Rheumatic symptoms as the first manifestations of underlying systemic disorders

Presenter: Dr. Megha Unadkat
Outline

• Case Summaries

• Management/Outcomes

• Literature Review
Objectives

• To demonstrate the importance of pursuing a diagnosis before initiating treatment for childhood arthritis.
Case One – Patient Information

• Name: CHG

• Sex: Female

• Date of presentation to Rheumatology clinic: 5/10/17

• Age at presentation: 2 years 2 months

• Date of admission to PHDU: 29/11/17

• Date of death: 7/12/17
**History**

- **Presenting complaint**
  - 5 month history of lower limb pain

- **History of Presenting Illness**
  - Developed left leg pain 5/12 ago, associated with fever
  - Treated as infectious – fever resolved
  - Pain progressed to involve right leg and bilateral upper limbs
  - Currently unable to walk completely
History...

• Functional Inquiry

  – Often wakes up due to nocturnal pain
  – No neck swellings noted
  – No respiratory, CVS, GIT, GUT or eye complaints
  – No convulsions
  – 1 episode of macular rash
  – ?1 episode petechial rash
History...

• Past Medical History
  – 4\textsuperscript{th} admission due to same illness

• Birth History
  – Unremarkable

• Family Social History
  – Has a sister 3 years old
  – No pets, no recent travel
  – Maternal grandpa – hx of Ca Prostate and arthritis
History...

- Admitted Nairobi hospital Aug 2017 with anaemia & thrombocytopenia

- Initial BMA work up ruled out leukemia- started on Rx for ITP (Prednisone)

- Nov 2017- recurrence of thrombocytopenia with purpuric skin lesions, melena & bleeding gums

- Hx of poor feeding, fevers and weight loss.

- Admitted to Getrude’s then referred to AKUHN
Examination

• General exam:
  – Sick-looking, febrile, gross edema, purpuric skin lesions, not pale, not jaundiced, not cyanosed

• R/S:
  – Tachypnea, no LCWI
  – Chest clear, good air entry bilaterally

• CVS:
  – Good volume pulses, S1S2 heard, no murmurs

• P/A:
  – Grossly distended
  – Massive hepatosplenomegaly
# Initial work-up

<table>
<thead>
<tr>
<th>Date</th>
<th>29/11</th>
<th>1/12</th>
<th>3/12</th>
<th>4/12</th>
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<td>CRP (mg/l)</td>
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<td>0.81</td>
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<td>Creatinine</td>
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<td>&lt;15</td>
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<td>118</td>
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<td>GGT (U/l)</td>
<td>53</td>
<td>57</td>
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<tr>
<td>SBR (umol/l)</td>
<td>57.7 (31.3)</td>
<td>82.9 (60)</td>
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<td>175 (151)</td>
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<td>AST (U/l)</td>
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<td>243</td>
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<td>403</td>
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<tr>
<td>ALT (U/l)</td>
<td>109.7</td>
<td>80</td>
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<td>33.9</td>
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</table>
Hematology work-up

• PBF:
  Increased total leucocytes, blasts 26%, neutrophils 24%, lymphocytes 33#, monocytes 7%, RBC normal morphology, platelets reduced

• Flow cytometry:
  • CD34 Negative
  • Tdt positive
  • CD 10 positive
  • CD 19 positive
  • CD 79a positive

SUGGESTIVE OF B-CELL ALL
Initial Management

• Started on IV Meropenem
• Allopurinol
• Ranitidine
• Paracetamol
• Mg supplementation
• Transfused with FFPs + Lasix
• Once afebrile-> 1\textsuperscript{st} dose induction given (IV Vincristine, Dexamethasone)
Outcome

• Later in PHDU – started desaturating on room air

• Still oozing blood from mouth, passing melena stools and spiking fevers

• Extensive ecchymotic lesions on skin

• Developed focal right sided seizures (secondary to hyperkalemia, ?Tumour lysis syndrome)
Outcome...

- On 6th Dec - worsening of respiratory distress
- Transferred to ICU - Sedated & intubated
- On vent - ACPC mode
- On 7th Dec - noted to become bradycardic, bleeding from nostrils, in DIC
- Code blue called – resuscitation efforts unsuccessful.
- Time of death - 9:22 pm.
Case Two – Patient Information

• Name: NM

• DOB: 26/09/14

• Age: 2 years 10 months

• Sex: Female
History

• Presenting complaint (1/8/17):
  – Bilateral foot pain for 8 weeks

• History of presenting illness:
  – Patient from Aga Khan Dar es Salaam
  – Initially limping but progressed to inability to walk within a month
  – Neurology assessment in TZ reported to be normal
  – Rheumatology review in Dar – diagnosed as JIA & started on prednisone & Methotrexate.
History

• Functional inquiry:
  – No photosensitivity, no heliotrope rash
  – No oral or nasal sores
  – No weight loss or night awakening
  – No seizures or developmental delay
  – No muscle weakness
  – No GIT GUT CVS complaints
  – No eye complaints
History

• Past Medical History
  – No chronic conditions
  – Recurrent URTI’s since joining school Feb 2017

• Allergy History
  – None known

• Perinatal history
  – Unremarkable

• Immunisation & Developmental History
  – Uptodate except varicella vaccine at 15 months and Hep A at 2 years
History...

