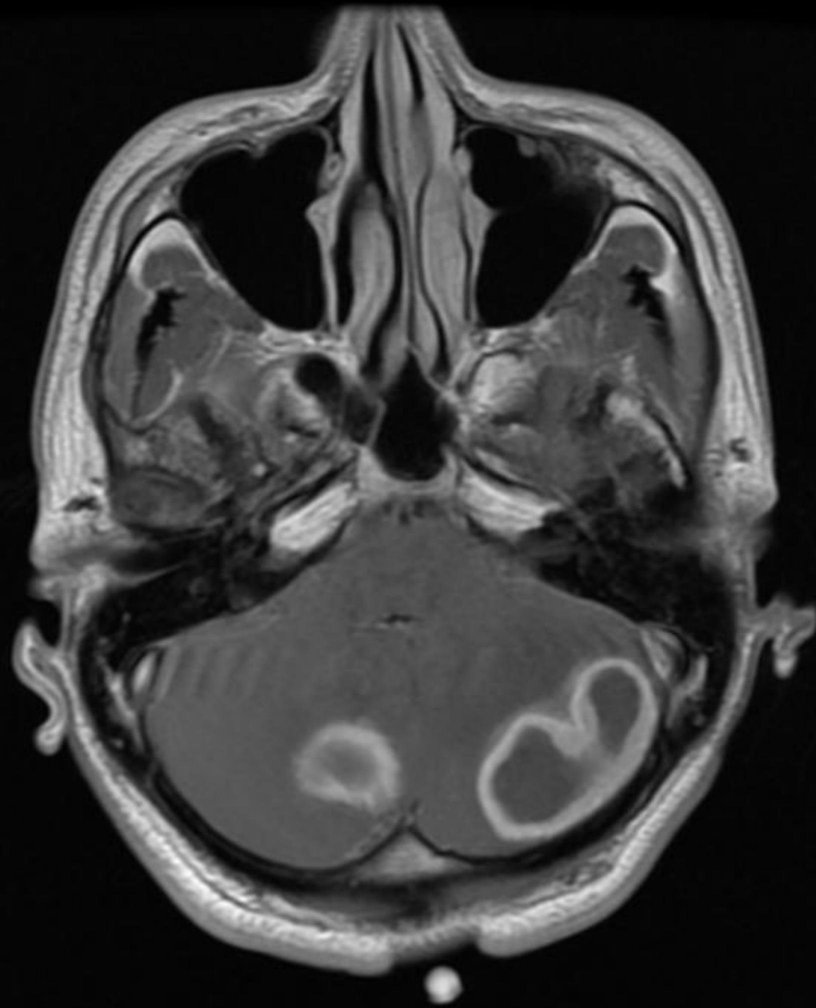
NEUROSURGERY FOR TRAVELLERS

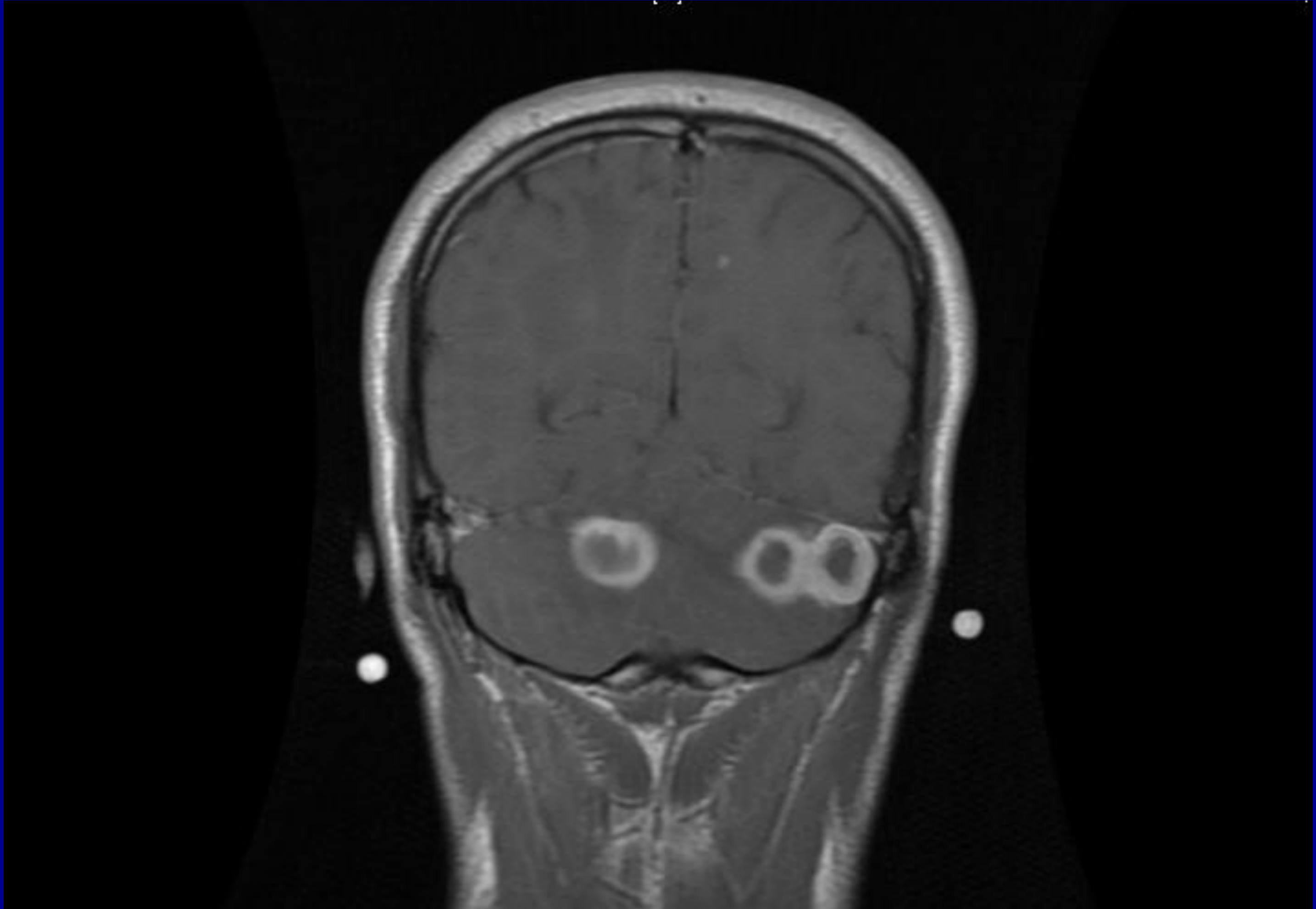
Dr Emma Bishop   Alfred Health

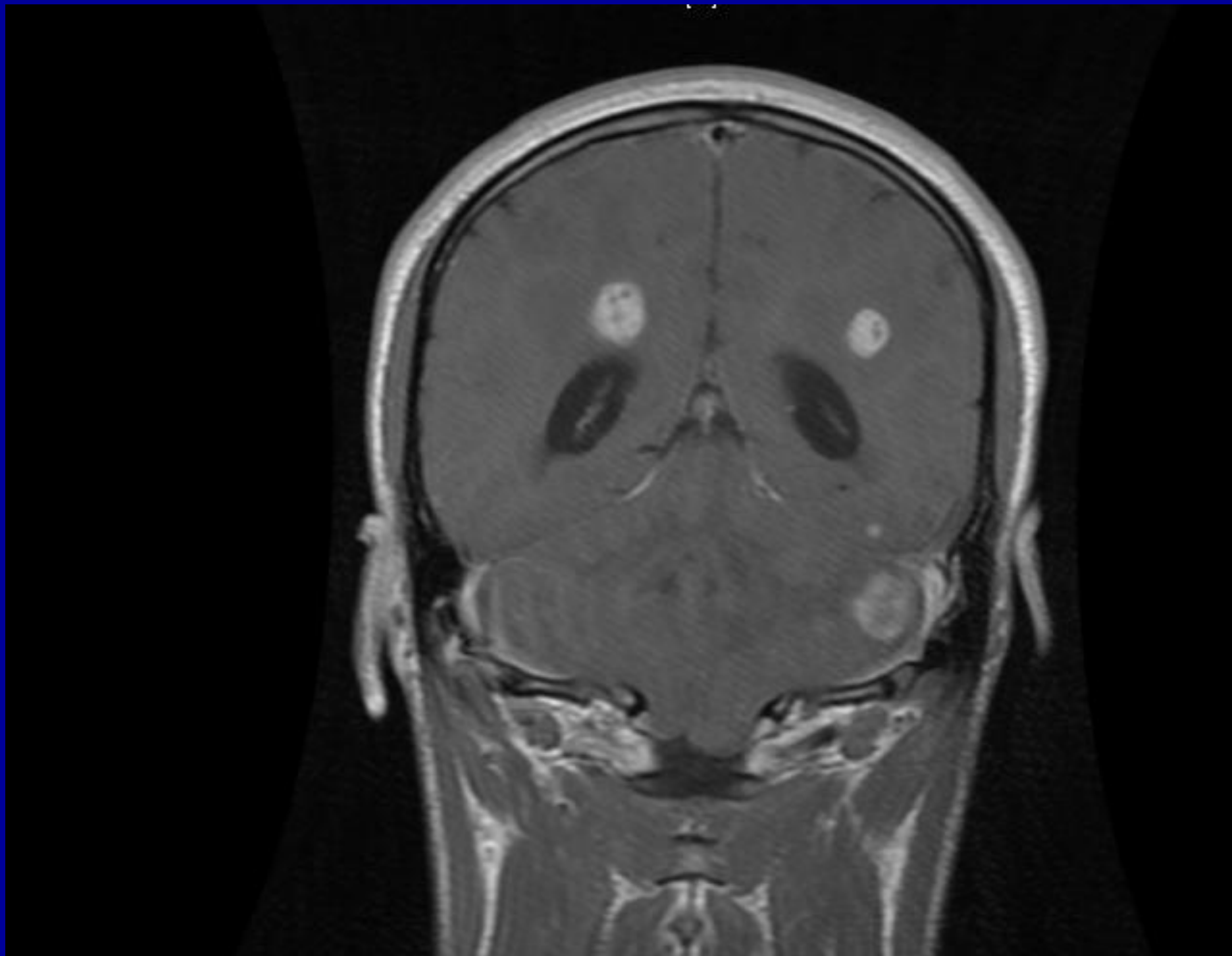
Case 1 - Mr B.V. 28 year old male

- Born in the Philippines, immigrated to Australia 2 years ago
  - No overseas travel since
- No significant past history or comorbidities
- Lives with wife and young daughter / prior work as pharmacist
- When taking daughter to G.P. for review of cough
  - commented on “persistent headache”
  - ordered CT brain, led to neurosurgical referral & MRI



Acq Date:
Acq Time:
MRN:
C+





History of the Presenting Complaint

- Headache, fatigue, dizziness for three months – vomiting 1 day

- Denied any:
  - Visual disturbance, diplopia
  - Recent fevers, night sweats or rigors
  - Significant weight loss
  - Cough, sputum, dyspnoea or haemoptysis
  - Abdominal or back pain

- 6 months prior:
  - few weeks of diarrhoea and fevers
  - stool samples negative for parasites + enteric pathogens

- No IVDU, no clear risk factors for HIV

