

“A day in the life”

MIDG

24/5/2011

Alistair Reid

Peter MacCallum Cancer Centre

Mrs SA

- 26yo female admitted to Peter Mac with AML on 2/2/2011
- Immigrated from Pakistan 2yrs ago.
- Married with 20 month old son.
- No other past medical history

AML

- 2 month history
 - Lymphadenopathy
 - headaches
 - Fevers
 - Bruising
- Had been on 1 month trial of clindamycin
- WCC 191 (predominantly blasts)
- BMAT staging AML M5
- 3/2/11 Induction chemo with “7+3+7”
 - (Cytarabine (Ara-C) + Idarubicin + Etoposide)

Serological screening

- Hep B negative, not immune
- Hep C negative
- HSV, CMV, Varicella all previous infection (IgG pos)
- Quantiferon positive
- HIV not tested
- Strongyloides not considered by treating unit

Prophylaxis

- Posaconazole day 1-day5
 - Ambisome day 7-day 22

- Valaciclovir day 1-day5
 - Aciclovir day 6-day 23

- Isoniazid not considered by treating unit

Day 6

- Febrile 38.7
- Bloody diarrhoea, abdo pain
- WCC 0.8, neutrophils 0.62
- Haemodynamically stable
- Tazocin commenced
- CT consistent with enterocolitis
 - extensive bowel wall thickening and oedema from mid-ileum to the descending and sigmoid colon
- Nil orally
- Prophylaxis changed to IV
- TPN commenced

Day 6 pm

- Hypotensive and tachycardic
- Stat dose gentamycin given and Vancomycin added.
- Transferred to ICU
- BP maintained without inotropes

- CXR normal

Day 9

- Ongoing fevers
- Now requiring Noradrenaline 20
- Acidotic
- Increasing respiratory requirements -> intubation
- Bilateral pulmonary infiltrates. ?overload
 - Frusemide infusion
- Tazocin changed to Meropenem

Day 12

- ALP 156
- GGT 166
- ALT 172
- Billi 56

- Ultrasound liver normal

- Day 13:
 - Vancomycin ceased as afebrile 48hrs and multiple BC's negative

Day 15/16

- Skin breaks and epidermal desquamation
- Low urine output, GFR falling; now 40
- LFT continue to deteriorate, INR 1.5
- Malena
- Tumor lysis
- Transfusion dependent (PRBC and platelets)

- Blood film excluded TTP/HUS

- CT top to tail
 - Brain normal
 - Chest showed early ground glass nodules consistent with pulmonary oedema or infection
 - Large amount of pelvic ascites and more small bowel thickening

Day 17/18

- Day 17:
 - Febrile
 - Vancomycin added
 - Ambisome changed to 3mg/kg daily
 - Cultures taken
- Day 18:
 - GPC in chains seen on BC
 - Teicoplanin started, Vancomycin ceased
- BC pos for VRE 19/2/2011 x2, 20/2/2011, 22/2/2011
- All lines changed. No growth on catheter tips

Day 19-22

- BMAT aplastic
- GCS 3 off sedation since day 16
- CVVHD started
- Neutrophil recovery day 22
- ALP 450
- GGT 311
- ALT 34
- Billi 192
- Albumin 28
- CRP 395

