FEVER

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ESIM 2013, Saas-fee

Case Presentation

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Clinical History

- A 26 year-old-man, actor , lives in Ankara in Turkey
- 20 days history of fever,night sweats, weight loss
- After beta-lactam antibiotic therapy ,maculopapular rash on his back and legs
- Admitted to our Infectious Diseases clinic due to persistent symptoms despite antibiotic treatment

Physical Examination

- T:39.7°C
- HR:108/min
- BP:120/80mmHg
- RR:18/min

- Hepatosplenomegaly
- maculopapular rash on his back and legs
- No lymphadenopathy
- No murmur

Additional Info

- No travel history
- No history of contact with animals
- No history of unprotected sexual contact
- He did not smoke or use illicit drugs
- No people around with similar symptoms
- No people around with tuberculosis history
- No herbal therapy
- No arthritis

Laboratory Results

- Hgb:9.7 g/dl (11.7-15.5)
- WBC:2000/mm3 (4100-11200)
- Plt:87,000/mm3 (159,000-388,000)
- Peripheral smear:

  %54PMNL,

  %42 lymphocyte,

  %4monocyte

  hypochromic

  normocytic erythrocytes,anisocytosis

  True thrombocytopenia

- ESR: 68mm/hr (0-20)
- CRP: 21 mg/dL (0-0.8)
- ALT:171(0-40)
- AST:260 (0-35)
- Renal function tests normal
- INR:1.55 (0.86-1.2)
- aPTT:33.6 (27-38)
- Fibrinogen:102 (219-403)
- D-dimer:18.8 (0-0.48)

Differential Diagnoses

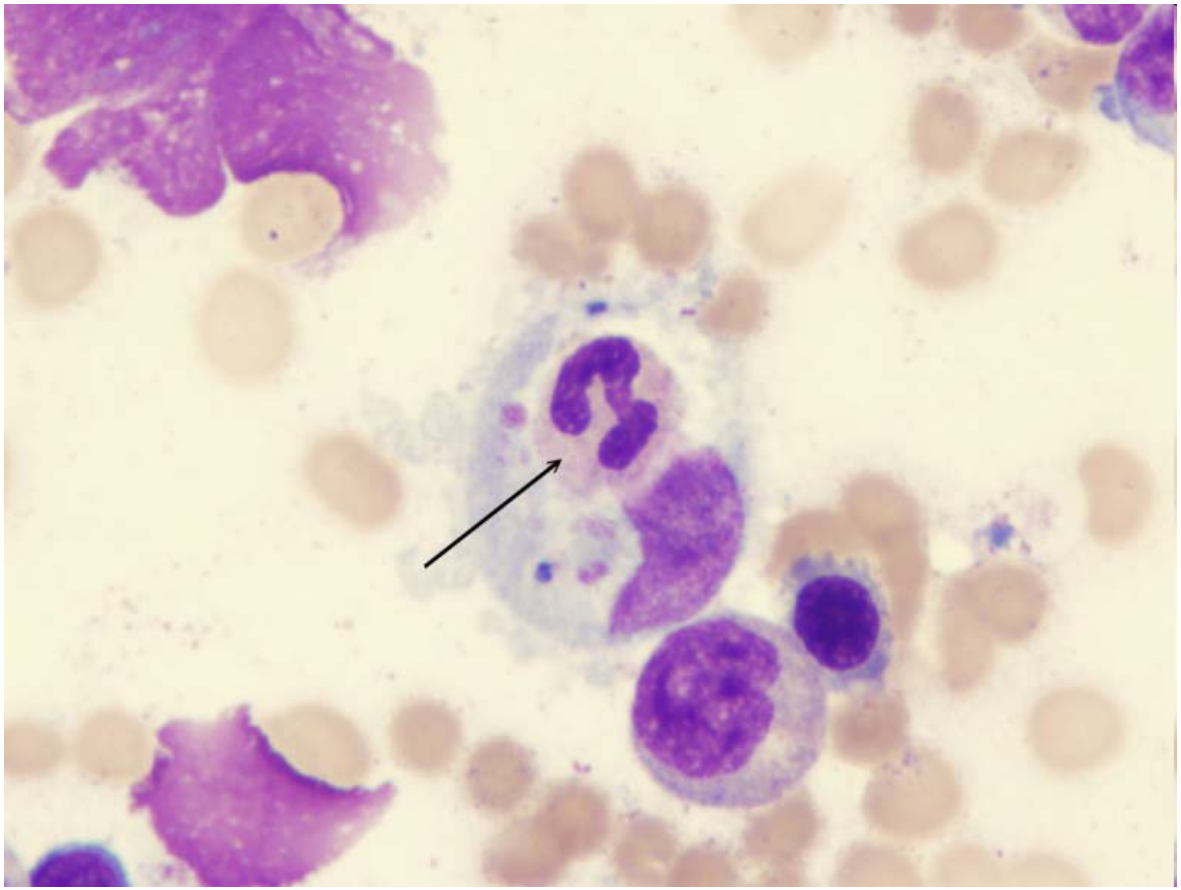
- Infectious mononucleosis
- Acute HIV infection
- Cytomegalovirus infection
- Tuberculosis
- Rheumatologic diseases
- Malignancies
- Infective endocarditis
- Brucellosis
- Syphilis
- …

Additional tests???