Examination Findings and Results

Afebrile HR 70 BP 130/80 RR 14 Oxygen sats 100% air

GCS 15, no upper limb ataxia, mild gait disturbance

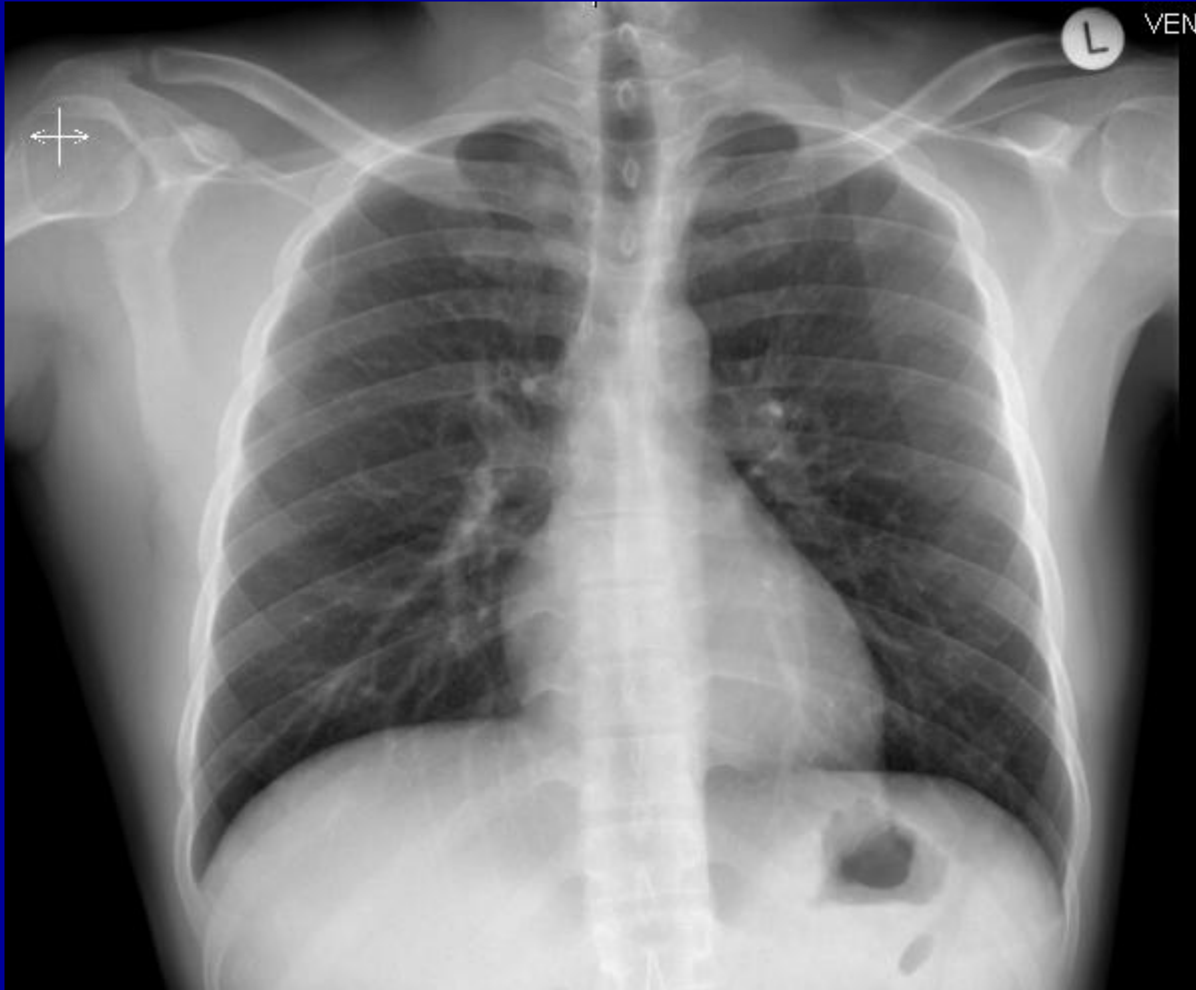
Chest clear, heart sounds dual, no murmurs

No hepatosplenomegaly

No palpable lymphadenopathy or bony tenderness

Hb 151 WCC 9.10 plt 274 neut 6.16 lymph 2.14 eosin 0.14

Serum creatinine 73 LFTS normal CRP 4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Neurosurgical Perspective

- 4th ventricle 50% occluded causing moderate hydrocephalus and tonsillar herniation

- **Planned for emergency:**

  - posterior fossa decompression

  - excision of cerebellar lesions with insertion of EVD

Differential Diagnosis?

Differential Diagnosis?

HIV

- Toxoplasmosis
- Nocardia
- Tuberculosis
- Cryptococcus
- Lymphoma

Differential Diagnosis?

HIV

- Toxoplasmosis
- Nocardia
- Tuberculosis
- Cryptococcus
- Lymphoma

Non-HIV

- Bacterial
- Tuberculosis
- Hydatid
- Fungal
- Amoebic
- Neurocystercicosis

Malignancy

Whilst awaiting progress……………….