x 1.584

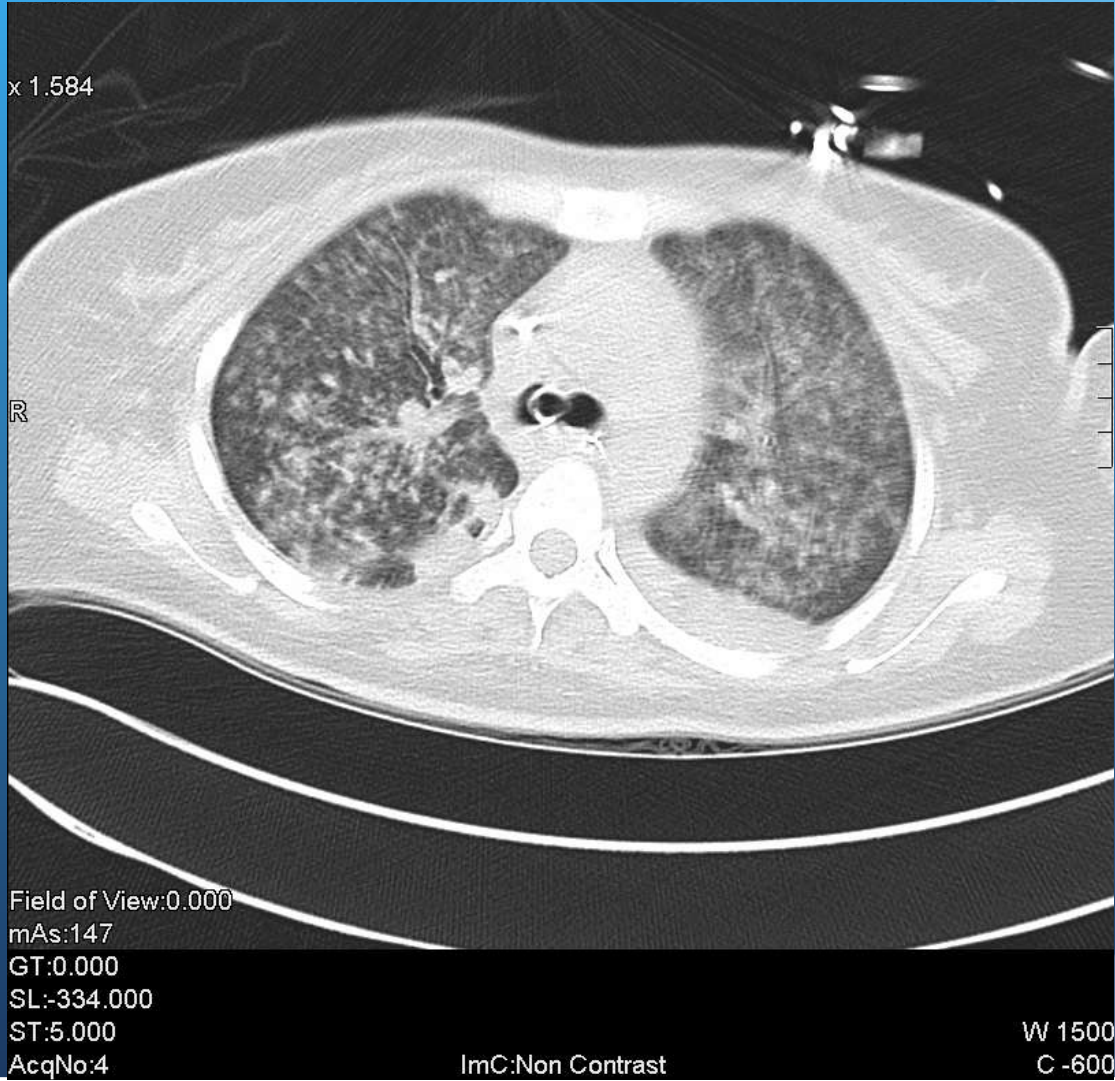
RHA



Field of View:0.000
mAs:398
GT:0.000
SL:0.000
ST:5.000
AcqNo:2

ImC:Non Contrast

W 80
C 40



Would you?

- Treat for TB?
- Respiratory isolate?
- Treat with antifungals?

ID opinion

- Single room
 - N95 masks for aerosol generating procedures
- TF to St Vincent's Hospital for respiratory isolation
- Bronchoscopy
- LP
- Start TB treatment
 - Continue meropenem
 - Isoniazid
 - Rifampicin
 - Moxifloxacin
- On hydrocortisone 100mg qid
- Ambisome re-started 3mg/kg

LP

- Prot 1.32
- Glucose 2.3
- Cryptococcal ag neg
- Blood stained
- Lymph 60
- Poly 150
- RBC >50000
- TB PCR neg, AFB stain neg, insufficient spec for culture
- VRE on culture

Bronchoscopy

- Moderate NOF
- Poly 0
- AFB stain neg
- TB PCR neg
- Galactomanin and aspergillus pcr negative

TF to SVHM day 23

- Bili 400
 - ALP 677
 - GGT 266
 - ALT 57
 - Alb 27
 - INR 1.3
-
- Liver biopsy showed mild cholestatic changes only
 - TB PCR on neg
 - no granuloma,
 - no hepatic injury.
 - MARS machine used 1-3/3/11



