Paediatric Infectious Diseases consults:

*your diagnosis please...*

Nicolette du Plessis
University of Pretoria
Kalafong Provincial Tertiary Hospital
nicolette.duplessis@up.ac.za
Cert ID(SA)

“The ID specialist is a uniquely trained clinician…”

“Effective clinical consultation and management”

“Interact effectively with colleagues”
“Part master diagnosticians, part medical sleuths, these specially trained doctors are often called upon to solve cases that baffle their colleagues.”

“We’re the Sherlock Holmeses of the medical world...”

Joyce Hessleberth
“You have to know the language of the entire spectrum and be able to deal with specialists in every field of medicine and surgery.”
It doesn’t hurt, too, to have a keen sense of history, which sometimes plays a pivotal role in reaching a diagnosis.

A keen sense of history is more enlightening than the evening news.

(Jeff Davidson)
“Like all top detectives, ID specialists are.., on the alert for that odd piece of data or seemingly trivial episode that may unlock an especially perplexing case.”

“A detailed history, one of the key investigative tools of the ID specialist.”
“And in listening to the details of a patient’s story, I can start to tingle a little bit when I start to see what the differential diagnosis might be and how to figure it out.”
12 year old girl

# chronic hip pain

- started at the age of 8 years
- chronic, fluctuating course

✓ bone pain in her upper legs

✓ not been associated with fever, swelling or loss of function

✓ no trauma history

Extensive investigations excluded malignancies and infective osteitis.
Social history: She is doing well in school.

There is no history of the following conditions in the family:

- ✔ Bone and joint disorders
- ✔ Inflammatory bowel disease
- ✔ Rheumatoid arthritis
- ✔ Psoriasis
- ✔ SLE
- ✔ Sjögren’s syndrome
- Well grown child
- Both hips have normal range of movement with no pain on passive or active movement.
- No swelling or erythema was noted.
- Skin: She has no acne, pustulosis, nail changes, vitiligo, pyoderma gangrenosum or erythema nodosum.
- Systemic exam was normal.
What next?

Sherlock...
MRI coronal STIR: high signal right calcaneus, left distal tibia and medial malleolus
MRI coronal T1 fat sat pre- and post-contrast images: Active lesion in right intertrochanteric region
Histology: Left medial malleolus biopsy shows granulomatous inflammation
Histology: Bone trabecle of right calcaneus with histiocytes, some epitheloid, mixed with plasma cells and lymphocytes
Malignancy

Ewing sarcoma
Leukaemia
Lymphoma
Osteoid osteoma
Metastasis

Bacterial osteitis, including TB osteitis
Langerhans cell histiocytosis
Sarcoidosis
SAPHO syndrome

An underlying auto-immune disease will likely be more evident as she goes through puberty...
No further investigation were done…
Read the reports again…

“Die beenpyn, multifokale been letsets, geen infektiewe oorsaak wat gevind kan word nie, respons op pyn medikasie, en die chroniese verloop, saam met die histologiese beeld, kan inpas by non-bakteriele osteitis.”

“The bone pain, multifocal bone lesions, failure to identify an infectious etiology, improvement with NSAIDs, and the chronic disease course have all been well described in NBO.”
After extensive review of IL’s disease progression and all the laboratory and imaging results, we are of the opinion that she has a form of non-bacterial osteitis known as Chronic Recurrent Multifocal Osteomyelitis (CRMO).
Since the first report of CRMO in 1972 the etiology is still unknown. A possible genetic cause is postulated with a chromosome 18 mutation in mice showing a similar disease phenotype. A clear diagnosis of CRMO may be impossible at presentation therefore it currently remains a diagnosis of exclusion. The differential diagnosis include:

- Pyogenic osteomyelitis
- TB osteitis
- Ewing’s sarcoma
- Leukemia
- Lymphoma
- Osteoid osteoma
- Metastasis
- Langerhans cell histiocytosis
Jansson et al suggested a diagnostic criteria:
  – TWO major or ONE major and THREE minor

Monitoring of the disease:
  – MRI scans are highly sensitive for both diagnostic and monitoring purposes
  – Whole body MRI (Heidelberger’s whole body MRI protocol) has been recommended for disease monitoring
  – Radio-isotope studies assist in establishing the diagnosis and in identifying initially silent lesions
Management strategies:

- First line treatment relies on NSAID’s.
- Second line agents
  - steroids, TNF-alpha blocking agents, methotrexate, or bisphosphonates
- Surgery is sometimes required
- A multidisciplinary team approach…

Outcome: The prognosis of CRMO is generally good with most patients (75%) experiencing symptom resolution after puberty
Take home message…

CRMO should be considered in all cases of nonclassic hematogenous osteomyelitis.

The characteristics of CRMO include:
- local bone pain with gradual onset
- multifocal lesions
- failure to cultivate an infectious organism
- improvement with anti-inflammatory drugs
- a protracted course for years with frequent exacerbations
1 year old boy

History: well grown, HUU

2/7 fever

2/7 swelling behind right ear

3/7 red rash started on face & neck and spread to limbs & trunk

# Lymphadenitis (to rule out TB)

# Viral exanthem
Odd piece of data…

Hands…

Appeared swollen (dactylitis)

General…

Extremely irritable / miserable

What would you do next…??
Diagnostic criteria for Kawasaki disease: fever must be present, with 4 of the 5 other criteria met.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Present for at least 5 days, typically high spiking and remittent, lasts an average of 10 days when untreated</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>Bilateral conjunctival injection, typically limbic sparing, non-exudative</td>
</tr>
<tr>
<td>Mucosal changes</td>
<td>• Erythema, cracking, peeling of lips</td>
</tr>
<tr>
<td></td>
<td>• “Strawberry tongue”</td>
</tr>
<tr>
<td></td>
<td>• Diffuse erythema of oral mucosa</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>Cervical lymphadenopathy; may be single node &gt; 1.5 cm in diameter or several smaller, firm, non-fluctuant nodes bilaterally</td>
</tr>
<tr>
<td>Polymorphous rash</td>
<td>Commonly maculopapular, but may be erythrodermic, urticarial, or erythema multiforme-like; may show early desquamation in the perineal region as well</td>
</tr>
<tr>
<td>Extremity changes</td>
<td>Erythema and induration of hands and/or feet seen in acute phase; periungual desquamation may follow in subacute phase</td>
</tr>
</tbody>
</table>
An evolving paradigm

Self-limited childhood systemic vasculitis

…predilection for the coronary arteries.

6 months and 4 years (> males)

Aetiology of KD unknown
Upcoming biomarkers

Inflammatory biomarkers

ESR ≥ 40 mm/h
Leukocyte count ≥16 * 10^9/L
Increased WBC count

Proteomic biomarkers (serum and urine)
elevated NT-proBNP
filamin C and meprin A
iNOS in monocytes

Genetic polymorphisms

six HLA class I genes
MICA alleles A4 and A5.1

fidssa 2015, 5-8 November 2015
Closing thoughts…

Sherlock Holmes….

“To a great mind, nothing is little,”

“There is nothing more deceptive than an obvious fact.”

“How often have I said to you that when you have eliminated the impossible, whatever remains, however improbable, must be the truth?”
Thank you