Consider another case the same week……………………………………..

Case 2 - Mr W. K 28 year old male

Past History

- Asthma (inhaled steroids seretide 200/25 mcg bd)

- Factor 11 deficiency

- Had never been administered Factor XI before
- Family history - father severe bleeding with tonsillectomy in Pakistan

Social History

- Married, works as engineer, no IVDU or risk factors for HIV

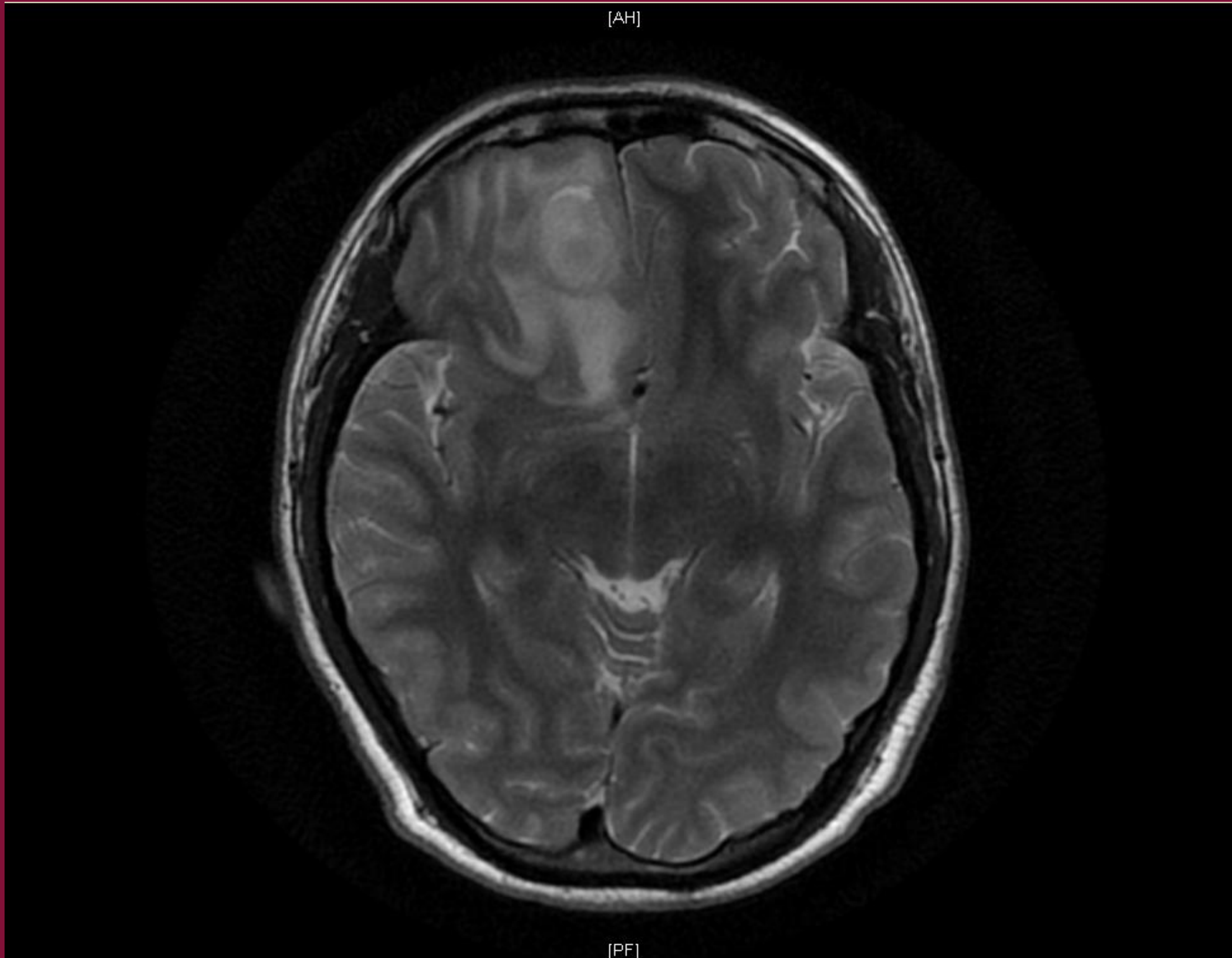
Travel History

- Born in Australia
- Frequent travel to Pakistan – most recent January 2011 for his wedding

History of the Presenting Complaint

Presented to G.P. with frontal headache, lethargy and fevers of several weeks in March 2011:

- **25/3/2011 Seizure**
  - MRI = cystic frontal lesion and nasal lesion
  - Neurosurgery/ENT to see as outpatient
  - Continued augmentin courses for headache and fever
- **3/5/2011 Worsening headache, fever**
  - Geelong hospital, blood cultures negative
  - Due to Factor XI deficiency, referred to Alfred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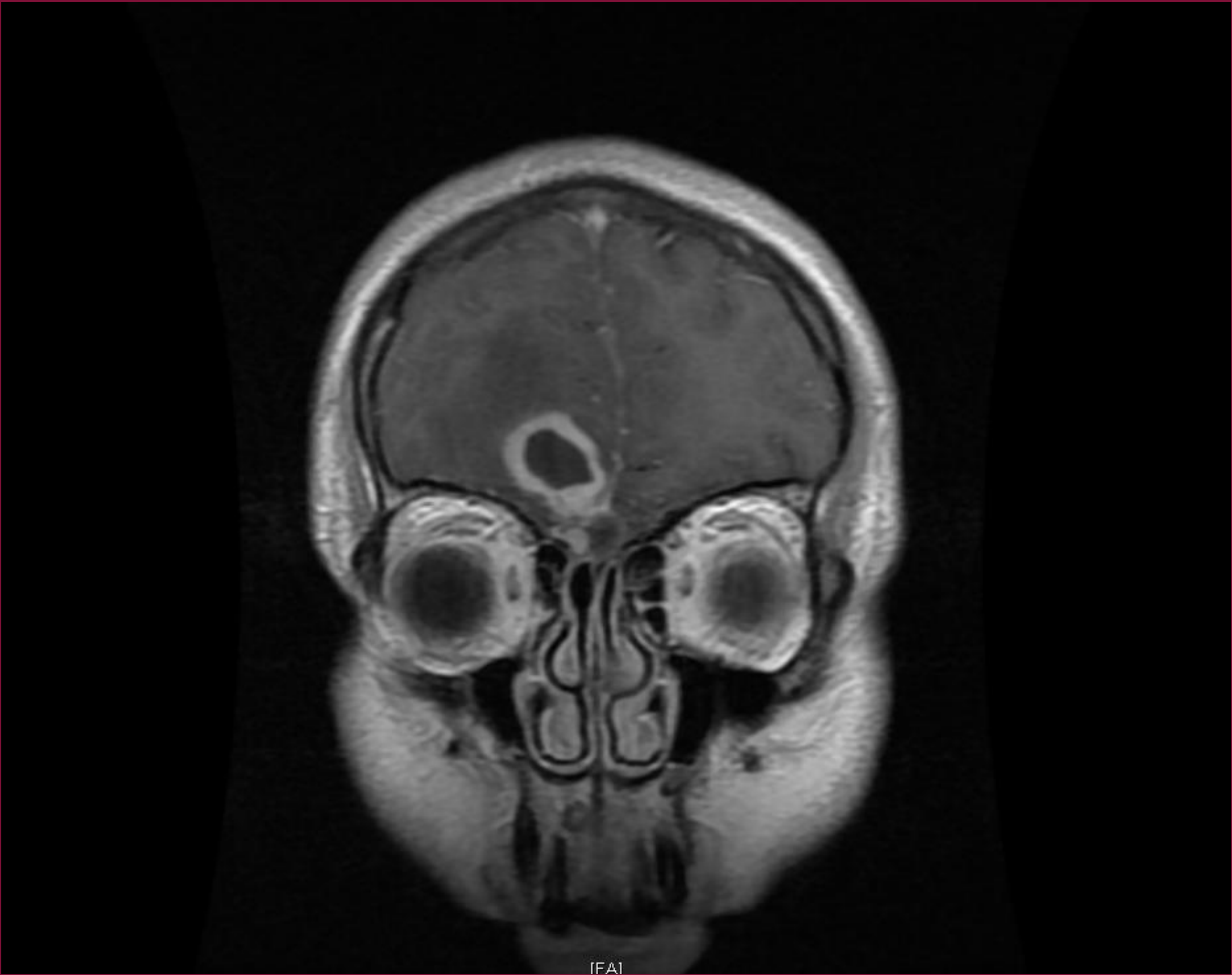
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Examination Findings and Results

