

EBV INFECTION EVOLVING TO SLE

UNIT IV
DEPT of Pediatrics
&
Pediatric Hemato-Oncology
Sri Ramachandra Medical Centre

August 2009

9 years old girl presented to us with

- High grade intermittent fever 5days
- Red spots in the leg 3 days
- Myalgia
- No other associated symptoms
 - Not investigated outside
 - Treated with oral medications- details not known
 - Past medical history nil significant


On examination

- Pallor+
- Petechiae +
- Normotensive
- No icterus/lymphadenopathy
- Abdomen – liver 3cm RCM, spleen 4cm along the axis
- Rest of the clinical examination- normal


- With fever, pallor, bleeding diathesis and hepatosplenomegaly- acute infectious illness like Dengue/malaria and DD of malignancy was suspected initially

LAB. INVESTIGATIONS

- Hb – 8 gm/dl
- Total counts- 5920 cell/mm DC P34% L 63%E 2%M1%
- **Platelets- 33,000**
- MCV – 99%
- Retic. count- 21% (repeated to double check)
- SGPT -121
- Sr.bilirubin – 1.65 Direct 0.6
- ESR normal

- 
- Peripheral smear- F/o microangiopathic hemolytic anaemia,
 - With high retics, anemia and smear showing hemolysis and thrombocytopenia, auto immune hemolytic anemia with Evan's syndrome suspected

- 
- DCT negative

- 
- Repeat smear - atypical lymphocytes seen
 - Suggested to look for evidence of EBV infection by pathologist
- (Clinically no lymphadenopathy or pharyngitis)

- 
- Viral serology – VCA IgG & IgM positive for EBV

- Sr.feritin -569
- Vit. B12/red cell folate normal
- G6PD level normal
- Blood C/S – no growth
- Widal – negative
- MP-negative
- Dengue serology – negative
- Leptospirosis negative
- ANA DSDNA negative
- Urine Microscopy nil significant
- Bone marrow increase in erythroid precursors & megakaryocytes, some megaloblastic changes reactive marrow
- LDH 454

Summary

9 year girl with

- Pallor and Petechiae
- Hepatosplenomegaly
- DCT negative microangiopathic hemolytic anaemia and thrombocytopenia
- Reticulocytosis
- Atypical lymphocytes
- EBV serology: positive


Final diagnosis

- Viral mediated hemolytic anaemia with thrombocytopenia
- (etiology- EBV infection)



- **MANAGEMENT**

- Empirical antibiotics
- supportive therapy
- Clinical improvement with stable Hb and rise in platelets. Reticulocytosis settled in 72 hrs

- 
- Reviewed in out patients fortnightly
 - Remained well, normal counts
 - Hepatosplenomegaly regressed

5 days after the last follow up
when she had normal counts

Nov 2009

Presented again with

- H/o myalgia and lethargy for one day after an “URI”
- Sudden onset of pallor and petechiae
- Hepatosplenomegaly+
- Normotensive

Child reevaluated

- Hb-6.4, Platelets- 30000, Proteinuria+
- Smear microangiopathic hemolytic anemia
- Normal retics
- Direct Coombs test – strongly positive
- ANA - positive
- AntidsDNA – positive
- Renal biopsy – class II lupus nephritis

DIAGNOSIS

SLE with class II lupus nephritis with
autoimmune hemolytic anemia & thrombocytopenia (EVAN s syndrome)
Following recent EBV infection (?coincidence or cause).

Multidisciplinary team – Pediatric Hematologist ,
Pediatric Nephrologist and Rheumatologist

Treated with steroids for 6 weeks and on tapering doses
of steroids Azathiopurine was added.

On Follow up

- Regression of hepatosplenomegaly
- proteinuria decreased
- liver enzymes were normal
- Blood counts – normal
- Viral serology (EBV) – decreasing titres of VCA
IgM & IgG – still positive



Relationship between SLE and EBV - Literature review

Co incidence or cause

CASE REPORTS

Few case reports for EBV induced SLE

Patients evaluated and diagnosed to have SLE, who had EBV infection (VCA positive) prior to this


R. Verdolini et al. (2002) Systemic lupus erythematosus induced by Epstein-Barr virus infection. *Br J Dermatol* **146**:877-881

Ozgur Kasapcopur et al. (2006) Systemic lupus erythematosus due to Epstein Barr virus or Epstein Barr virus infection provoking acute exacerbation of systemic lupus erythematosus? *Rheumatol int* **26**:765-767

Ren Fail. 2009;31(2):144-8. Kikuchi-Fujimoto disease and systemic lupus erythematosus: the EBV connection?

Mechanism of EBV evolving to SLE (molecular mimicry)

- Ability of antibodies against EBNA 2 antigen of EBV to cross react with Sm D1 , that leads to an autoimmune response.
 - Homologous between EBNA 1 antigen and PPPGMRP peptide of Cterminal region of Sm antigen
- Autoimmun Rev. 2009 Feb;8(4):337-42. Epub 2009 Jan 22.

- 
- Patients with SLE have abnormally high frequencies of EBV-infected cells in their blood, and this is associated with the occurrence of SLE disease flares.
 - Abnormal regulation of EBV infection in SLE patients reflects the sensitivity of the virus to perturbation of the immune system.

J Immunol. 2005 Jun 1;174(11):6599-607.

- 
- Exposure to EBV infection may predict a disease phenotype of mild SLE disease with cutaneous and joint manifestations
 - Ann N Y Acad Sci. 2009 Sep;1173:658-63.

Learning objectives

- EBV infection could work as a trigger in some cases of SLE, particularly if the patient is genetically susceptible.
- In contrary to the existing evidence in literature EBV associated SLE could be severe with Evan's syndrome and lupus nephritis
- SLE patients have increased risk of EBV infections and found to have chronic EBV infection

- 
- Thank you