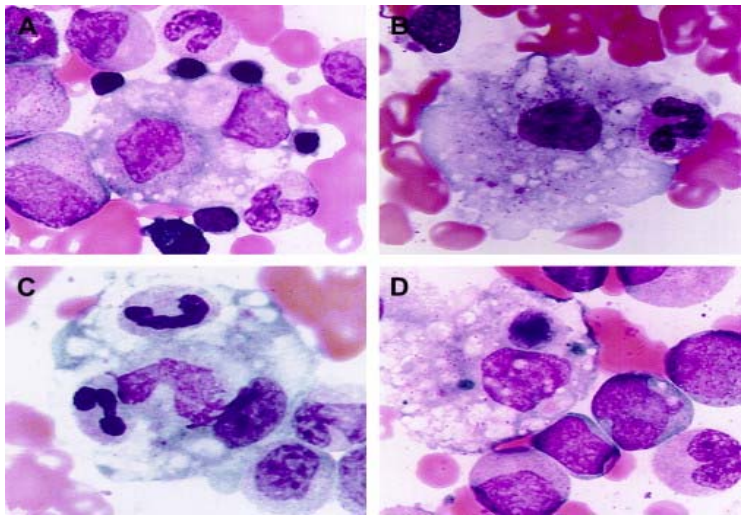
- ANA(-) anti-dsDNA(-)
- Anti HIV(-) hepatitis markers (-)
- Brucellosis agglutination (-)
- VDRL(-) TPHA(-)
- CMV IGM(-)
- EBV VCA IGM(+)
- Echocardiography:EF %65,no vegetation
- Ferritin:88967 Triglyceride :654
- Bone marrow aspirate culture negative for tbc

- Bone marrow aspiration and biopsy→
  - Activation of macrophages,
  - EBV associated hemophagocytosis

HEMOPHAGOCYTIC SYNDROME



- Pathologic finding of activated macrophages engulfing erythrocytes, leukocytes, platelets, and their precursors.
- Uncommon, life-threatening hyperinflammatory syndrome caused by severe hypercytokinemia due to a highly stimulated but ineffective immune process.



CLASSIFICATION

- **Primary**
  - Familial/Genetic
  - Associated with Immune Deficiencies
- **Acquired**
  - Infections
    - Viral: HSV, EBV, CMV
    - Bacterial
    - Fungal
    - Protozoal
  - Malignancy
    - Lymphoma
  - Rheumatologic Diseases(macrophage activation syndrome)

DIAGNOSTIC CRITERIA

- Familial disease/known genetic defect
- Clinical and Laboratory (5/8)

-Fever
-Splenomegaly
-Cytopenia (at least 2 cell lines)
HGB < 9
PLA < 100,000
ANC< 1000

-Hypertryglyceridemia and/or hypofibrinogemia
Fasting TRY > 265 mg/dL
Fibrinogen < 150 mg/l

-Hemophagocytosis in bone marrow, CSF, or lymph nodes
-Decreased/absent NK cell activity
-Ferritin > 500 ug/l
-Soluble CD25 > 2400 U/ml

TREATMENT

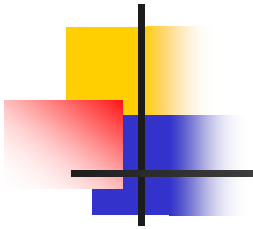
- Steroid + Etoposide + Cyclosporine A
- Other considerations
  - ATG
  - IVIG
  - Rituximab
  - Plasma exchange
- Bone Marrow Transplant
  - Familial Disease
  - Non-familial: only if fail immuno-/chemo- therapy

Take home messages…

High fever lasting for long periods and unresponsive to antibiotics can be life-threatening and has to be handled carefully.

Although HFS is an uncommon event described in critical patients, it is possibly underdiagnosed.

Awareness of the disease and high level of clinical suspicion are essential, especially in patients with fever, hepatosplenomegaly and pancytopenia that do not respond to GSC-F and antibiotics.



Thanks for your patience and attention…

See you soon again in ESIM 2013, in Cappadocia ☺

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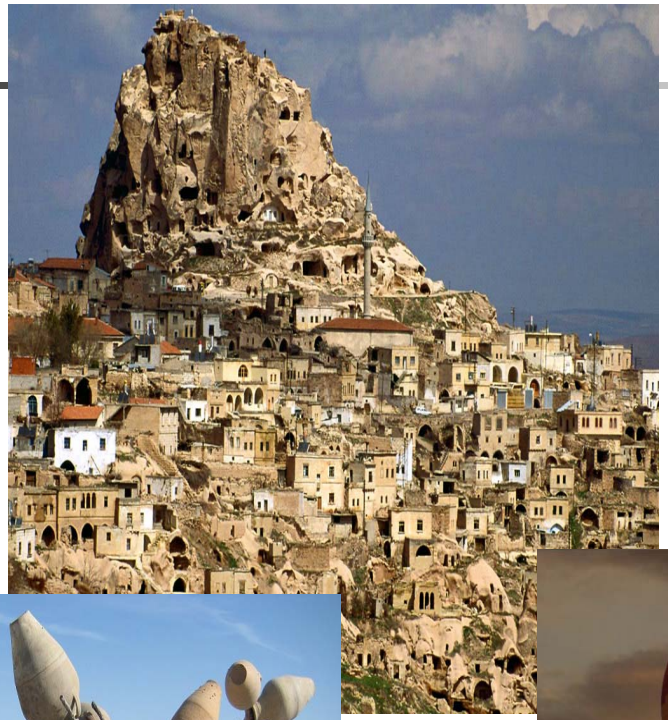

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