Headache Temp. 38.5 BP 140/80 HR 90 RR 16 0_2sats 99% air

GCS 15 No neurological signs

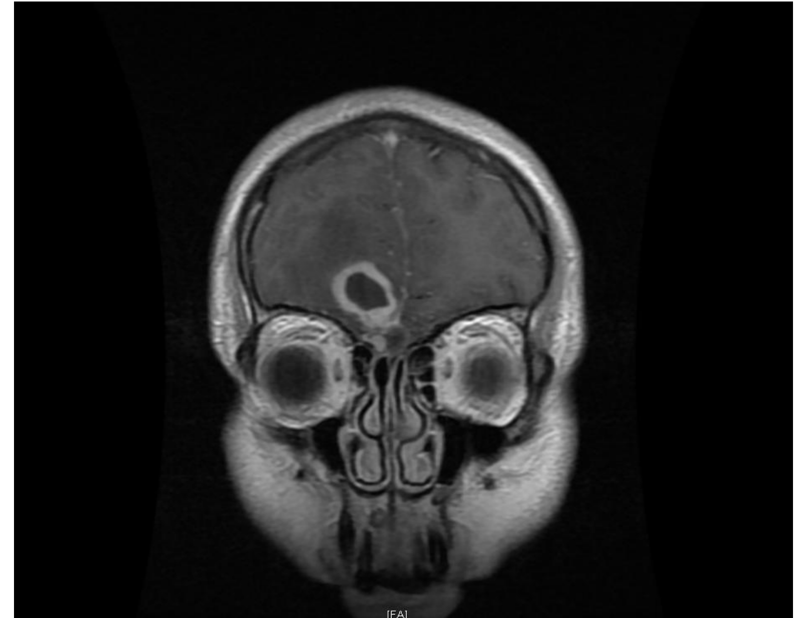
Chest clear, Heart sounds dual, no murmurs

No hepatosplenomegaly, no palpable lymphadenopathy

Bloods
CRP 23 ESR 30
PLT 145 no malarial parasites
All other routine bloods normal

Factor XI 1.5% (Normal range 50-150%)

Plan



- Blood cultures (negative)
- Antibiotics
  - Vancomycin
  - Ceftriaxone 2g bd
  - Metronidazole 500mg tds

WAIT FOR THE FACTOR XI

Differential Diagnosis?

Differential Diagnosis?

HIV

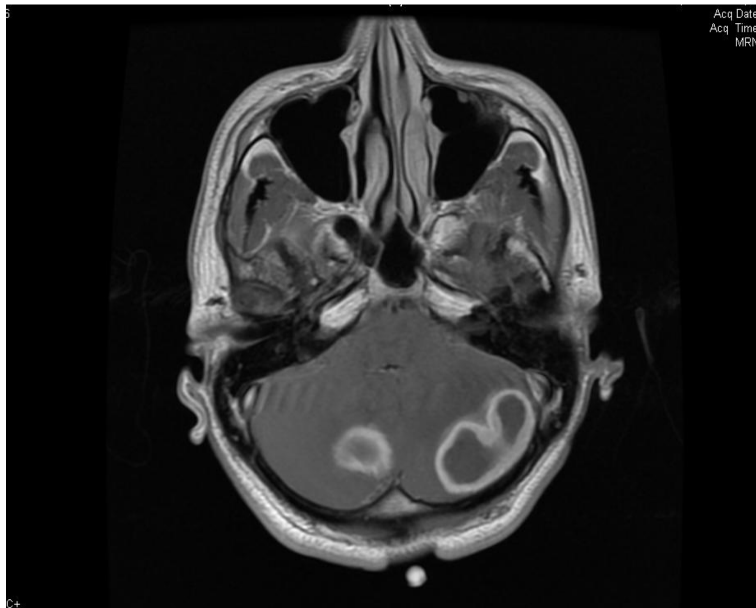
- Toxoplasmosis
- Nocardia
- Tuberculosis
- Cryptococcus
- Lymphoma

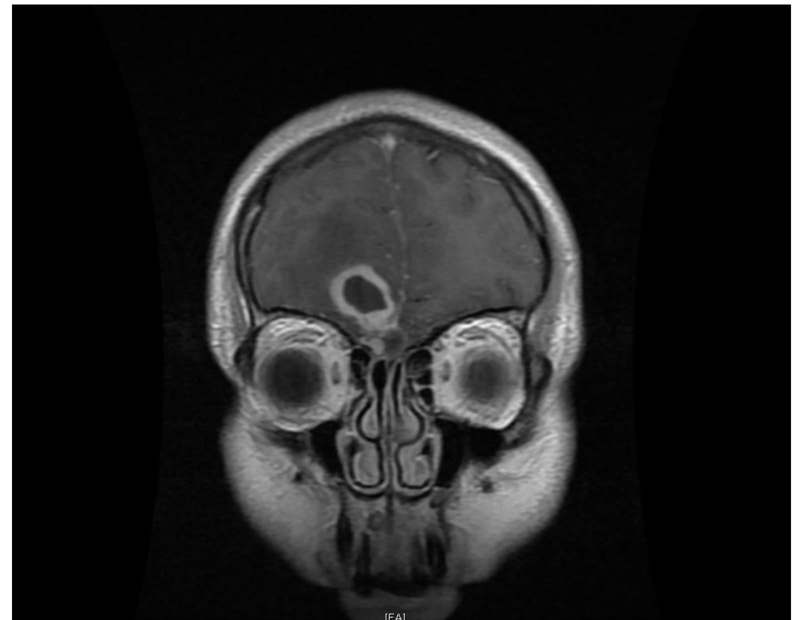
Non-HIV

- **Bacterial (sinusitis associated)**
- Tuberculosis
- Hydatid
- Fungal
- Amoebic
- Neurocystercicosis

Malignancy

A Tale of Two Brain Abscesses !



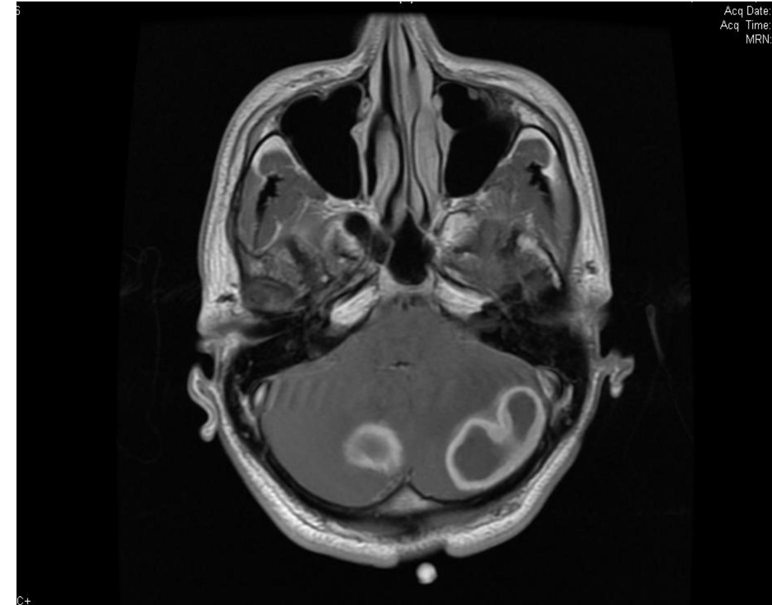


PHILIPPINES

PAKISTAN

Case 1 (Philippines) - Progress

HIV	**Negative**
Cryptococcal Antigen	Negative
Toxoplasma	IgG - IgM -
Hydatid serology	Negative
HTLV	Negative
Quantiferon	**Positive (Ag 12.0 IU.ml)**
CD4 count	1,130 (42%)
Immunoglobulins	Normal
Serum electrophoresis	Negative
Hepatitis C	Negative
Hepatitis B	sAg, sAb, core Ab NEG
E. histolytica serology	NEG

