Adult onset Still Disease

Hospital Raja Permaisuri Bainun
CPC
21 Jan 2011
Case 1

2010 December

• 45 year old Malay man
• Multiple joints pain with fever for more than 2 weeks
• Fever especially evening together with joint pain
• Sore throat for 2 weeks
Case 1

• Preceded by evanescent, non pruritic macular rashes mainly over the trunk and extremities

• Joint pain involved shoulder, knee, hip, wrist and small joints of the hands until he can hardly ambulate
Case 1

• Similar history on Dec 2008 and also Dec 2009
• Dec 2008- seek treatment and treated as rheumatoid arthritis, started MTX but patient defaulted the treatment after the joint pain resolved
• Dec 2009- The joint pain and rashes resolved after taking NSAIDs bought over the counter
Case 1

Physical Examination:

• 39.0 C
• BP 126/75 mmhg  PR 75 bpm
• Throat –slight injected
• Lungs clear , no organomegaly
• Synovitis-wrists, elbows, ankles , knees and small joints of the hands
## Case 1

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 3</th>
<th>Day 5</th>
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</thead>
<tbody>
<tr>
<td>Hb</td>
<td>11.5</td>
<td></td>
<td>12.3</td>
</tr>
<tr>
<td>White cell counts</td>
<td>20.6 (94.7% N)</td>
<td></td>
<td>23.9 (93.0% N)</td>
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<tr>
<td>Platelet</td>
<td>182</td>
<td></td>
<td>310</td>
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<tr>
<td>Creat</td>
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<tr>
<td>AST</td>
<td>92</td>
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<tr>
<td>ALT</td>
<td>157</td>
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<tr>
<td>ALP</td>
<td>148</td>
<td>169</td>
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<tr>
<td>Bilirubin</td>
<td>17.5</td>
<td>9.4</td>
<td>9.2</td>
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<tr>
<td>ESR</td>
<td>101</td>
<td></td>
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<tr>
<td>CRP</td>
<td>265.4</td>
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</tbody>
</table>
Case 1

- Serum ferritin > 10,000 ug/l
- Anti CCP, ANA and Rheumatoid factor were all negative
- Blood and urine cultures revealed no evidence for bacterial, fungal or viral infection
- Computerized tomographic scan of the thorax and abdomen was normal.
Case 1

• Based on Yamuguchi and Ohta criteria
• Diagnosed to have Adult-onset Still’s disease
• Started on Cap Cerebrex 200mg bd and T prednisolone 30 mg od.
Case 1

- 5 days after prednisolone, patient became afebrile
- Joint pains improved slightly and patient ambulating by himself
- Discharged with Cap cerebrex 200mg prn, prednisolone 30mg (tapering dose), calcium lactate 300mg bd and rocaltrioi 0.25 mg od
Case 1

• 2 days after discharge, patient presented back to clinic with multiple itchy papules over the chest wall and upper limbs
• Different from the previous rashes
• ? Allergic to the rocaltrioil or calcium lactate given??
Case 1

• Started on tab piriton and both the rocaltrieol and calcium lactate were off.
• 8 days later, patient readmitted with generalized body weakness, polydipsia and polyuria.
• DXT 27.1 mmol/l, HbA1c 10.5%
• The allergic rashes resolved but joint pain just slightly improved compare since discharged
Case 1

• Started on insulin to control the blood sugar
• MTX 7.5mg weekly initiated with folate 5 mg weekly (liver enzymes normalized)
• T prednisolone decreased to 10 mg (sugar difficult to control)
• Cap cerebrex 200 mg prn
Case 2

June 2010

• 17 yo man
• Fever 1 month
• Associated with sore throat, multiple joint pains involved knees, elbow and small joints of hands
• Rashes during febrile episodes
Case 2

• Admitted to hospital taiping
• Septic workout done and all negative
• Not responding to empirical course of antibiotics.
Case 2

• Temperature hovering around 39 and 40 c
• Tender joints but not swollen
• Evanescent rash affecting abdominal wall and forearms
• Blood investigations: liver enzymes raised, serum ferritin > 5000 ug/l.
• Echo and chest x ray all normal
Case 2

• Diagnosis of AOSD was made
• Treated with indomethacin 50 mg tds and prednisolone 20mg bd.
• Improved and discharge well
• Patient defaulted the follow up !!!
Case 2

• Readmitted 3 months later with fever for 2 weeks.