Antibiotics revised at SVHM

- Linezolid started instead of teicoplanin
- moxifloxacin changed to ciproflocacin
- metronidazole added
- Rifampicin/isoniazid/ continued
- Meropenem ceased
- Intragam Given
- Ambisome stopped
- BMAT 3/3/11 no malignancy. Recovering marrow

Results thus far

- TB smear and PCR negative on
 - Bronchoscopy
 - LP
 - Bone marrow
 - Liver biopsy
- Cultures pending

Re-admitted to Peter Mac day 32

- Abdo distended, lactate 10
- Eyes tracking off sedation
- CVVHD
- Billi 293, ALP 364, ALT 146, GGT 49, Alb 19
- Still on noradrenaline
- WCC 49

Imaging

- Repeat CT
 - Bilateral intracranial septic emboli (right temporal, left frontal)
 - Diffuse leptomenigeal enhancement
 - Total splenic infarction
 - Clustered bilateral liver nodules, ? Abscesses
 - New right lower lobe cavitating lesion
 - Marked ascites
 - No free gas in abdomen

ImNo:34

x 1.584



Field of View:0.000

mAs:198

GT:0.000

SL:185.800

ST:5.000

AcqNo:7

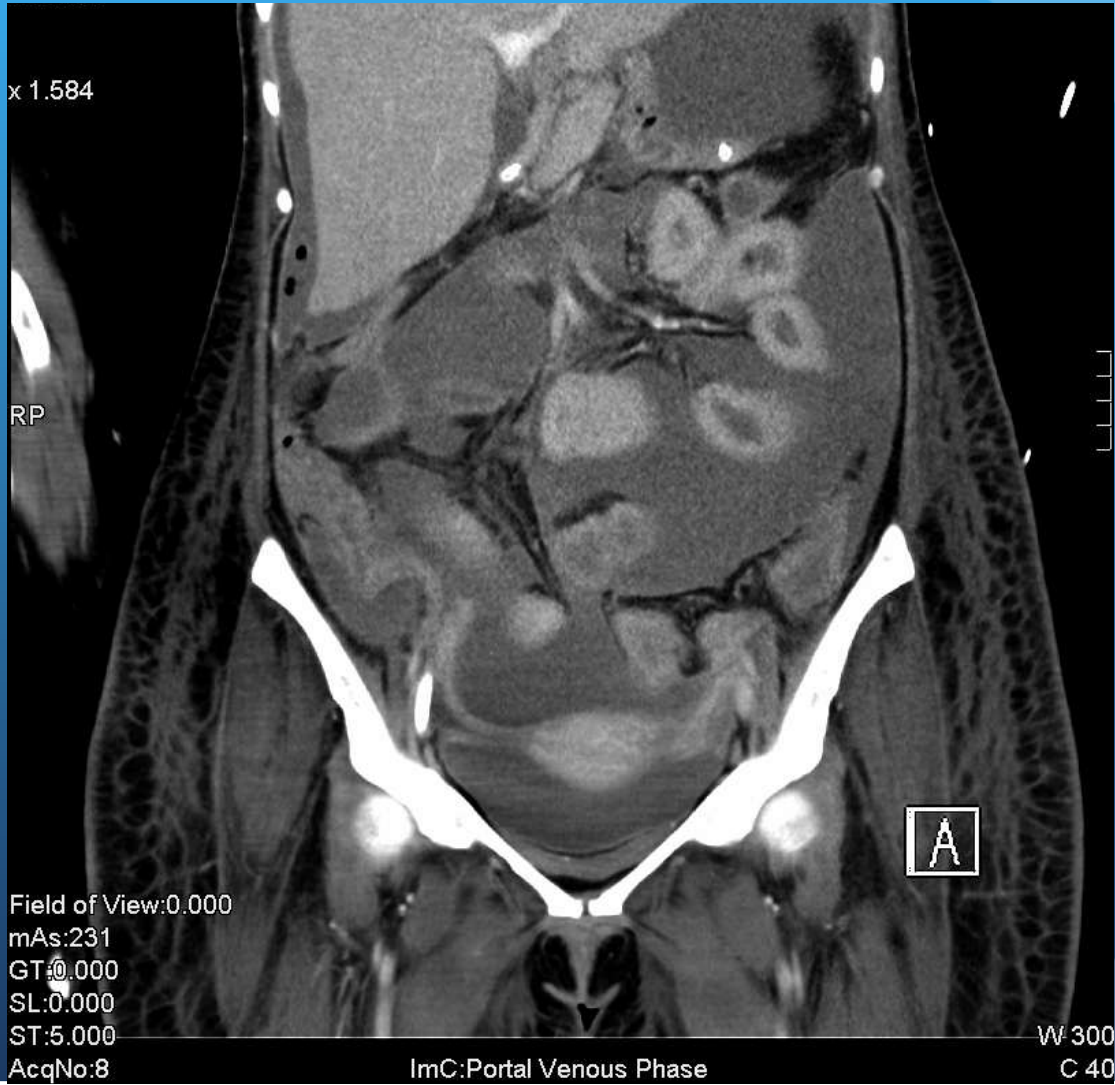
ImC:Arterial Phase

W 1500

C -600

Day 36 further deterioration

- Repeat CT shows free gas in abdomen
- Theatre for laparotomy and wash out and formation of stoma
- 6.5l enteric contents drained
- Multiple small abscesses
- Perforation just proximal to ileo-cecal valve





Day 37

- Post op coagulopathic
 - INR 1.8
 - APTT 53
 - Pts 93
 - Hb 52
- Bleeding from wound +++
- 14 units blood and 14 units FFP

Candidaemia

- BC from day 32 and 36 pos for c.parapsilosis
- Caspo started day 37, changed to fluconazole day 41
- Echo 23/3 NAD

Day 40/41

- Back to theatre
 - Washout and closure of open wound
- Still no urine output, on CVVHD
- Not waking up
- Taken out of respiratory precautions after 2 weeks treatment.

Day 41

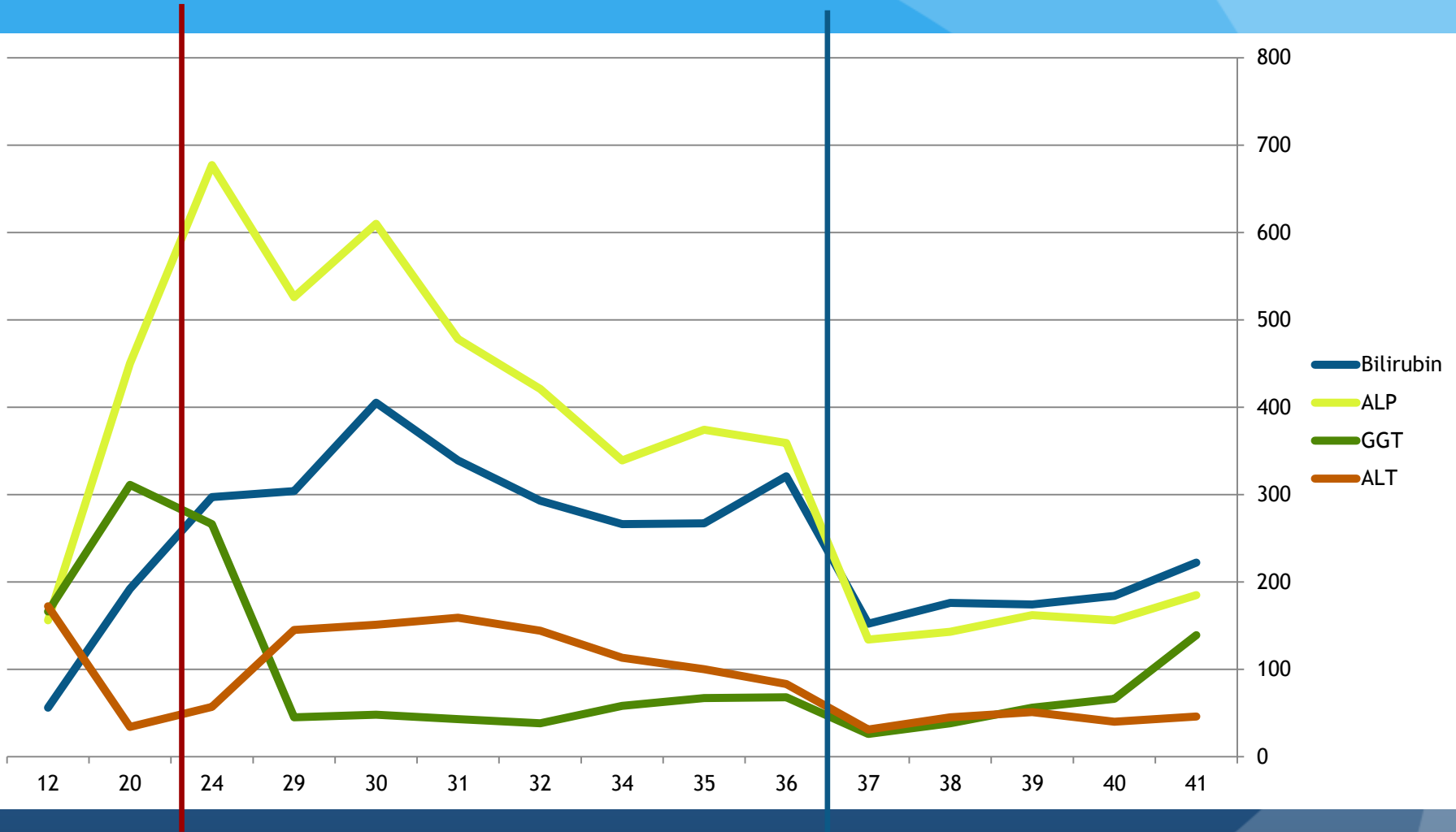
- Current meds
 - Caspofungin
 - Metronidazole
 - Ciprofloxacin
 - Linezolid
 - Rifampicin
 - Isoniazid
 - Pyridoxine
 - Hydrocortisone
 - Exomeprazole