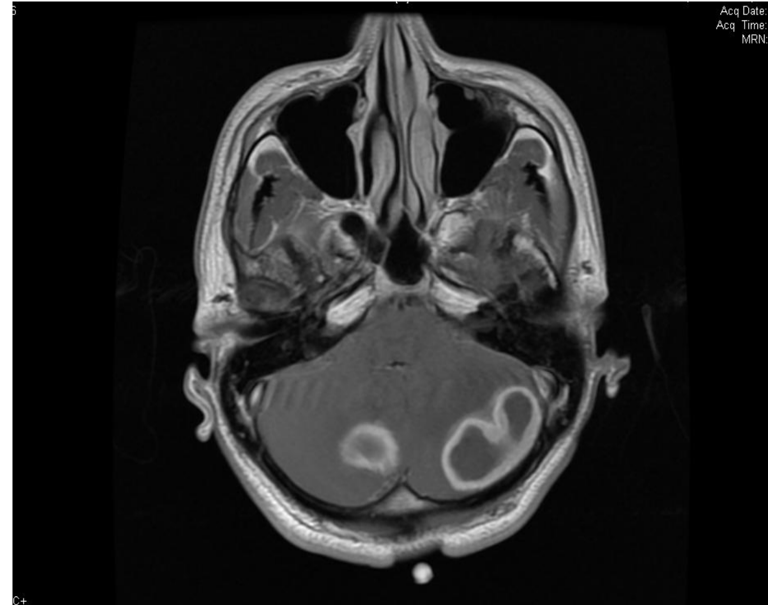


Case 1 (Philippines) - Progress

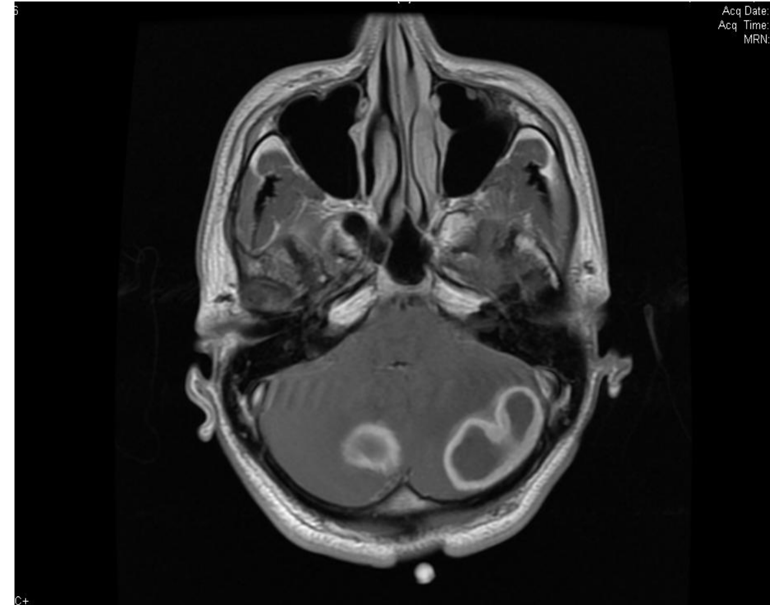
Brain biopsy:

- Caseous material macroscopically
- Frozen section
  - – no malignancy/ inflammatory tissue

No antibiotics given



Case 1 (Philippines) - Progress



Brain biopsy:

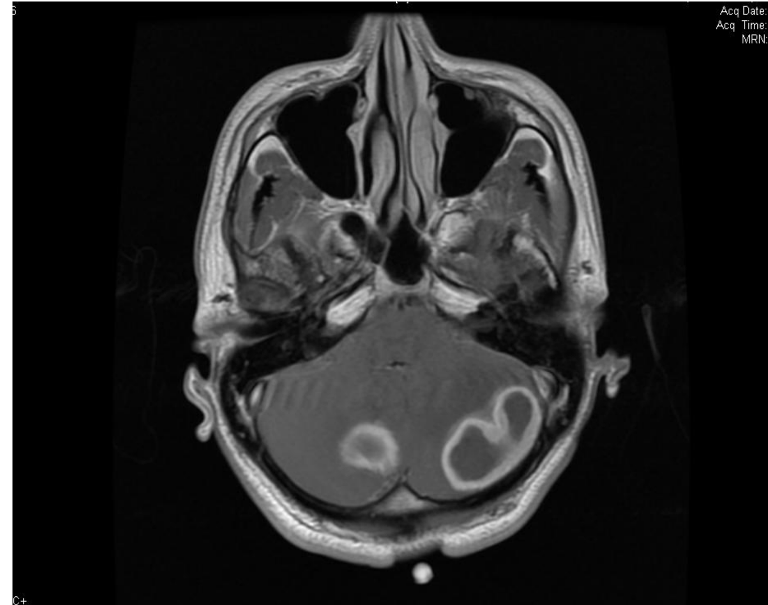
- Caseous material macroscopically
- Frozen section
  – no malignancy/ inflammatory tissue

No antibiotics given

Day 3 = Formal Pathology results

- Necrotizing Granulomatous inflammation
- AFB smear negative
- TB PCR ordered
- Standard 4 drug therapy & Prednisolone 40 mg daily

Case 1 (Philippines) - Progress

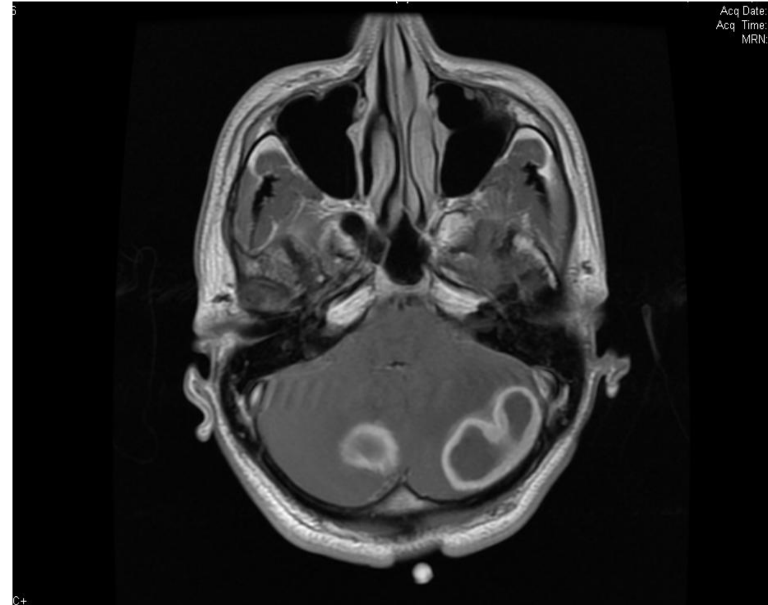


Fresh Brain Biopsy Tissue

- 1+ polymorphs
- No organisms seen on gram stain
- AFB smear negative
- fungal culture negative

