ORBITAL NK/T CELL LYMPHOMA AS FIRST PRESENTATION OF HIV IN OVERSEAS VISITOR

ASHM Case Presentation Breakfast
8th November 2017

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Mrs CN - 1st Presentation

- 37-year-old Zimbabwean female visitor
  - 1 week of frontal headache, subjective fever, nasal congestion
  - 4 days of right-sided facial pain and swelling
- Past medical history:
  - Recurrent sinusitis - maxillary sinus surgery
- Nil regular medications
- Lives with husband and 3 children

1st presentation

- Examination findings:
  - Right peri-orbital swelling
  - No cranial neuropathy
  - Purulence within right maxillary antrum
- CT head – pansinusitis
- Diagnosis: Right sinogenic peri-orbital cellulitis

1st Presentation

- Management:
  - Intravenous piperacillin/tazobactam
  - Single dose intravenous dexamethasone
  - Xylometazoline nasal spray
- Discharged home 36 hours later
  - Oral amoxicillin/clavulanic acid
  - Nasal decongestant

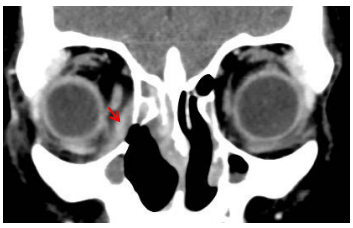
2nd Presentation – 6 days later

- Recurrence of right periorbital swelling and pain

- Examination findings
  - Normal vision 6/6
  - Mild infra orbital cellulitis
  - Right periorbital swelling
  - No cranial neuropathy

2nd Presentation – 6 days later

- CT head



- Blood tests
  - WCC - 5.01 x 10^9/L
  - Lymphocytes - 0.92 x 10^9/L
  - C-reactive protein - 57mg/L

- Incision and drainage
- Intravenous piperacillin/tazobactam

Progress

- Right nasal tissue culture:
  - Methicillin susceptible *Staphylococcus aureus*
  - *Enterococcus faecalis*
  - Acid fast bacilli not seen, no fungal growth

- Ongoing fevers, progressive lymphopenia

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Further investigation

HIV Serology (CMIA):		
HIV-1/2 antigen/antibody		Reactive
HIV-1/2 Western Blot:		
	p17..:	NOT Detected
	p24..:	Detected
	p55..:	Equivocal
	p31..:	Detected
	p51..:	Equivocal
	p66..:	Detected
	gp41.:	Detected
	gp120:	Detected
	gp160:	Detected
	HIV-2:	NOT Detected
Western Blot Interpretation:		POSITIVE

HIV-1 Antibody . . . Detected

HIV work up

- CD 4 absolute count – 26 x 10^6/L (2%)
- Viral load – 281,838 copies/ml
- No previous exposure to Hepatitis B or C
- Schistosoma/Strongyloides/Syphillis serology negative
- Cryptococcal antigen negative
- Myco/F lytic blood culture collected

- Chest x-ray normal

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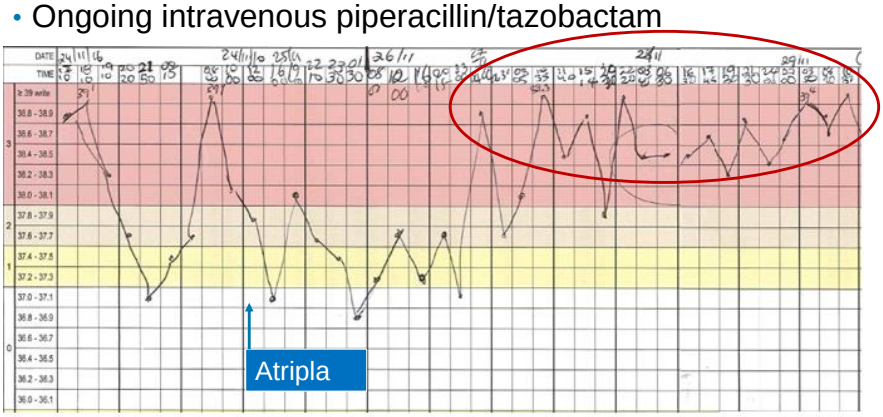
Progress

- Commenced on Atripla, fluconazole for oral candidiasis, azithromycin and cotrimoxazole prophylaxis
- Ongoing intravenous piperacillin/tazobactam



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Progress

- Increased right periorbital swelling
  - Repeat debridement

	28/11
Hb	123
WCC	3.43
Neutrophils	2.52
Platelets	203
ALT	99
ALP	276
GGT	680

- Abdominal ultrasound – no hepatic lesion

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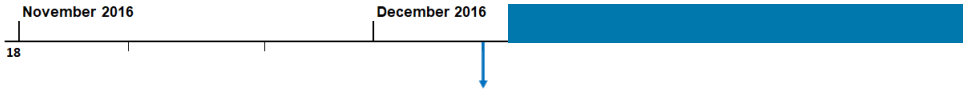
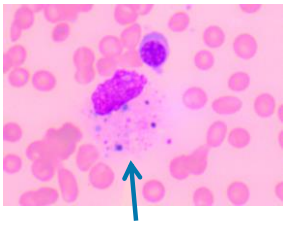
Progress

