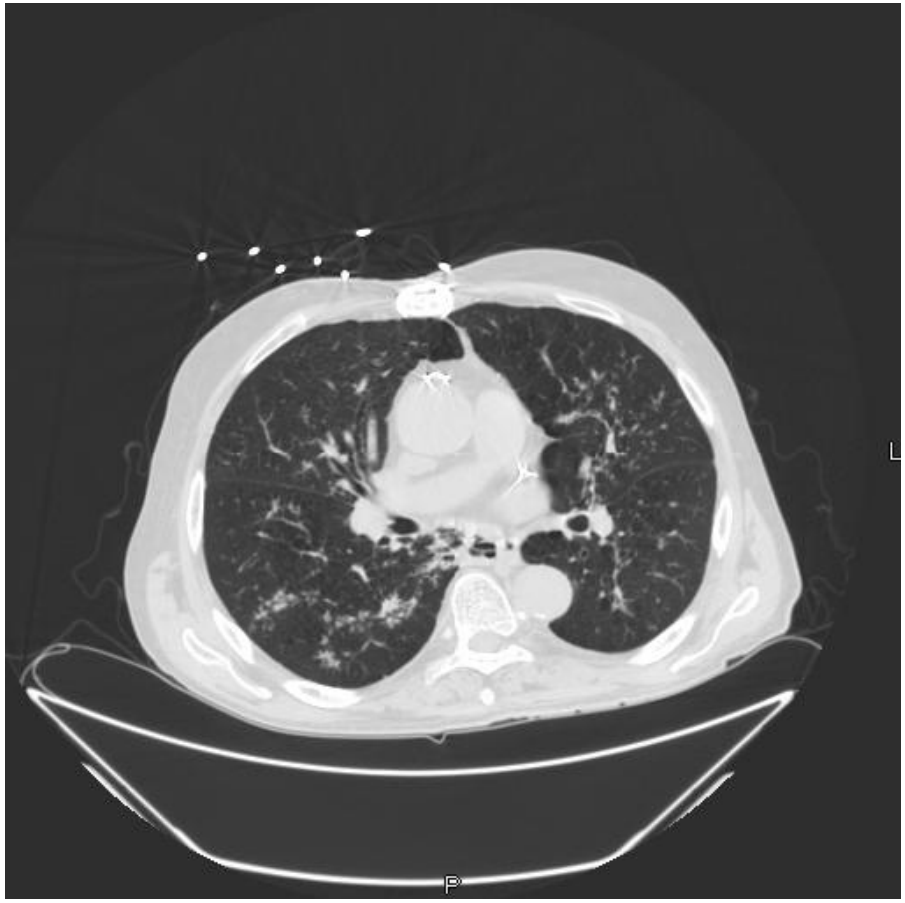
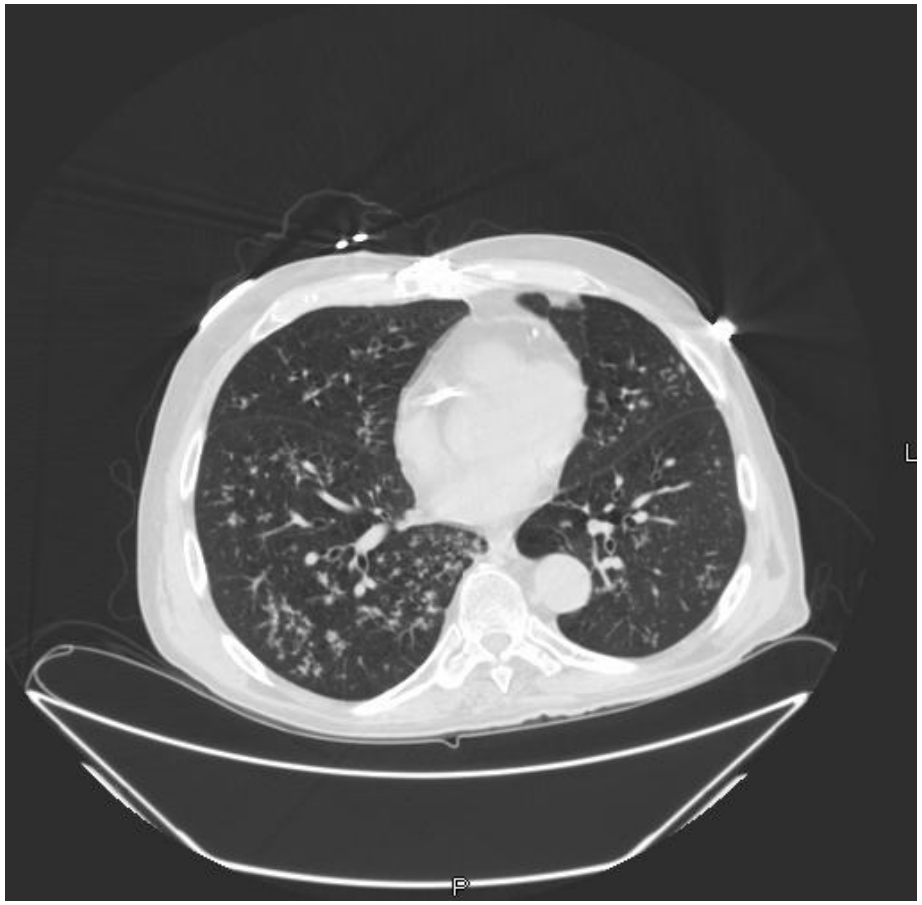
Chest CT





