Imaging HIV – and the problem of TB Co-infection in Children

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Why HIV is important for me

• 2/3 of all HIV infections = sub-Saharan Africa
• 91% of newly HIV infected children = born in Africa
• ..the result is ...top 30 infant mortality rates = in Africa

• > 90% of children with TB live in developing world
• Incidence TB sub-Saharan Africa = 2X S-E Asia (350/100,000)
• Cape Town South Africa has the second highest rate of TB in the world (935/100,000)

• Of global 8.6 million TB cases 13% are HIV +ve and of these 75% = in Africa (WHO 2013).
What I will show you today

HIV

CHEST

CNS

Co-infection with TB
HIV and imaging the Chest
CXR differential in HIV is wide

<table>
<thead>
<tr>
<th>Infections</th>
<th>Neoplastic</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Bacterial / TB / MAC</td>
<td>• Lymphoma</td>
<td>• LIP</td>
</tr>
<tr>
<td>• Fungi / Pneumocystis</td>
<td>• Kaposi</td>
<td>• IRIS</td>
</tr>
<tr>
<td>• Viral</td>
<td></td>
<td>• Interstitial</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Bronchiectasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Aspiration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cardiac</td>
</tr>
</tbody>
</table>
Please choose:

- Milliary TB
- Pneumocystis
- Kaposi LIP
- Strep
- TB
- Aspergilosis
- Varicella
- Kaposi
"Una Faccia Una Razza" (One Face, One Race)
Sav’s three tricks in HIV:
CD 4 Trick:
Fever + CD4 > 200 = bacteria or TB

<table>
<thead>
<tr>
<th>Any CD 4</th>
<th>Bacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TB</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 &lt; 200 c/mm³</td>
<td>Pneumocystis</td>
</tr>
<tr>
<td></td>
<td>Cryptococcus</td>
</tr>
<tr>
<td>CD4 &lt; 50 c/mm³</td>
<td>Coccidiodomycosis</td>
</tr>
<tr>
<td></td>
<td>CMV</td>
</tr>
<tr>
<td></td>
<td>MAI</td>
</tr>
<tr>
<td></td>
<td>Aspergillus</td>
</tr>
</tbody>
</table>
### CXR lung parenchyma trick

<table>
<thead>
<tr>
<th><strong>Bacteria</strong></th>
<th><strong>Unilateral ---- (bilateral)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>TB</td>
<td>Focal -------------------(multifocal)</td>
</tr>
<tr>
<td></td>
<td>Segmental-----(lobar)</td>
</tr>
<tr>
<td><strong>Pneumocystis</strong></td>
<td><strong>Diffuse bilateral</strong></td>
</tr>
<tr>
<td>CMV</td>
<td></td>
</tr>
<tr>
<td>LIP</td>
<td></td>
</tr>
<tr>
<td>Kaposi</td>
<td></td>
</tr>
<tr>
<td>Cardiac failure</td>
<td></td>
</tr>
<tr>
<td>Aspiration</td>
<td><strong>Dependent</strong></td>
</tr>
</tbody>
</table>
## CXR Exclusion trick

<table>
<thead>
<tr>
<th>NOT in</th>
<th>bacteria and aspiration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lymphadenopathy</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Effusion</strong></td>
<td>PJP / LIP</td>
</tr>
<tr>
<td><strong>Cavities / cysts</strong></td>
<td>lymphoma / Kaposi</td>
</tr>
</tbody>
</table>
However, clinicians usually want to know one thing: before starting HAARTreatment, can we ‘exclude’ TB?
Diagnosis of TB in children
=
identify lymphadenopathy
Lymphadenopathy on AP:
Hilum should be a hippo’s open mouth
Nodes = a cauliflower in the mouth

Right hilar lymphadenopathy

Left hilar lymphadenopathy

Calcified lymphadenopathy
Airways are a up-side-down tree
Lymphadenopathy = ‘compressed air-way branches’
Lateral radiograph
Lymphadenopathy on Lateral

- Normal structures (=horseshoe)
- Diverging vessels (=tentacles)
- Lymphadenopathy (=‘doughnut’)

Lateral: doughnut replaces the horse-shoe and tentacles
What makes the doughnut?

Subcarinal and left hilar lymphadenopathy

And there is the doughnut........