• Dietary history
  – Mainly consists of milk, porridge, fruits, potatoes, rice

• Family Social History
  – Family from Dodoma, Tanzania
  – Has an elder sister - who is well
  – No pets
  – Maternal grandfather has osteoarthritis
  – No family hx of JIA, periodic fever syndromes, IBD, celiac diseases or other autoimmune diseases
Examination

• General exam:
  – Alert, not pale, not jaundiced, no lymphadenopathy

• Skin: No vasculitic, photosensitive or pruritic rash

• ENT: Normal oral cavity and dentition, no oral or nasal sores, normal otoscopy and nasal exam

• Eyes: Brisk bilateral pupillary light reflex
Examination

• Respiratory system:
  – Chest clear

• CVS:
  – S1S2 normal

• Abdomen:
  – Soft, non-tender, no organomegaly

• MSS:
  – Nail fold capillary exam normal
  – Soles and palms normal
  – Bilateral ankle joints effused and tender
Differentials

• ?
Outcome

• Patient went back to Tanzania

• BMA done at Muhimbili National Hospital

• ALL was confirmed

• Patient has now completed induction phase of chemotherapy

• Doing well
Case Three- Patient information

• Name: NC

• Age: 4 years old

• Sex: Female

• Date of presentation: 2/8/17
History

• Presenting complaint:
  – Multiple joint pains for 1 and a half weeks

• History of presenting illness:
  – 19/7: right shoulder pain after gymnastics, relieved by brufen
  – 21/7: right elbow pain associated with abdominal pain & fever 37.8’c
  – Assessed at AKUHN- **CRP 89.49,** CBC normal
  – Treated with 5 day course of augmentin, brufen and paracetamol- symptoms resolved
  – Had another episode of shoulder and knee pain- awakening her at night
History

• Limitations
  – Reluctant to get off bed, opts to roll out of bed
  – No other disabilities noted

• Functional inquiry
  – No skin rashes
  – No oral or nasal sores
  – No lymphadenopathy
  – No weakness
  – No weight loss but reduced appetite
  – No bleeding tendencies
  – No Resp/GUT/GIT/CVS symptoms
History...

• Past Medical History
  – Recurrent ear infections since age of 2 years
  – Initially every 6 months, now every 3 months
  – Several courses of antibiotics (augmentin, orelox)
  – No past admissions or chronic illnesses

• Allergies
  – Initially allergic to milk and tomato paste- now ok
  – Allergic to oats

• Perinatal
  – unremarkable
History...

• Immunisation & Developmental history
  – Uptodate

• Dietary history
  – 3-4 portions of milk per week
  – Cereals, berries, bananas, chicken and vegetables

• Family Social history
  – American family - only child
  – Have a pet dog
  – Travelled to Mombasa 15^{th}-17^{th} July
  – No family hx of arthritis, periodic fever syndromes, celiac disease, SLE
  – Maternal grandmother has colitis
Examination

- Febrile Temp 38.5’c
- Skin: no rash
- Eyes: brisk bilateral pupillary light reaction
- ENT: normal
- Resp: good air entry bilaterally
- CVS: S1S2 normal
- Abdomen: soft, no organomegaly
- MSS: arthritis of right elbow (tenderness and limited ROM)
Differentials?
# Work-up

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<tr>
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<td>Hb</td>
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<tr>
<td>Plt</td>
<td>328</td>
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<td>330</td>
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<td>CRP</td>
<td>89.49</td>
<td>179.42</td>
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<td>Urine/blood</td>
<td>No growth</td>
<td>No growth</td>
<td>No growth</td>
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<tr>
<td>MPS</td>
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<td></td>
<td></td>
<td>absent</td>
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<tr>
<td>ESR</td>
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<td>60</td>
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<tr>
<td>LFTs</td>
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<td>Normal</td>
<td>Normal</td>
<td></td>
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<tr>
<td>ASOT /ANA/Anti DS DNA</td>
<td>NEGATIVE</td>
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<tr>
<td>Uric acid</td>
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<tr>
<td>LDH</td>
<td></td>
<td></td>
<td>342</td>
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</table>
The visualized bones are normal. There is no fracture or dislocation seen. Peri-articular soft tissues are normal.
Follow-up visit (30/08/17)

- Assessed by ID specialist, orthopedic and heamato-oncologist
- Infectious cause & malignancy ruled out
- Ophthalmology and audiology assessments also normal
- Still spiking fevers and multiple joint pain
- CRP persistently high
Outcome

• Went back to America for further work-up

• Had a BMA at the NIH

• Confirmed B cell-ALL
Summary of cases

• Rheumatic diseases- recognition of clinical patterns essential because no single diagnostic test

• Primary mimics of rheumatic disease are infection and malignancy

• Exclusion of such is necessary before initiation of treatment for a presumptive diagnosis, especially steroids.