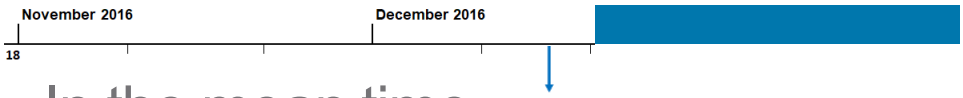
	28/11	2/12	5/12
Hb	123	91	88
WCC	3.43	3.1	1.79
Neuts	2.52	2.49	0.47
Platelets	203	187	194
ALT	99	185	92
ALP	276	549	621
GGT	680	1270	1500
Ferritin		90800	
LDH		2270	
Triglyceride		1.8	



Haematology consult

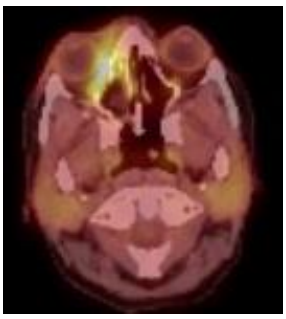
- Possible macrophage activation/haemophagocytic lymphohistiocytosis (HLH)
  - ? HIV associated
  - ? Other co-infection
  - ? Underlying lymphoma
- Bone marrow aspiration and trephine
- Dexamethasone 20mg daily





In the mean time…

- Histology nasal mucosa:
  - Extra-nodal NK/T cell lymphoma, nasal type
  - CD 2/7/56 + and EBER +
  - Other T cell markers: CD 3/4/5/8 negative
  - T cell gene rearrangement non-contributory
- EBV viral load
  - 2.96 x 10^2 IU/ml
- Bone marrow not involved
- PET scan
  - Stage 2 disease



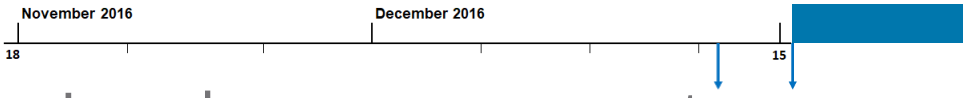
Pyschosocial wellbeing

- Confidentiality
  - Family unaware of diagnosis except husband
- Stigmatization and discrimination
- Healthcare cost
  - Antiretrovirals
  - Cost of chemotherapy and choice
  - Inpatient cost

Medicare Ineligible PLHIV

- Jurisdictional arrangement
- Western Australia:

"All fees and charges associated with notifiable sexually transmitted disease management are to be waived by the Health Service Provider managing the care of the patient. This applies to all patients regardless of Medicare eligibility status." [1]



Lymphoma management

- What is the cost? What are the options?

- CHOEP Cycle 1
  - Cyclophosphamide, doxorubicin, etoposide, vincristine and prednisolone
  - Antiretrovirals changed to Truvada + Dolutegravir

- Is that the best option?

Lymphoma treatment - options

Ideal	Compromise

• SMILE;
  • Dexamethasone
  • Methotrexate
  • Ifosfamide
  • L-asparaginase
  • Etoposide
• Response Rate 66%[2]
  • 4 cycles + RTX 50Gy
• 5-year overall survival 50%[2]
• TRM >7%![3]
	• CHOEP;
	  • Cyclophosphamide
	  • Doxorubicin
	  • Etoposide
	  • Vincristine
	  • Prednisolone
	• Response rate 58%[3]
	  • 4 cycles + RTX 45Gy
	• 3-year overall survival 59%[3]
	• 65% progressed on treatment[3]

The dilemma…

- HIV treatment fully accessible
- Decision regarding optimal lymphoma treatment influenced by
  - Medical consideration
  - Financial reasons
- Medicare eligible Australian
  - Likely different treatment to what she was offered

HLH in HIV

- 'Secondary' HLH
- Immune dysregulation and excessive inflammation[4]
  - Macrophage activation
  - Lack of negative feedback from NK cells and cytotoxic lymphocytes
- All stages of HIV[5-7]

HLH in HIV

- Trigger:
  - Viruses, bacteria, mycobacteria, fungi, protozoa[8,9]
  - Neoplasm
- Diagnostic challenges
  - Many symptoms can just be HIV itself
- Fulminant and aggressive[10]

NK/T cell lymphoma

- More common in Asia, Central and South America[11-13]
- Limited reports in the HIV +ve population
  - 6/199 (3%) in a 20-year review in South Africa[14]
- Male predominance (2:1)
- EBV +
- Types:
  - Nasal (80%)
  - Non-nasal (20%)
- “Lethal midline granuloma”
- Haemophagocytosis is a late complication

Back to our patient…

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