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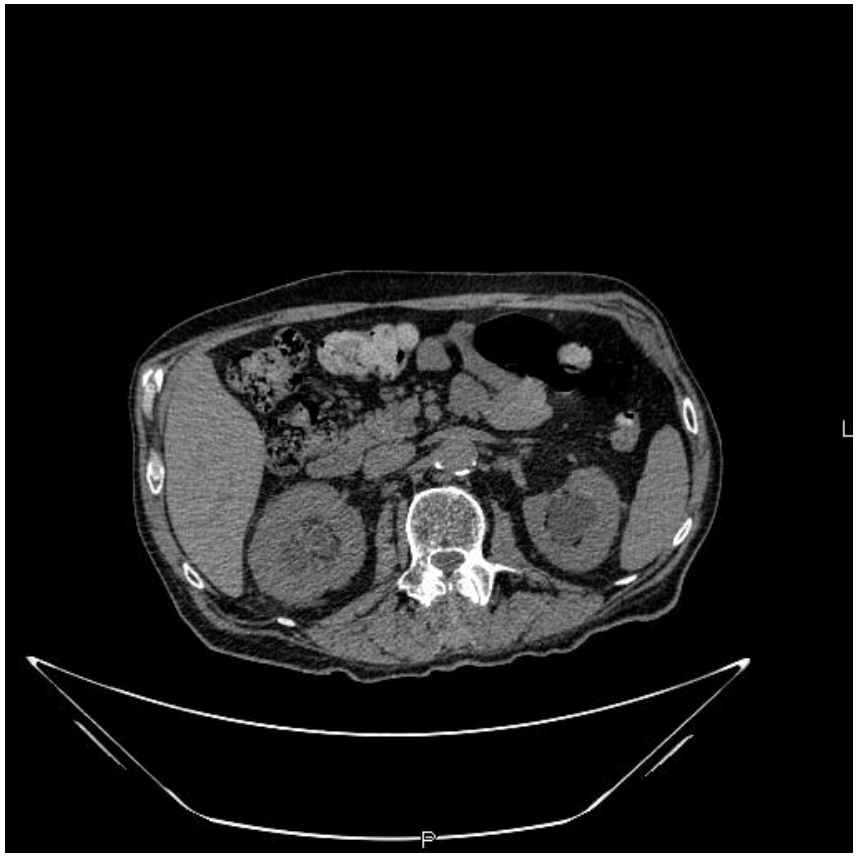
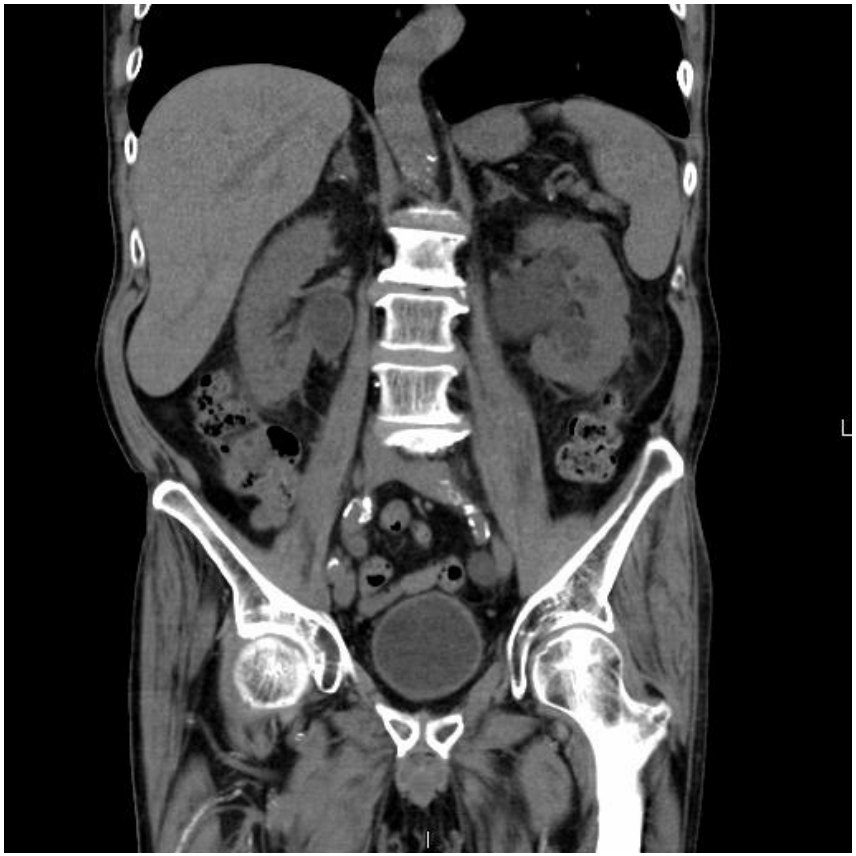
CT evidence of hydronephrosis