• Prompt referral to haemato-oncologist for confirmation of diagnosis and early treatment
Literature Review

• Joint and limb pains frequent complaints among 10-20% school-age children. ¹

• Major reason for referral to paediatric rheumatology clinics.

• Differential diagnosis of joint pain and swelling include both benign and serious conditions.

• Majority are of benign origin.

• Studies have found <=1% of MSS complaints are caused by neoplasia, mostly ALL. ¹

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Literature Review...

- Leukemia accounts for approximately 31% of all malignancies in children <15 years of age. ²

- In Kenya, Leukemia is the third most common tumour comprising 13%. ³

- A systematic review showed that MSS symptoms feature prominently as presenting symptoms in leukemia (limb pain – 43%). ⁴

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²- Nelson textbook of pediatrics, 20th edition
Literature Review...

• A retrospective analysis of patients attending Pediatric Rheumatology Clinic (Sau Paulo) 2013-2015, 5 out of 250 (2%) had a cancer diagnosis.  
  – ALL(3), AML(1), Neuroblastoma(1)

• Retrospective analysis of 166 new leukemia and 95 new lymphoma patients (Budapest).  
  – 20% of leukemic (33 children) and 2% of lymphoma patients (2 children)
  – MSS symptoms at first presentation

• Haemograms initially normal (3 out of 61 patients), or may have subtle changes in the cell lines.

Table 1 - Musculoskeletal signs and symptoms at presentation of leukemia (n = 61)

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>n</th>
<th>%</th>
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<tbody>
<tr>
<td>Limb pain and/or joint pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>daytime</td>
<td>19</td>
<td>50</td>
</tr>
<tr>
<td>nighttime</td>
<td>4</td>
<td>10.5</td>
</tr>
<tr>
<td>continuous</td>
<td>15</td>
<td>39.4</td>
</tr>
<tr>
<td>Difficulty walking</td>
<td>24</td>
<td>39.3</td>
</tr>
<tr>
<td>Arthritis (anamnesis)</td>
<td>14</td>
<td>22.9</td>
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<tr>
<td>Arthritis at physical examination</td>
<td>8</td>
<td>13.1</td>
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6- Musculoskeletal manifestations as the onset of acute leukemias in childhood Cássia Maria Passarelli Lupoli Barbosa,1 Cláudia Nakamura,2 Maria Teresa R.A. Terreri,3 Maria Lúcia de Martino Lee,4 Antonio Sergio Petrilli,5 Maria Odete E. Hilário6
A multicenter study done to discriminate diagnosis of ALL from Systemic JIA at disease onset showed that:

- Median age disease onset higher in leukemia patients than in JIA

- Frequencies of limb pain, hepatomegaly, weight loss, hemorrhagic manifestations higher in leukemia

- Three most important predictive factors for leukemia were leukopenia, thrombocytopenia, nighttime pain.

# Worrisome findings!

<table>
<thead>
<tr>
<th>JIA</th>
<th>Leukemia</th>
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<tbody>
<tr>
<td>Pain of low to moderate intensity</td>
<td>Bone pain initially intermittent (especially metaphyseal region)</td>
</tr>
<tr>
<td>Mainly in the morning and accompanied by stiffness</td>
<td>Progresses to continuous and preferably nocturnal pain</td>
</tr>
<tr>
<td></td>
<td>Severe pain disproportionate to physical findings</td>
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<tr>
<td></td>
<td>Poor response to NSAIDs or Corticosteroids</td>
</tr>
<tr>
<td></td>
<td>Early significant osteopenia or lytic bone lesions (pathologic fractures)</td>
</tr>
<tr>
<td></td>
<td>Inability to bear weight, refusal to walk</td>
</tr>
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</table>
Take-Home Points

• Awareness of possibility of malignancy in child presenting with MSS pain.

• Lab tests: CBC, LDH, BMA, Imaging fundamental for early diagnosis

• If such procedures initially normal – repeat to avoid delay in establishing diagnosis.

• Malignancy should be eliminated before introduction of steroids/immunosuppressive therapy
Thank you!