Midsagital: subcarinal nodes

Far para-sagital: Left hilar nodes
Doughnuts and other foods

No mass behind bronchus intermedius
When child is HIV-infected:
You’ve gotta be Sherlock Holmes and uncover TB

Air space and airway
Air space, cavity and airway
Air space expansile and airway
Air space, effusion and airway
Milliary nodules
If you don’t see the TB you may get IRIS

Before HAART

After initiation of HAART
Is POC US the answer for Africa?
Point of Care US:
for TB and Pneumonia

Tsung 2012
Some research going on

- **Research projects** using US at the Red Cross Children’s Hospital in Cape Town, South Africa for mediastinal TB lymphadenopathy and pneumonia
- Others are using TCD for TB and HIV

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**The value of transcranial Doppler imaging in children with tuberculous meningitis.**

van Toorn R, Schaal HS, Solomon R, Laubscher JA, Schoeman JP.

**Abstract**

**PURPOSE:** Transcranial Doppler imaging (TCDI) is potentially a valuable investigational tool in children with tuberculous meningitis (TBM), a condition often complicated by pathology relevant to Doppler imaging such as raised intracranial pressure (ICP) and cerebral vasculopathies.

**METHODS:** Serial TCDI was performed on 20 TBM children with the aim of investigating cerebrovascular haemodynamics and the relationship between pulsatility index (PI) and ICP.

**RESULTS:** We observed a poor correlation between ICP and PI in children with communicating hydrocephalus ($p = 0.72$). No decline in PI was noted following 7 days of medical therapy for communicating hydrocephalus ($p = 0.78$) despite a concomitant decline in ICP. Conversely, a decline in PI was noted in all four children with non-communicating hydrocephalus who underwent cerebrospinal fluid diversion. High blood flow velocities (BFV) in all the basal cerebral arteries were observed in 14 children (70%). The high BFV persisted for 7 days suggesting stenosis due to vasculitis rather than functional vasospasm. Complete middle cerebral artery (MCA) occlusion, subnormal mean MCA velocities ($<40$ cm/s) and PIs ($<0.4$) correlated with radiologically proven large cerebral infarcts.

**CONCLUSIONS:** TCDI-derived PI is not a reliable indicator of raised ICP in children with tuberculous hydrocephalus. This may be attributed to individual variation of tuberculous vascular disease, possibly compromising cerebral vascular compliance and resistance. Basal artery stenosis secondary to vasculitis is observed during the acute stage of TBM in the majority of children.

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HIV and the CNS
What can be seen with imaging?

‘HIV ENCEPHALOPATHY’ (HIVE)
- Atrophy
- White matter abnormality

‘CONSEQUENCES of HIV’
- Calcifications
- Infections
- Vascular events / lesions
- Maliganancy [uncommon]

Additional:
monitoring disease progression and treatment response
What can I show you to look for?

- To look for atrophy as a marker of HIVE
- To identify HIVE and PML (progressive multifocal leukoencephalopathy) white matter signal patterns
- Understand that HIV is a major cause of BG calcification
- Look for vascular events
- Look for infections
- To understand the effects of HIV on TBM
HIV Encephalopathy (HIVE)

Atrophy and

White matter abnormality
What about atrophy?

- It is the most common finding (90%) in HIV imaging (Kauffman et al 1992, Safriel et al 2000, Kieck and Andronikou 2004)
- It’s the imaging representation of HIV encephalopathy
- It correlates with severity and viral load
- It is reversible or can be halted on HAART (Di Carli et al 1991)
- It is measurable on imaging
- But it is a late finding - we need something earlier in the disease
Volume loss

White matter:
- Expanded ventricles (in presence of large SAS)
- deep sulci (near ventricles)

Doesn’t it remind you of chronic evolution of HIE???
An objective, automated method of measuring volume loss: Matlab
Corpus Callosum: a surrogate marker of WM volume?
Results:

Brain volume only showed a trend relationship with nadir CD4.

Correlation degree of mental development and motor segmental CC thickness

Correlation of the CC length with immunity and microcephaly
What about the white matter signal?
Encephalopathy (HIVE):
T2 high signal

Bilateral ‘symmetric’
Spares sub-cortical U-fibres
Progressive multifocal leukoencephalopathy (PML)

- Much less common
- Have the JC virus
- Confused with HIVE but...
- More focal
- Asymmetrical
- Common posterior parietal
- Involve U-fibres
- Advanced cases - ‘bar-bell’ sign
Summary HIVE vs. PML

No mass effect or contrast enhancement

PML/HIVE

Distribution
- Uni-/bilateral asymmetric
  - PML
- Bilateral symmetric
  - HIVE

Location
- Subcortical U-~
  - PML
- Subcortical WM sparing
  - HIVE
More subtle WM abnormalities?