Day 41

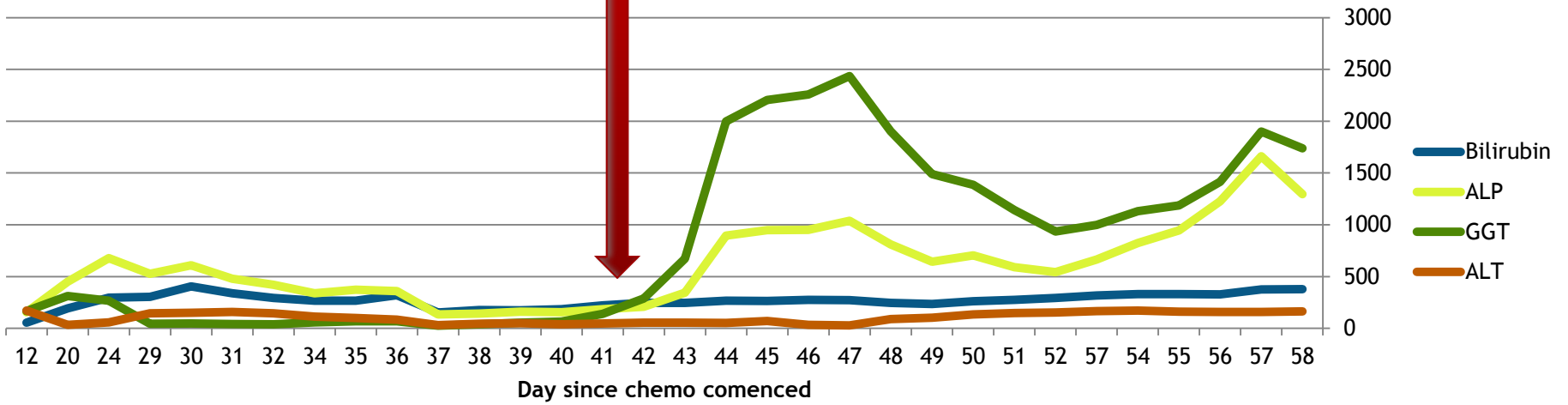
- Current meds
 - Ciprofloxacin
 - Metronidazole
 - Hydrocortisone
 - Exomeprazole
 - Caspofungin
 - Linezolid
 - ~~• Rifampicin~~
 - ~~• Isoniazid~~
 - Pyridoxine
- TB meds stopped as per haematology

TB therapy started here

14 units PRBC given here



TB therapy stopped here



Is it TB?