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Case presentation – here we go again

- Cystoscopic findings
  - wide caliber urethral stricture
  - bladder
    - lots of debris
    - brownish cobble-stone appearing material
    - L ureter tight distal stricture with dilated ureter above
    - R ureter distal stricture not as dense as the left, primarily obstructed by the bladder wall
  - bilateral stents placed and foley placed

  the urologist felt that the findings were compatible with the diagnosis is renal TB

Case presentation – here we go again

- Biopsy
  - necrotizing granulomatous inflammation
    - AFB seen [>100 per hpf]
- Cultures
  - bladder washings and biopsy ultimately grew MTB
  - urine
    - 5-10 AFB per hpf/ bacterial culture negative; grew MTB
  - throat culture
    - negative for bacteria
    - positive for MTB

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Case presentation – here we go again

- At the hospital, the patient was started on 4 drug standard therapy and discharged a few days later.
  - to receive DOT through the Southeast Region
  - BUN/Cr was variable but fell from 92/4.45 to 55/2.36
    - HCO3 remained low 15 on discharge
  - LFT normal when checked early in the admission
    - » ALT 19
    - » AST 15
    - » alk phos 126
    - » bili 0.4
- He followed up in our clinic within a week of DC.

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Case presentation – here we go again

- In clinic
  - pt complaints
    - significant fatigue and weakness
    - severe anorexia
    - weight loss
    - mild dyspnea
  - PE - Looked puny, not toxic, thin – looked dry
    - VS: wt 154
    - mild temporal wasting, purulence from R tonsillar area
    - no cervical or axillary adenopathy
    - lungs coarse without significant crackles, wheezes or rub
    - heart RRR no murmur; abd soft, benign; no CVAT
    - ext were cool to touch

Case presentation – here we go again

- lab results came back the following day
  - elevation of the BUN and Cr
  - worsening of a metabolic acidosis
  - some elevation of his transaminases
- the pt was called and encouraged to increase fluids
  - planned on repeat labs the following day
  - contacting pt to determine how he was doing
- the next day, we were told patient was doing poorly
  - arranged for admission to the hospital
  - son confirmed that his father was not making it at home

Case presentation – here we go again

- Hospital admission
  - pt admitted – seemed significantly dehydrated
    - IV fluids
    - hold TB medications
    - lab evaluation
      - » BUN/Cr 95/4.2
      - » WBC 11.8 – pt hemoconcentrated
      - » elevated transaminases peaked after several days AST/ALT → 450/214; alk phos 200 bili 0.7
      - » hep C seropositive

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What would you do now?

1. Start 4 drug RIPE (or a variation) a few agents at a time
2. Do a gene Xpert looking for rifampin resistance
3. Do a HAINS test looking for INH resistance
4. Call Dr Jon for guidance and moral support
5. Call Dr Ashkin for his guidance
6. All of the above
7. Consider adding levofloxacin
8. Add an injectable in case there is resistance