White Matter Signal Abnormalities in Children with suspected HIV-Related Neurologic Disease on Early Combination Antiretroviral Therapy.


Abstract

BACKGROUND: The natural history and manifestation of HIV-related neurological disease have been ameliorated by combination antiretroviral therapy (ART). We describe the characteristics of white matter signal abnormalities (WMSA) on magnetic resonance imaging (MRI) in children with HIV-related neurological disease.

METHODS: We reviewed MRI scans of children with suspected HIV-related neurological disease despite early ART, and correlated with clinical, neurodevelopmental data, virological markers and time on ART. These children were also on the Children with HIV Early Antiretroviral (CHER) trial.

RESULTS: MRI scans were performed at a mean age 31.9 months (range 8-54) on 44 children: 10 on deferred and 34 on early treatment arms, commencing ART at mean age of 18.5 and 8 weeks respectively. Multiple high signal intensity lesions on T2/FLAIR were documented in 22 patients (50%), predominantly in frontal (91%) and parietal (82%) white matter. No differences in neurodevelopmental scores comparing children with and without WMSA were found. Neither lesion load nor distribution showed significant correlation with neurodevelopmental scores or neurological examination. Normal head growth was more common in the WMSA group (p=0.01). There was a trend for association of WMSA and longer time on ART (p=0.13) and nadir CD4% (p=0.08).

CONCLUSION: Half of children referred with HIV-related brain disease had WMSA on T2/FLAIR. Our findings of the association with normal head growth and duration of ART require further study. We suspect that WMSA can occur early and that initiating ART by 8 weeks of life may be too late to prevent HIV from entering the CNS.

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Prevalence of WMSA “HIV related brain disease” = 50%

Of the 22 patients with WMSA:
- 17 patients pinpoint lesions < 1cm
- 8 confluent lesions
- 2 patients lesions > 1cm
- Lesion size: 5 - 12mm  
  (mean 7.2mm)
WMSA

- Half of children referred for HIV-related brain disease had WMSA on T2MRI
- Involved mainly frontal and parietal lobes.
- **Positive correlation of ‘time on ART’ and presence of WMSA**
- Trend correlating nadir CD4% and presence of WMSA.
HIVE with a normal signal?
Work in HIV infected adults: DTI and FA

• Normal looking subcortical WM and CC
• BUT...areas where FA decreased
• Patients with lowest FA had most advanced HIV  [Filippi CG et al 2001]

• Abnormalities corpus callosum in patients with HIV, associated with dementia severity and motor speed losses  [Wu Y et al 2006]
• Reasons: trafficking of virus from ventricular CSF
DTI:
FA group comparison of HIV infected vs. Controls
Consequences
Calcification
Basal ganglia calcification

• Commonest cause of BG calcification in children is HIV
• Up to 1/3 of children with HIV have calcification
• Usually affect palidus and putamen
• Less often frontal white matter / cerebellum
• Not seen before 10 months age
Infections:
Infection:

TBM: best feature is basal enhancement

Pyogenic meningitis:
Surface collections; Venous infarctions
Vascular: Infarction / aneurysms
Infarction
Other findings on the scan
Parotidomegally - painless bilateral Lymphadenopathy - cervical
HIV and TB together: Add petrol to the fire?
HIV and TB

• Because the body fails to contain TB in the lungs.....
• HIV predisposes to blood borne and extra-pulmonary TB......
• BUT
• HIV also affects imaging appearances of TB
MRI findings in children with tuberculous meningitis: a comparison of HIV-infected and non-infected patients

Gerrit Dekker · Savvas Andronikou · Ronald van Toorn · Shaun Scheepers · Andrew Brandt · Christelle Ackermann

TB and HIV co-infection: CNS
It’s the immune response to bacilli in the meninges that results in pathological features of TBM...
Diagnosis of TBM:

MRI diagnosis of pediatric TBM = basal enhancement (93%)
Basal Enhancement in HIV

BE = infrequent, less prominent, atypically distributed, milliary nodules (100%)
Ventriculomegally in HIV

CSF space = result of atrophy; hydrocephalus less frequent and exclusively communicating
So now you know....

HIV

CNS

CHEST

Co-infection with TB