- Cultures all negative at 17 day mark when meds stopped
- PCR and smear negative on 4 different tissue samples.

- Indian study of 14000 TB cultures by MIGT
 - 91% of all positive cultures were positive by 2 weeks from MIGT
 - Median time to positive MIGT culture for smear negative patients was 16 days (1487 patients)

Antituberculosis drug hepatotoxicity

Journal of Antimicrobial Chemotherapy Advance Access published May 17, 2011

Journal of
Antimicrobial
Chemotherapy

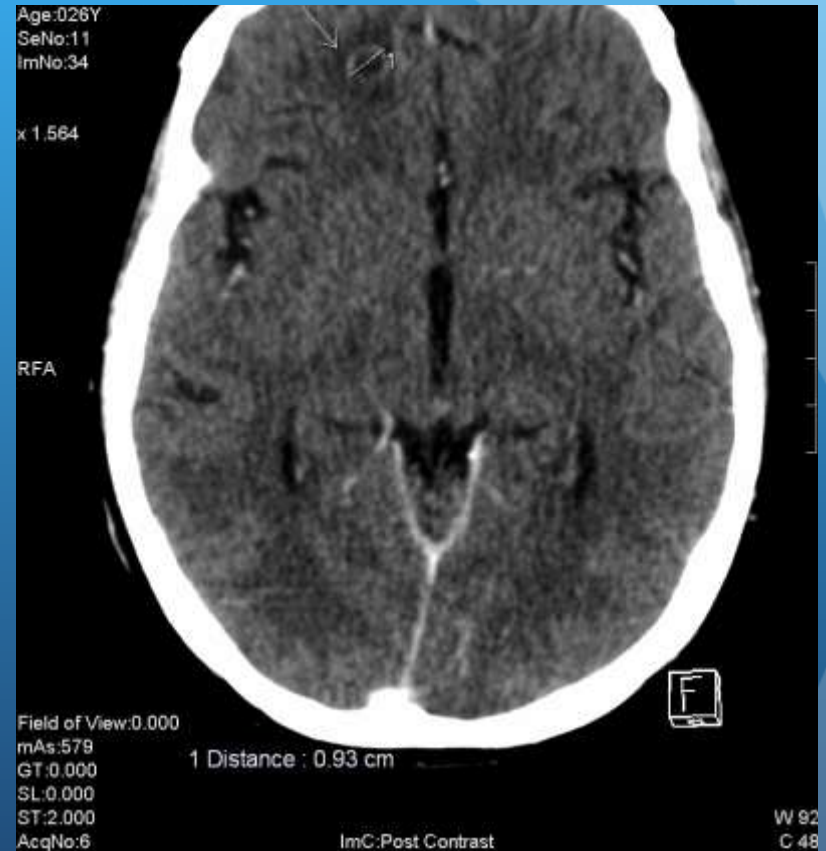
J Antimicrob Chemother
doi:10.1093/jac/dkr159

Hepatic safety of antibiotics used in primary care

Raúl J. Andrade^{1,2} and Paul M. Tulkens^{3,4*}

- Liver injury is characterized by hepatocellular necrosis for both Isoniazid and Rifampicin
- LFT abnormalities expected to be predominantly transaminitis
 - Rifampicin may cause cholestasis

Day 44



- Ambisome re started
- Bactrim commenced

Day 47

- LP
 - Lymph 2
 - Poly 4
 - Clear
 - No growth
 - Rbc 1
 - Toxo pcr neg
 - Pan fungal pcr neg
- BMAT normal marrow, no AML

