PERSISTENTLY POSITIVE PROBLEMS

MATTHEW PULLEN MD

81YO WHITE MALE FROM MINNEAPOLIS…

- Presented to OSH from his home with “a day or two” of fevers and loose stool described as “just watery brown stuff” once per day
- Complained of malaise that he felt had been progressing for several weeks, but sharply worsened in the past few days
- He was admitted, blood cultures were collected, and he was started on vitamins V and Z (vancomycin and zosyn)

HISTORICAL DETAILS

- His only past medical history is de novo AML that was being treated with a trial drug, SGI-110
  - DNA methyltransferse inhibitor, which is thought to block and/or reverse the hypermethylation seen in some cancers, reversing (or stopping the progression of) tumor suppressor gene silencing
  - Last infusion was two weeks prior to admission at the OSH
  - Chronically neutropenic as a result
- AML was diagnosed 9 months prior, after presenting to his PCP with malaise, leg/trunk itching, and pancytopenia (diagnosis confirmed on subsequent marrow biopsy)
- Lives with his wife in Minneapolis, former smoker (quit in the 1960s), does not drink or use illicit drugs, no pets, no foreign travel
- Had been treated for MRSA cellulitis the month prior without any recurrence

MICRIOBIOLOGY

- At the OSH, his cultures were quickly stained, both positive for gram positive cocci in clusters and pairs.
- He was continued on vancomycin and zosyn pending speciation of the GPCs
- Two days later, when nothing has grown in culture, they restained the blood samples and modified their report, now saying these were NOT gram positive cocci, but they weren't entirely sure WHAT they were, so they sent them to another hospital with a larger lab…

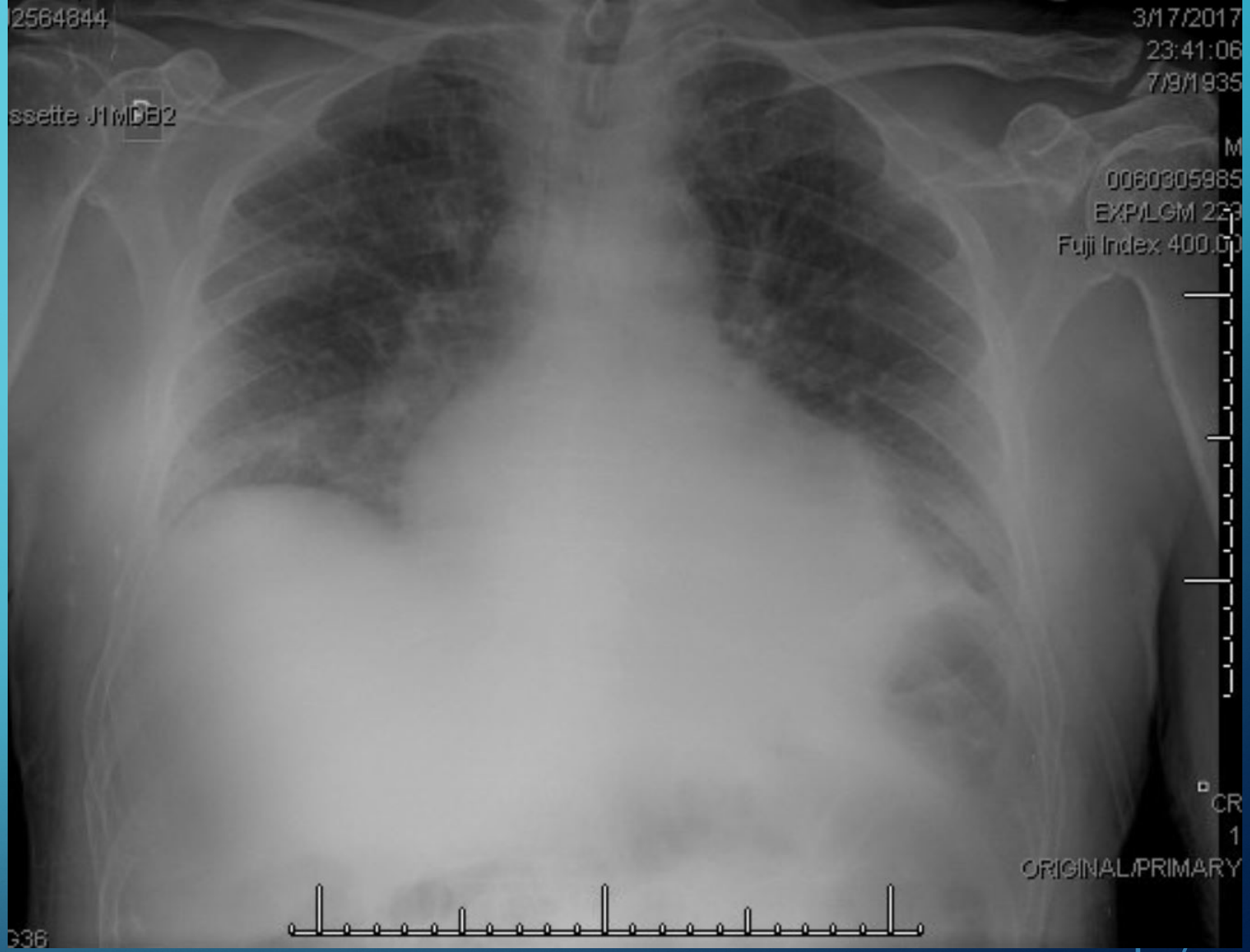
TRANSFER

- By the time the amended report was called out by the lab at the OSH, the patient was in severe rigors, confused, and still febrile
- ID was consulted at that hospital, who recommended changing zosyn to ertapenem, continuing vancomycin, and transferring the patient to UMMC.
- He was brought to our ICU, new cultures were collected, abx continued, and ID consulted…
  - ICU also added aztreonam fur further GN coverage, and he was continued on home posaconazole ppx