CSF – nil cells, no growth

Case 1 (Philippines) - Progress



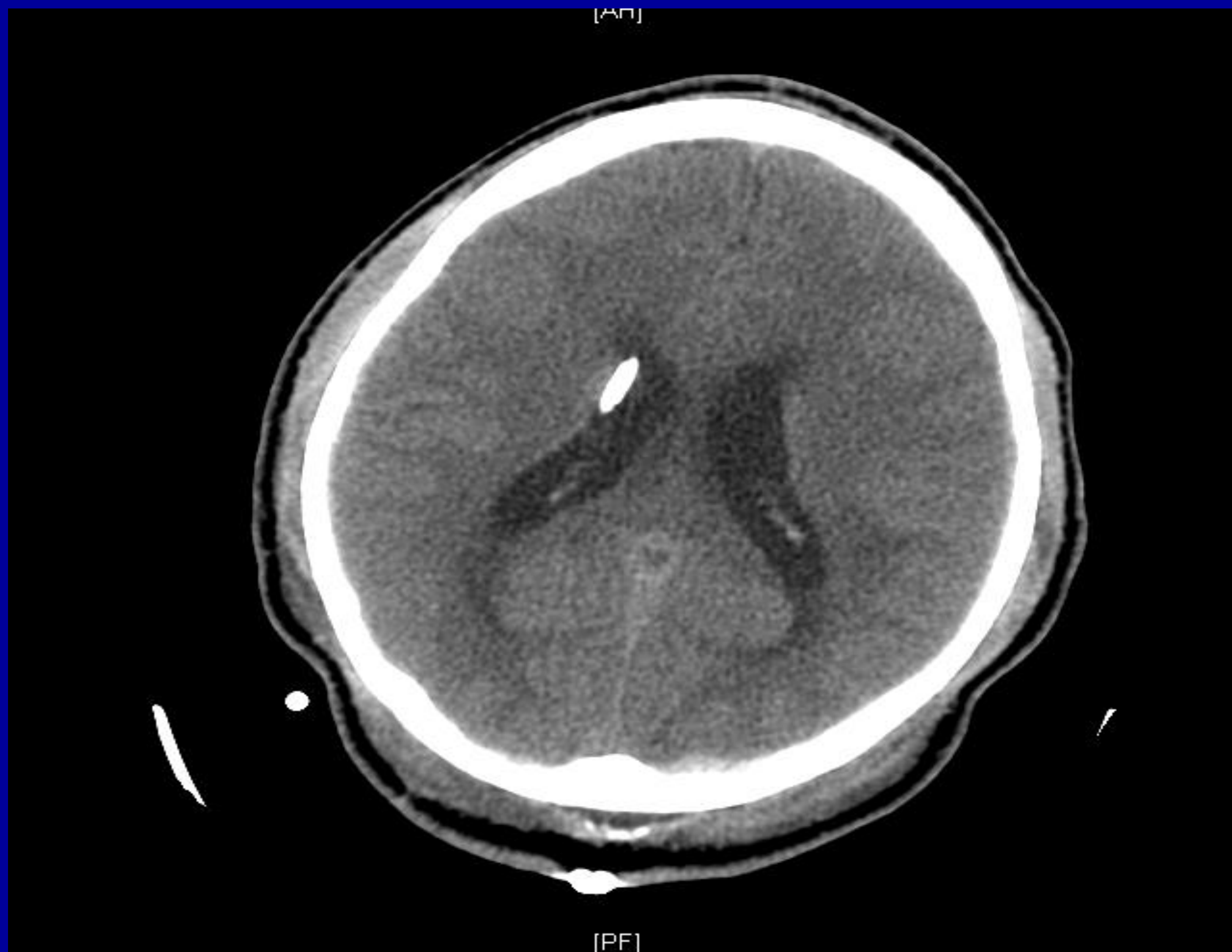
Fresh Brain Biopsy Tissue

- 1+ polymorphs
- No organisms seen on gram stain
- AFB smear negative
- fungal culture negative

CSF – nil cells, no growth

Day Five

- branching GPB from enrichment broth
- ZN and modified ZN negative >> added penicillin/meropenem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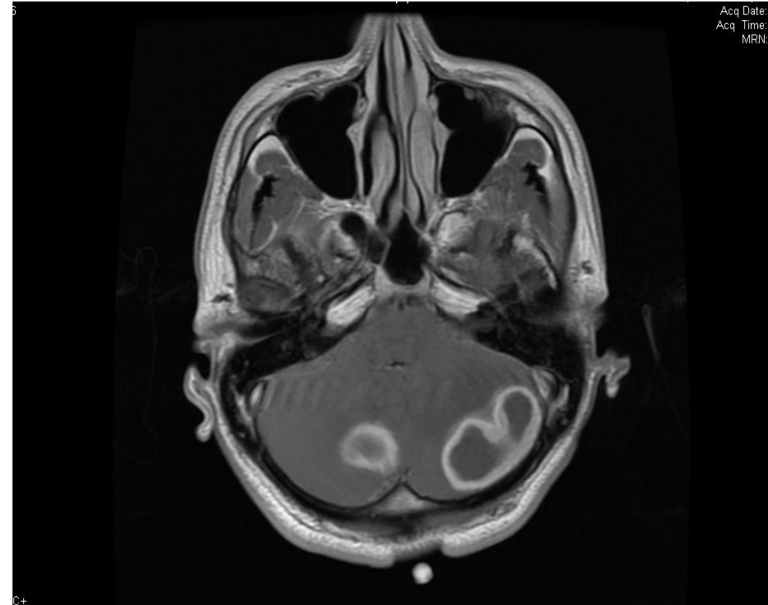
Case 1 (Philippines) - Progress



Day Six

- **TB PCR positive !!!**
  micro + histo one possible AFB each!

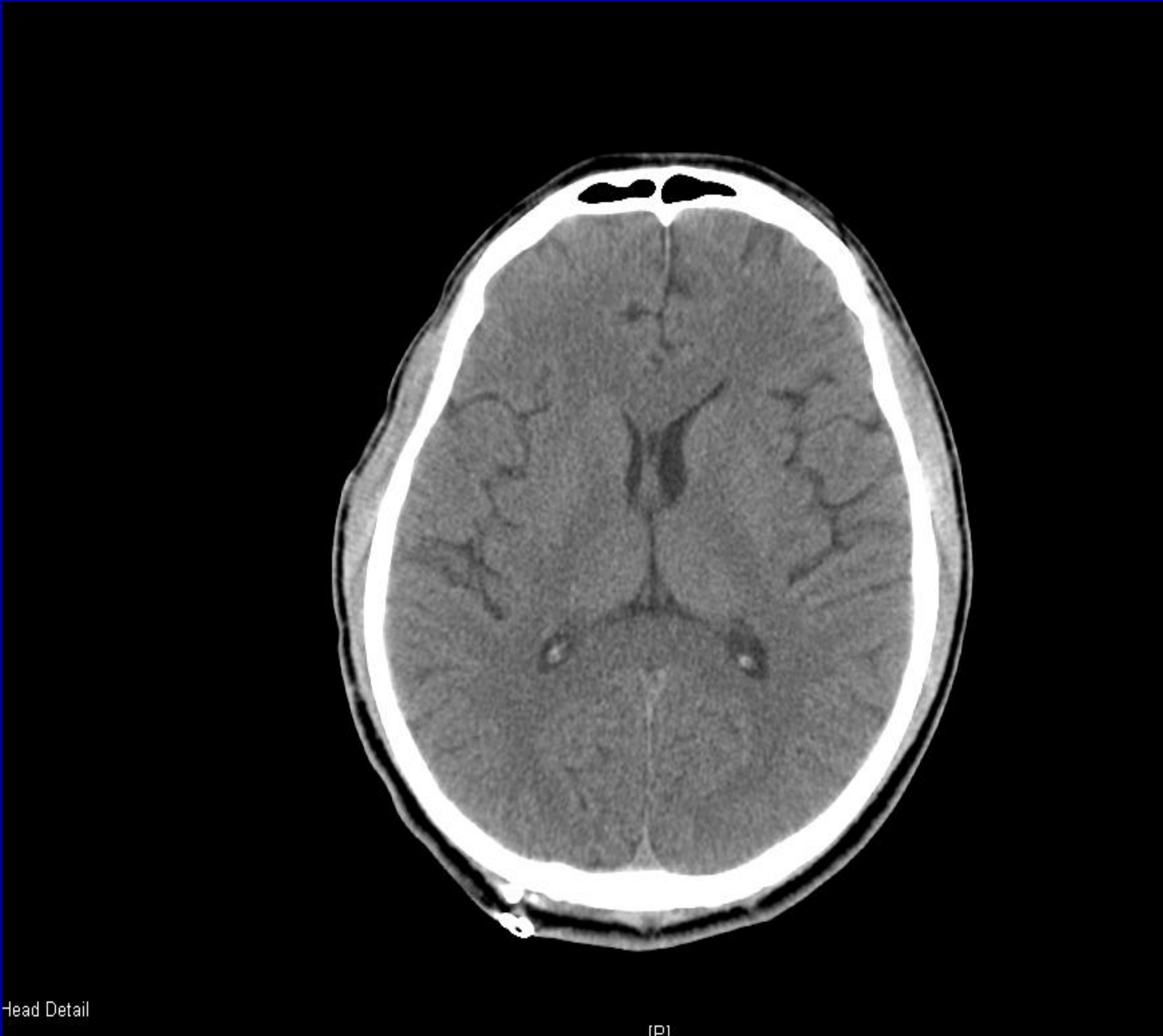
- Antibiotics ceased

Then he had problems …………………………………

Case 1 (Philippines) - Progress

Post-operative complications

- Persistent fever – no other cause than TB found
- Persistently raised ICP and high EVD outputs
- **Day 18 – CT brain – planned for VP shunt**



Head Detail
[P]

A Narrow Escape!