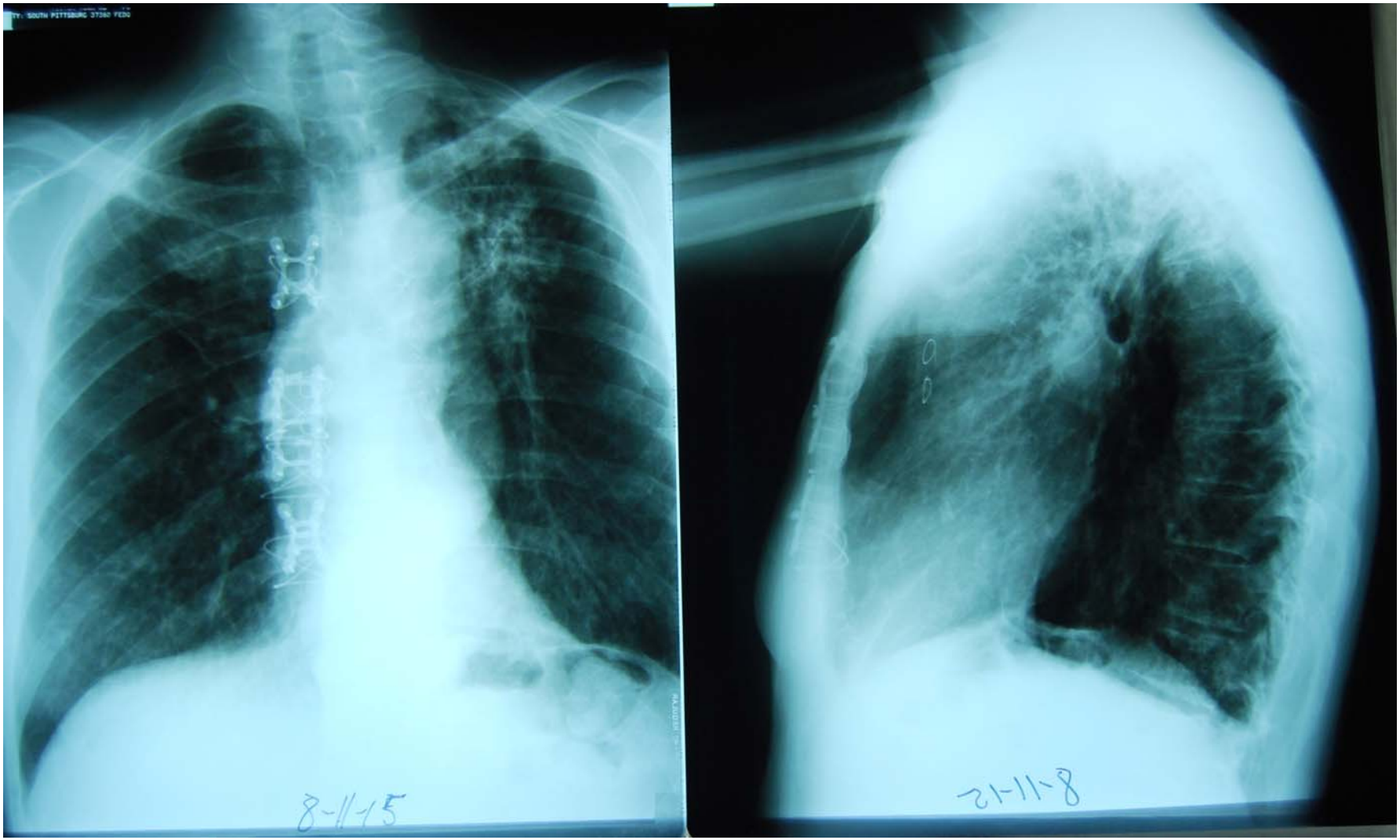
Case presentation – here we go again

- Hospital course
  - TB meds held until we had genetic resistance data
    - no resistance mutations for INH or rifampin
    - started PZA, ethambutal and rifabutin
    - INH added 5-7 days later
      - » LFTs actually fell over a week or so back to normal
      - » Hep C viral load was negative
    - pt tolerated the above regimen
    - organisms actually isolated again from urine and now sputum
  - anorexia resolved – son brought in food
  - received IVF as well for a prolonged period

Case presentation – here we go again

- Hospital course (cont)
  - Cr improved with IV hydration but only into 2.5-3.0
  - off IV fluids the Cr started to rise again
  - US of the kidneys showed bilateral hydronephrosis
  - urology consulted → benefit from nephrostomy tubes?
    - tubes were recommended by urology
    - pt then balked at the offer
      - » with encouragement from all services
      - » with long discussions with patient and son
    - pt finally consented
    - BUN/Cr came down nicely after the tubes 51/2.2 and continued to fall in the outpatient setting

CXR August 2015



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Case presentation – here we go again

- Outpatient course has lately been uneventful
  - Our management
    - Pan-sensitive organism