• Classical Stills rash and other similar presentations like previous admission

• This time there was hepatosplenomegaly
Case 2

- Septic workout was again negative
- Serum ferritin remained high ( > 5000ug/l)
- Treated with T indomethacin 50mg tds and Prednisolone 20mg tds
- 3rd day of admission developed chest pain and ECG classical features of pericarditis
Case 2

• Echo repeated showed EF dropped to 44% from 61% on previous admission
• Rim of pericardial effusion with no vegetations
• Joint pain worsen.
• MTX 10mg weekly started
• He complained of shortness of breath and the unable to lie flat. SaO remained 100% on RA
Case 2

- IV Methylprednisolone 500mg given for 3 days
- Significant resolution of symptoms and fever resolved
- ECG normal, Echo normalized to 57%
- Another problem ARISED!
Case 2

• The blood sugar charted 19 mmol/l with no FH of DM.
• Steroid induced hyperglycaemia and was started on insulin
• Discharged with:
  T MTX 10mg weekly, folic acid 5mg weekly, Prednisolone 20mg bd, Brufen 400mg prn, Sc Actrapid 20 u tds and humulin N 6 u ON
Case 2

During the follow up:

- the joint pain persisted but no more fever or rashes
  - T ARAVA 20 mg od was started to replace T MTX
  - Patient improved with T ARAVA
Yamaguchi Criteria 1992

Major criteria:
fever of 39°C or higher, lasting 1 week or longer
arthralgia lasting 2 weeks or longer
typical rash
leukocytosis (10,000/mm³ or greater) including 80% more of granulocytes

Minor criteria:
Sore throat
Lymphadenopathy and/or splenomegaly
Liver dysfunction
Negative RF and negative ANA

Exclusions:
I. Infections (especially, sepsis and infectious
   Mononucleosis)
II. Malignancies (especially, malignant lymphoma)
III. Rheumatic diseases (especially, polyarteritis
    Nodosa and rheumatoid vasculitis with
    Extraarticular features)

Classification of adult Still's disease requires 5 or more
criteria including 2 or more major criteria.
Any disease listed under “Exclusions” should be excluded.
Clinical Manifestations

Fever > 39.0 °C
- Mainly early evening

Rashes
- Evanescent, salmon-pink, maculopapular eruption
- During febrile attacks
- Proximal limbs and trunks
- Last for hours
- Skin biopsy nonspecific inflammation and mild perivascular inflammation
Clinical Manifestations

Sore throat
• Throat culture negative

Arthralgia and arthritis
• Commonly involved knees, wrists, ankles and elbows
• Narrowing of carpometacarpal and intercarpal joint spaces
• Destructive arthritis in 25% patients, carpal joints mostly affected
Clinical Manifestations

- Lymphadenopathy
- Hepatosplenomegaly
- Pericarditis, Pleurits
- Central nervous system (Fits, encephalopathy)
Laboratory investigations

- Leukocytosis
  (More than 80% granulocytes)
- Raised ESR
- Raised liver enzymes
- Pancytopenia
- RF and ANA generally negative
- Synovial and serosal fluids inflammatory type
Laboratory investigations

High level of ferritin

• Consequence of cytokine secretion induced by reticuloendothelial system or hepatic damage
• Correlate with disease activity
• However, normal levels of serum ferritin not exclusion criteria of diagnosis of AOSD
Treatment

AOSD diagnosis

NSAIDs or Aspirin (During the time of investigations)

Response

[-] Prednisone

Response

[-] Methotrexate

Response

[-] Anti-IL1 (Anakinra)

[-] TNF-blockers

Anti-IL6 (Tocilizumab)?

Cyclosporin A?

Other conventional treatments?

Regular monitoring (Initially tight)
- Clinic
- CBC, ESR/CRP, LFT

Careful treatment tapering
Once remission is achieved
Trials

• infliximab

• adalimumab

• etanercept

• anakinra

• Tocilizumab