Day 19 - EVD clamped, shunt cancelled due to small ventricles

Discharged

- Residual mild ataxia, slowed gait, no cranial nerve palsies
- Weekly LFTS at GP
- Weaning dexamethasone over 4 weeks
- Neurosurgery/ ID/ Opthalmology outpatient review

A Narrow Escape!

Day 19 - EVD clamped, shunt cancelled due to small ventricles

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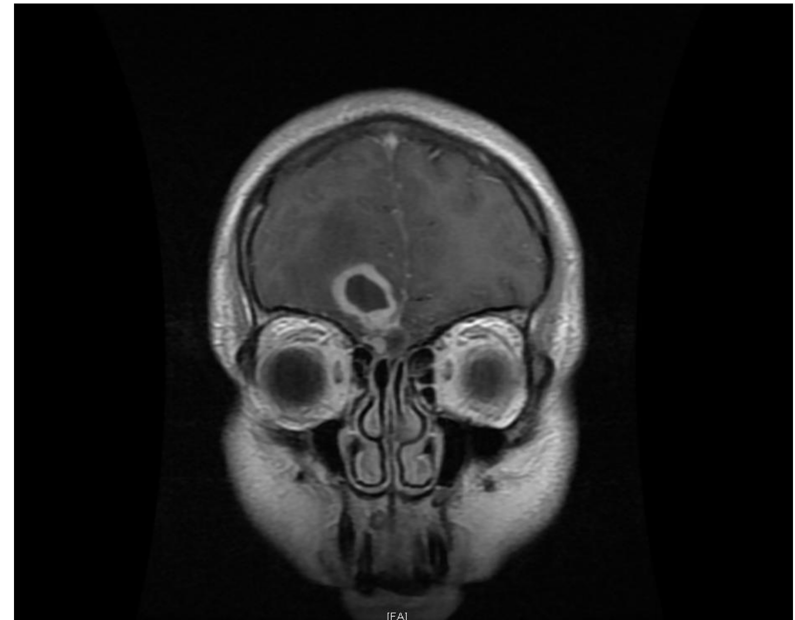
Residual mild ataxia, slowed gait, no cranial nerve palsies
Weekly LFTS at GP
Weaning dexamethasone over 4 weeks
Neurosurgery/ ID/ Opthalmology outpatient review

M.tuberculosis grown from brain tissue = fully sensitive isolate

Case 2 (Pakistan) - Progress

HIV	**negative**
CXR	Normal
Transthoracic echo	Normal
Hydatid	negative
Quantiferon	negative
Hepatitis C	negative
Hepatitis B	sAg -
Immunoglobuins	normal
Serum electrophoresis	normal
E.histolytica	NEG



Case 2 (Pakistan) - Progress

- **Second MRI on 7 days therapy worsening**
- Craniotomy and resection of abscess performed with repair of defect into frontal lobe
- Factor XI levels measured and replacement given around surgery + transexamic acid

Case 2 (Pakistan) - Progress

Cerebral Abscess - Microbiology:

- Five cerebral tissue specimens
  3+ polymorphs
  2+ Gram positive cocci resembling staph
  Grew 2+ **methicillin susceptible *S.aureus*** *(*penicillin resistant only)
- No acid fast bacilli seen/fungal cultures negative

Dermoid tissue - Microbiology

- no polymorphs
  no organisms seen
  Grew 2+ **methicillin susceptible *S.aureus*** *(*penicillin resistant only)
  No acid fast bacilli seen/fungal cultures negative

Histopathology:

Brain **–** acute on chronic inflammation, no mycobacteria or fungi
Dermoid – acute on chronic inflammation in squamous epithelial cell lined sinus tract

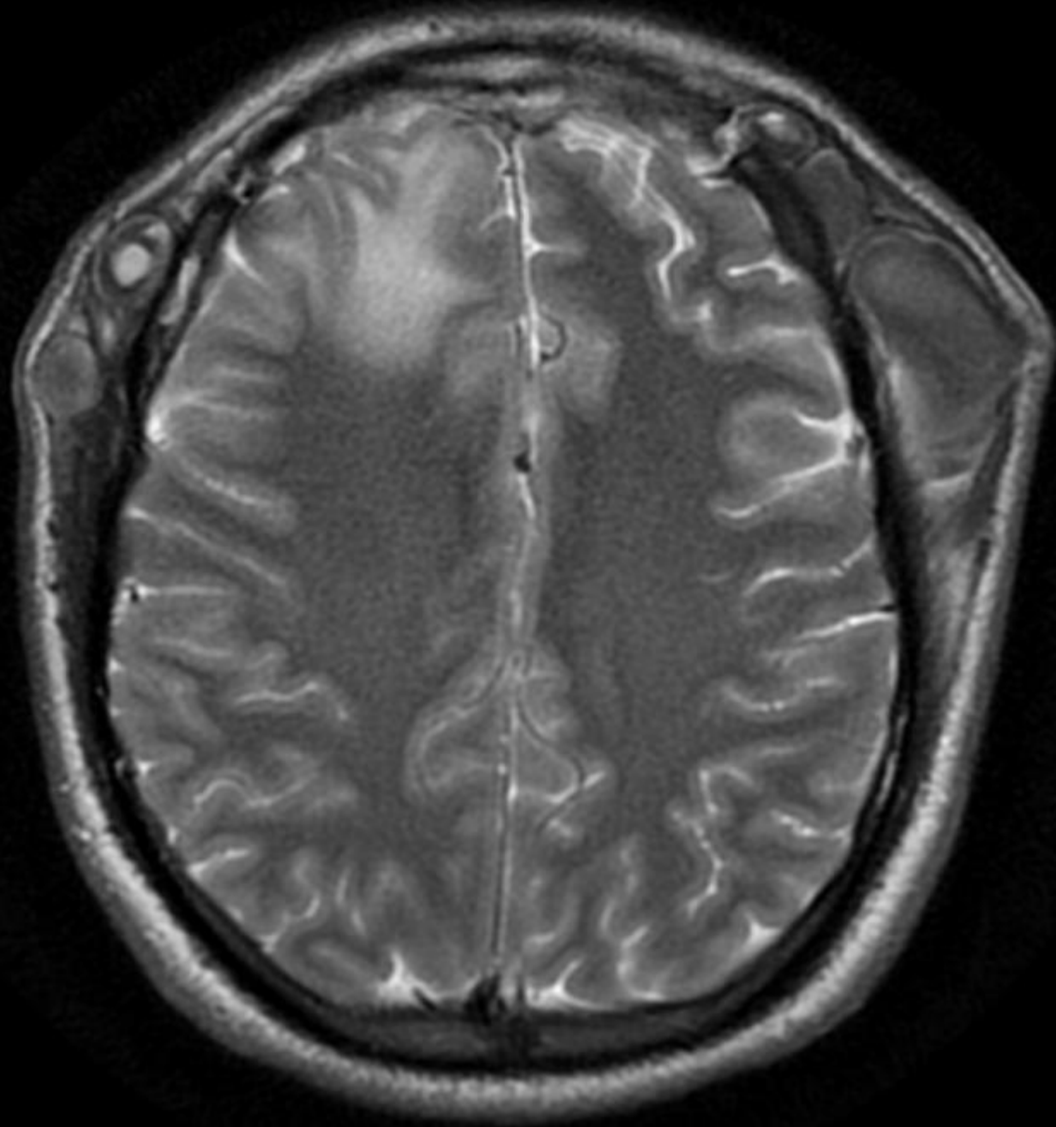
Case 2 (Pakistan) - Progress

Planned for second operation to remove dermoid

- Day 14 = CRP 9, afebrile on flucloxacillin
- Awaiting sourcing of Factor XI from overseas