      - RIPE but substituted rifabutin for rifampin (liver)
      - presently on INH/rifabutin/B6 5 days a week
    - drug levels – only needed to increase rifabutin
    - can't get blood
    - Jerry rigged nephrostomy tube
    - Cr has fallen into the 1.5 range
    - weight 153 →189.5 at last clinic visit

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Case presentation – here we go again

- Urology
  - repeat cystoscope
    - the bladder mucosa appears normal
    - found urethral stricture – repaired that surgically
  - contrast injection into nephrostomy tubes
    - right
      - » mid ureter multifocal stricture
      - » some contrast gets to bladder
    - Left
      - » high grade distal stricture
      - » lots of reflux – no contrast into the bladder
  - MAG 3 lasix scan
    - excretion of the isotope on the R; reflux no excretion on the L

Why Failure?

- inadequate duration
- sub therapeutic drug levels
- occult alcohol abuse
- uncontrolled DM
- immune compromise
- resistance [no evidence]

HOW LONG DO I TREAT???

References

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- Lee P-H, Lin H-C, Huang AS-E, Wei S-H, Lai M-S, et al. (2014) Diabetes and Risk of Tuberculosis Relapse: Nationwide Nested Case-Control Study. PLoS ONE 9(3): e92623. doi:10.1371/journal.pone.0092623

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