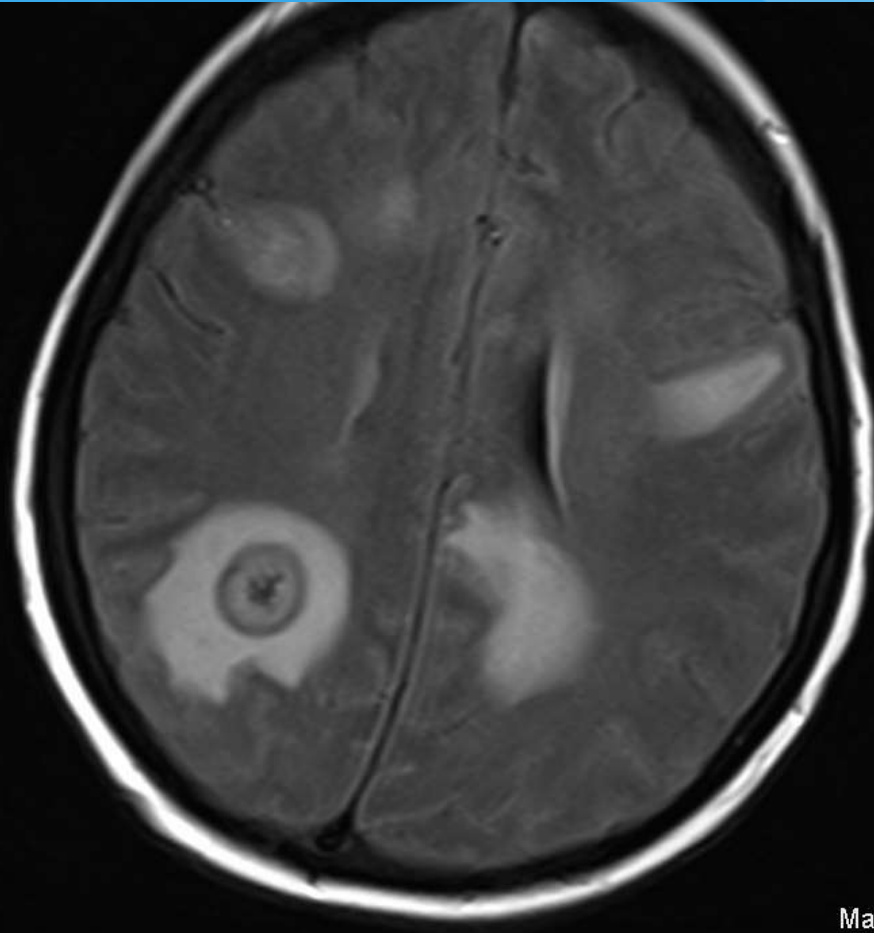
Day 54



Sen0.2
ImNo:14

x 3.138

RAF



SO:IR/SAT1
Type:ORIGINAL/PRIMARY/M/...
TE:93.000
TR:8500.000
TI:2500.000
TT:0.000

Matrix:0/320/168/0
ST:5.000
SL:81.104
SV:SK/SP/MP/OSP
W 870
C 390

Progress

- Day 53: *Aspergillus fumigatus* from sputum
- Ambisome increased to 5mg/kg
- Day 57: TF to SVHM for brain biopsy and returned to Peter Mac same day
- Day 58: blew a pupil
 - Urgent CT brain

Day 58



Outcome

- RIP
- Brain biopsy grew *Aspergillus fumigatus*
- Galactomanin from day 55 positive

Summary

- Aspergillus probably every where but nowhere we looked
- Could account for
 - Lung lesions
 - Brain lesions
 - Splenic infarct
 - Liver lesions and abnormalities
- In retrospect probably had aspergillus on presentation
 - 2 months symptoms AML prior to presentation
 - likely functionally neutropenic
 - Consistent with early presentation of enterocolitis

Summary

- Consult medicine is difficult
- Cancer medicine is difficult
- Under resourced medicine is difficult

Galactomanin on BAL in HM SCT pts

- Retrospective study 67 patients
- More sensitive than cytology (0%, 0/14), BAL culture (27%, 4/15), transbronchial biopsy (40%, 2/5), or serum GM (67%, 10/15) for diagnosing IPA.
- BAL GM was ≥ 0.85 and ≥ 0.5 in 86% (6/7) and 100% (7/7) of patients with proven or probable IPA who received a mold-active agent for ≤ 3 days.

Did her race effect the outcome



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Genetic factors influencing cytarabine therapy

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- Ara-c likely subject to genomic variations
- Rumors of increased toxicity of AML induction on Indian sub-continent



Summary of antifungals

- Posaconazole: day 1-5
- Ambisome prophylaxis: day 7-17, 21-22
- Ambisome treatment: day 18-20, day 23
- Caspofungin: day 37-41
- Fluconazole: day 41-45
- Ambisome treatment: day 45-58