Day 19

- sudden swelling over frontal region
  >> MRI ? Pus ? Blood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Case 2 (Pakistan) - Progress

Planned for second operation to remove dermoid

- Day 14 = CRP 9, afebrile on flucloxacillin
- Awaiting sourcing of Factor XI from overseas

Day 19

- Sudden swelling over frontal region >> MRI brain

Day 26

- Excision of dermoid septal cyst

Discharge Plan:

- Complete 6 weeks IV flucloxacillin
- 3 months oral flucloxacillin – review in ID/Neurosurgery/ID Geelong

Discussion

- Differential Diagnosis of Brain Abscess in this context
- What is a Dermoid sinus tract?
- Factor XI deficiency and its implications
- **CNS Tuberculosis**
  - diagnosis
  - use of TB PCR for diagnosis
  - treatment recommendations in tuberculous brain abscess

Differential Diagnosis

Indian Perspective on Multiple Ring Enhancing lesions:

Prospective case series 2004-2006 Lucknow India (Uttar Pradesh)

- 110 consecutive patients (4 HIV +)
- Entry criteria = Contrast CT 2 or more ring enhancing lesions (at least 1 < 20mm D)
- HIV, ELISA for taenia solium, CSF – gram, india ink, AFB, cytology
  No histopathology performed
- 59% "probable etiologic diagnosis"
  If diagnosis unclear, received empiric antituberculous treatment + oral steroids
- Repeat CT brain at 6 months

Garg RK et al. J. Neurological Sciences 2008;266:92-96

Differential Diagnosis

Indian Perspective on Multiple Ring Enhancing lesions:

Diagnosis	Number
Tuberculosis	45
Neurocystercicosis	10
Neoplastic	24
Toxoplasmosis	2
Cryptococcus	2
SLE	2
Brain abscess	1
Undiagnosed	28

Nasal Dermoid Sinus

- **Result from congenital fusion abnormalities at the nasal root**
- Dermoids are epithelium-lined sinus tracts that extend from the root of the nose through the nasal septum to the anterior cranial fossa
- Frequency approximately 1:20,000 – 1:40,000 births
  - Account for 1% of all dermoid cysts
  - Autosomal dominant inheritance has been described
- Nasal dermoids with intracranial extension should be surgically excised
  - due to the risk of cerebral abscess
  - can mimic recurrent sinusitis

Edmonds et al. Current Problems in Diagnostic Radiology 2007 36(1) : 43-47.
Maniglia AJ et al. Archives of Otolaryngology- Head and Neck Surgery. 1989 115(12): 1424-1429.

Factor XI Deficiency "Rosenthal syndrome" or "Haemophilia C"

- Plasma glycoprotein
  - in the contact phase of blood coagulation
  - generates additional thrombin, down regulates fibrinolysis

- Generally not associated with spontaneous bleeding
  - surgery tissues with high intrinsic fibrinolytic activity i.e. nose, oral cavity

- Congenital condition
  - Severe deficiency < 15% homozygote or compound heterozygote
  - Family being tested through haemophilia centre at Alfred

- Any further surgery at Alfred as haemophilia centre for state
  - support the obtaining of supply of pooled human factor XI nationally
  - only a few vials of Factor XI produced by CSL every few months

Central Nervous System Tuberculosis

3 Clinical Entities

- Meningitis (dominant form)
- Tuberculoma (meningeal or parenchymal)/abscess
- Spinal tuberculous arachnoiditis

CNS = approximately 10% of all patients with tuberculosis globally

Immunocompetence

- 1% of all of TB + 6% of extrapulmonary TB
- A polymorphism in Toll-interleukin 1 receptor appeared to affect susceptibility to meningeal TB in a study of 175 HIV-negative patients and 392 controls

Hawn et al. J Infect Dis 2006; 194:1127 CDC, reported tuberculosis, 2004.
Farer LS et al. Am. J. Epidemiol. 1979:109(2):205-217 Dube MP et al. Am J Med 1992 93:520
Hejazi N and Hassler W. Infection 1997 41(4):233-239
Farrar DJ et al. Am J Med 1997;102:297-301

Central Nervous System Tuberculosis

Pathogenesis of Meningitis:

- tubercles established in the brain, meninges, primary TB or late reactivation in immunodeficiency
- chance occurrence of a subependymal tubercle with progression and rupture leads to meningitis

Complicating Hydrocephalus

- communicating hydrocephalus from extension of inflammatory process to affect resorption of CSF is common: Noncommunicating, brainstem tuberculoma obstructing the aqueduct is rare

Signs of active TB outside the CNS are often absent
1/3 of pts with TB meningitis have miliary tuberculosis on presentation

Jinkins JR. Neuroradiology 1991;33(2):126-35
Al-Deeb SM et al. Clinical Neurology and Neurosurgery 1992. 94:S30-S33

Central Nervous System Tuberculosis

Tuberculoma

- Granulomatous inflammatory tissue that contains epithelioid and giant cells

- Uncommon in the West
  Accounts for 20-30% of all intracranial TB in India and Asia

- Often located in the basal ganglia, thalamus and hypothalamus
  - varying in size from a few mm to several cm in diameter

Harder E et al. Am.J. Med. 1983 74(4):570-6 / Dolin PJ et al. Bull. World Health Organ. 72(1994) 213-220.

Central Nervous System Tuberculosis

Tuberculous Brain Abscess

- May resemble astrocytoma due to edema and low grade gliosis
- Mainly supratentorial and rarely in cerebellum / pus with capsule of granulation tissue
- Rare presentation of CNS TB – 57 reported cases in literature to 1978
- Approximately another 20 reported to 2002
  - one case associated with superior sagittal sinus thrombosis
- Most case reports in HIV-infected or immunocompromised patients
- India 2002 – 1 case drainage "in ED" recovered with antituberculous therapy

Whitner DR. Archives of Neurology 1978;35(3):148-53. Barber PA et al. Acta Neurological Scandinavica 1999;99:202-3.
Babu ML and Shavindaer MC. JK-Practitioner 2002;9(4):262-263 Ildan F et al. Neurosurgical Review 1994;7(4):317-20.
Velasco-Martinez JJ et al. AIDS 1995;9:1197-9. Tangviriyapaiboon T & Suwansirikul S . J Infcet Dis Antimicrob Agents 2005.

Sensitivity of TB PCR

Early Case Report 1999

- Diagnosis of en plaque tuberculoma in a 62 year old
- Solitary lesion, deep in a sulcus in relation to the meninges

- CSF 200 lymphocytes, protein elevated, glucose low
  - AFB smear and mycobacterial culture negative , TB PCR +

J.Clin. Micro 1999 37(2):467-470

Meta-analysis of NAATs for tuberculous meningitis 2003

- Pooled sensitivity of commercial assays was 56%
- Difference in sample volume
- Difference in target sensitivity

Pai M et al. Lancet Infect Dis 2003;3:633

Sensitivity of TB PCR

Target for PCR in this case:

- IS6110 a *m.tuberculosis* complex-specific insertion sequence
- Real-time PCR [ct was 34.26, threshold 40, relatively weak signal]
- Good target as multiple copies (5-20) in most strains MTB [range 0-30]
- Also described in the genome of *M.smegmatis*
- Does not detect the "Vietnamese" strain
- Can perform panmycobacterial PCR if required (ITS)

Chawla K et al. J Infect Developing Countries

- Evaluated an IS6110 assay for 104 different tissue samples (in saline) in comparison to histopathology
- Caseating granulomas or AFB positive
- 74% sensitivity and 96.1% specificity

Treatment Recommendations: No randomised controlled trials

American and British Thoracic Society/IDSA
- 2 month intensive
- Continuation phase 12-18 mths, depending on clinical response

Australian Therapeutic Guidelines
- 12 months, with consideration longer therapy if slow to respond

Tuberculous Brain Abscess
- Combined surgical excision + ATT increased survival (case series)
- Serial CT scanning to abscess resolution
- Sequelae: calcifications, encephalomalacia

Tuberculoma/Abscess
- Rare paradoxical progression with therapy (> 35 cases reported)

Hejazi N and Hasslet W. Infection 1997 (4): 233-239
Ng SK et al. Singapore Med J 2011 42(7):325-327
Whitener DR. Archives of Neurology 1978;35(3):148-53.