EXAMINATION

- VITALS: 102.6F, 111 HR, 30 RR, 130/55 BP, 98% on RA
- GEN: Disoriented to place and time, appears very acutely ill and exhausted, shaking vigorously on bed with teeth chattering
- HEENT: EOMI, PERRLA (though prefers eyes being closed), OP clear, MMM
- CV: Tachycardic, regular rhythm, s1/s2, no m/r/g
- PULM:: Coarse breath sounds in upper and mid lung fields bilaterally, no w/c, no cough
- GI: soft, non-distended, non-tender, +BS, no HSM
- SKIN: No rashes or lesions, no ports/intravascular devices
- NEURO: CN 2-12 intact, no focal deficits noted

IMAGING



- CXR: Prominent perihilar opacities and pulmonary vasculature may be related to pulmonary edema. Left basilar atelectasis and/or consolidation. Small left pleural effusion. Low lung volumes.

LABS

- Na – 138
- K – 3.4
- Cl – 105
- CO2 – 24
- BUN – 12
- SCr – 1.02

Tbili – 0.4
Aphos – 81
Tprot – 5.7
Alb – 2.0
AST – 68
ALT – 76

WBC – 1
ANC - 200
ALC - 800
Hgb – 7.8
Hct – 23.6
Plt – 49

- The day he arrived at UMMC (three days after blood cultures were drawn), we called the lab at the OSH and they had just noted something growing in their cultures…

GROWTH!

- The previously called GPCs were now actually identified as AFB of unknown species.
- We started the patient on clarithromycin and ciprofloxacin while awaiting MDH's species probe of the now AFB-positive blood cultures.
- The patient had relief of rigors, but did continue to have fevers and some loose stool.
- Broad work-up for other infections in blood and stool were negative, though our blood cultures would continue to grow AFB for 9 consecutive days (initially at 3 days of incubation, then gradually extending to 7 days of incubation.

OUTCOME

- Patient continued to have daily fevers as additional agents were gradually added, eventually ending up on a regimen of linezolid, clarithromycin, cefoxitin, and amikaxin with occasional levofloxacin depending on how his QTc looked every 48 hours.
- MDH probe identified the cbacteria as Mycobacterium abscessus
  - National Jewish performed resistance testing, found resistance to fluoroquinolones, augmentin, minocycline, doxycycline, imipenem.
- Extensive work-up for source of the bacteremia was only significant for possible increased FDG uptake in some pulmonary nodes and inguinal nodes.
- Despite a short rebound, patient quickly decompensated and passed away (DNR/DNI) on hospital day 23

MYCOBACTERIUM ABSCESSUS

- Member of the “rapid growers” club in Mycobacterium genus
  - M. fortuitum, M. chelonae
  - Runyon IV (rapid growing, non-pigmented)
- Environmental bacteria, often found in soil, vegetation, water, sewage.
- Initially thought to be a subspecies of M. chelonae, but unlike M. chelnoae, M. abscessus tolerates higher NaCl concentrations in growth media and cannot use citrate as a carbon source.
- Sometimes confused for diphteroid bacteria in broth (was this the source of our initial confusion?)

PRESENTATION

- Most common presentation is lung disease (most often as a “chronic disease” picture)
- Can also cause cutaneous disease and wound infection, most commonly in immunosuppressed/deficient persons
  - These are often culture negative, though only due to lack of testing for AFB
- One of the more famous presentations was culture-negative skin infections at acupuncture sites
  - Largest known outbreak included 40 patients in Seoul, Korea…all from one clinic in a 7 month period!
- Risk factors for disease include:
  - Pulm: CF, bronchiectasis, immunosuppression
  - HAI: surgical wound infections (lots of cases of breast implant infections documented)
  - SSTI: trauma with water exposure,
  - Disseminated: Immunosuppression

DIAGNOSIS

- Diagnosed similarly to other AFB with smear and stain of suspected infected tissue/site.
- American Thoracic Society criteria for NTM pulmonar disease diagnosis:
  - Chest imaging without cavitations
  - At least two separate positive sputums or one bronch wash.lavage
  - Exclusion of other diseases, mainly TB

TREATMENT

- Well-known for frequent and various resistances. Most M. abscessus isolates will have slightly elevated (even if not quite to the intermediate resistance range) MICs for clarithromycin, cefoxitin, and amikacin.
  - Presence of the *erm* gene removes macrolides from your options.
  - M. abscessus abscessus has erm gene more often, M abscessus boletti does not.
- For this reason, combination therapies are the gold standard for lung disease, and becoming more common ofr all M. abscessus infections.
- SKIN: Clarithromycin/azithromycin alone or PLUS parenteral agent (cefoxitin, amikacin, imipenem) for up to 4 months.
- BONE: Similar drug options, but treated for 6 months (at least) plus surgery if possible
- PULMONARY: Clarithromycin for at least 12 months with parenteral agent for first 2-4 months.
  - Goal is 12 months of clear sputum. No regimen has been shown to be superior to another.
- For all of these, if macrolides are out, then tigecycline or linezolid may be secondary options.

PROGNOSIS

- Considered an incurable, chronic lung disease
- Precludes lung transplantation
- Frequent recurrences often necessitate retreatment or chronic suppressive antibiotics

REFERENCES

- CDC “M. absceussus Study Team” Report: https://wwwnc.cdc.gov/eid/article/22/3/pdfs/15-0828.pdf
- UpToDate
- John’s Hopkins Reference
- Clinical Infectious Diseases