A 13 YEAR-OLD BOY WITH RECURRENT EPISODES OF FEVER, LYMPHADENOPATHY AND HEPATOSPLENOMEGALY

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INITIAL HISTORY

- Male, 13 years-old
- Consanguineous marriage
- 2 healthy sisters

Chief complaint:

recurrent episodes of fever since 2 months of age
HISTORY OF CURRENT ILLNESS

- Recurrent episodes of fever, associated with odynophagia, painful cervical lymphadenopathy and hepatosplenomegaly.
- Lasted for 3 to 4 days, twice a month since he was 2 months old until the age of 9 years old. Then, these symptoms occurred every 2 months.
- Occasionally, he also presented vomiting, diarrhea and abdominal pain that lasted for 2 to 3 days.
- Several times, it was diagnosed as adenitis or tonsillitis and treated with antibiotics.
- Also presented recurrent episodes of suppurative otitis.
TIME LINE

2mo • 1st episode of fever

3mo • Lymphadenopathy

6mo • Pneumonia
    • Hepaosplenomegaly

3y 5mo • Skin lesions in upper thighs and lower limbs

4y 1mo • Liver biopsy = granuloma
         • Mycobacteriosis?

6y 9mo • Pneumonia with pleural effusion
TIME LINE

- 7y 5mo: Herpes zoster
- 7y 6mo: Inflammatory acute abdomen, Suppurative otitis
- 7y 9mo: Submandibular adenitis
- 8y 3mo: Pneumonia
- 8y 9mo: Cervical adenitis, Suppurative otitis
- 8y 10mo: Cervical adenitis, Oral pustule
TIME LINE

9y 5mo
- Pneumonia with pleural effusion
- Exanthema

10y 2mo
- GI subocclusion

11y 2mo
- Suppurative otitis

11y 9 mo
- Cervical and submandibular adenitis

12y 3mo
- GI subocclusion
- Cervical adenitis

12y 4mo
- Obstructive acute abdomen
PHYSICAL EXAM

- Underweight
- Short stature for his age
- Pale
- Tonsilar hypertrophy*
- Enlarged cervical, supraclavicular, axillary, and inguinal lymph nodes*
- Hepatosplenomegaly*

* Observed only during attacks
LABORATORY EXAMS

- Anemia
- Leukocytosis (up to 40,000/ml)*
- High levels of C-reactive protein (23.8-284.5 mg/dL)*
- Elevated erythrocyte sedimentation rate (50-70mm)*
- IgG levels ranging from 1,458 up to 2,457 mg/dL
- IgA levels ranging from 614 up to 975 mg/dL
- Normal lymphocyte immunophenotyping
- Normal myelogram
- Abdominal ultrasound: hepatosplenomegaly

* higher levels during attacks
SUMMARY

- 13 year-old boy
- Recurrent episodes of fever
- Associated with adenopathy and hepatosplenomegaly
- Infections: 5 pneumonias, suppurative otitis, tonsilitis
- Acute abdomen and surgery
- Laboratorial tests: anemia, leukocytosis, high levels of IgG, IgA, CRP and elevated ERS
ANALYSIS OF MVK GENE

- mutation in homozygosis  C.709 A>T, P. T237S
  - Change in position 709 in the exon 8 – thymine for adenine
  - Change in amino acid threonine for serine

MEVALONATE KINASE DEFICIENCY
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- Autosomal recessive disorder

- SEVERE
  - Mevalonic aciduria – no MK activity
    - Severe CNS involvement, mental retardation, ataxia, myopathy, poor growth, and early death

- MILD
  - Hyper-IgD – reduction in MK activity (1-10% of normal levels)
MVK gene

- Long arm of chromosome 12 (12q24)
- 11 exons
- 396-amino acid-long enzyme
CLINICAL FEATURES OF HIDS

**General**
- Fever
- Malaise
- Headache
- Cold Chills

**Mucocutaneous**
- Maculopapular rash
- Urticaria
- Purpura
- Erythema nodosum
- Oral ulcers
- Genital ulcers

**Lymphoid tissue**
- Cervical lymphadenopathy
- General lymphadenopathy
- Splenomegaly

**Gastrointestinal**
- Vomiting
- Diarrhea

**Abdominal**
- Abdominal pain
- Hepatomegaly
- Serositis
- Abdominal adhesions

**Blood**
- Acute phase reaction
- Elevated serum IgD
- Elevated serum IgA

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## SYMPTOMS DURING ATTACKS

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>% of patients</th>
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<tbody>
<tr>
<td>Lymphadenopathy</td>
<td>87.4</td>
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<tr>
<td>Abdominal pain</td>
<td>85.4</td>
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<tr>
<td>Arthralgia</td>
<td>83.5</td>
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<tr>
<td>Diarrhea</td>
<td>71.6</td>
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<tr>
<td>Vomiting</td>
<td>70.9</td>
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<tr>
<td>Skin lesions</td>
<td>68.9</td>
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<tr>
<td>Headache</td>
<td>63.3</td>
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<tr>
<td>Cold chills</td>
<td>62.7</td>
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<tr>
<td>Arthritis</td>
<td>55.3</td>
</tr>
<tr>
<td>Aphtous ulcers</td>
<td>48.5</td>
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<tr>
<td>Splenomegaly</td>
<td>32.4</td>
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<tr>
<td>Hepatomegaly</td>
<td>21.6</td>
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<tr>
<td>Serositis</td>
<td>18.6</td>
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</tbody>
</table>

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LABORATORY FINDINGS

- Elevated erythrocyte sedimentation rate
- C-reactive protein
- Leukocitosis
- High levels IgD
- Elevated IgA
- Urinary mevalonate levels
DIAGNOSIS

- MVK mutations

TREATMENT

- Antiinflammatory
- Simvastatin
- Etanercept
- Anakinra
TREATMENT

- Simvastatin was prescribed
- Initially the patient didn’t take the medication regularly
- Currently he is doing well, but still has recurrent attacks