International Journal of Contemporary Pediatrics
Kamalamma R et al. Int J Contemp Pediatr. 2016 Nov;3(4):1474-1476
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20163705

Case Report

Evans syndrome with severe thrombocytopenia: a rare presentation

Rugmini Kamalamma, Siddaraju ML, Swathi Badam*, Niranjan Mahankali

Department of Pediatrics, Adichunchanagiri Institute of Medical Sciences, B.G. Nagara, Karnataka, India

Received: 22 August 2016
Revised: 03 September 2016
Accepted: 04 October 2016

***Correspondence:**
Dr. Swathi Badam,
E-mail: swathi.badam961@gmail.com

ABSTRACT

Evans syndrome is a rare disease characterized by the sequential or simultaneous presence of autoimmune haemolytic anemia and immune thrombocytopenia with a chronic relapsing and remitting course. Most of them present with severe anemia and moderate thrombocytopenia while neutropenia is associated in some cases. Associated laboratory parameters include unconjugated hyperbilirubinemia, decreased total serum IgG and IgM levels, presence of non-cross reacting auto antibodies against erythrocytes, platelets and in some cases against neutrophils. Management of evans syndrome includes glucocorticosteroids as the first line therapy and IVIG as second line treatment. Resistant cases are treated with cyclosporine, mycophenolate mofetil, vincristine, danazol, rituximab (monoclonal anti-CD20 antibody), alemtuzumab (humanized monoclonal anti-CD52 antibody). Autogenic or allogenic hematopoietic stem cell transplantation (HSCT) is the only curative option available. Here we are presenting an adolescent boy with Evans syndrome who presented with severe thrombocytopenia and moderate degree of haemolytic anemia and responded well to first line oral corticosteroid therapy.

Keywords: Evans syndrome, Immunosuppressive therapy, Severe thrombocytopenia

INTRODUCTION

Evans syndrome is a rare disease characterized by the sequential or simultaneous presence of autoimmune haemolytic anemia and immune thrombocytopenia with a chronic relapsing and remitting course. Evans syndrome is defined as the simultaneous or sequential association of autoimmune hemolytic anemia (AIHA) and immune thrombocytopenic purpura (ITP).[1,2] Most of them present with severe anemia and moderate thrombocytopenia while neutropenia is associated in some cases. Associated laboratory parameters include unconjugated hyperbilirubinemia, decreased total serum IgG and IgM levels, presence of non-cross reacting auto antibodies against erythrocytes, platelets and in some cases against neutrophils. Management of evans syndrome includes glucocorticosteroids as the first line therapy and IVIG as second line treatment. Resistant cases are treated with cyclosporine, mycophenolate mofetil, vincristine, danazol, rituximab (monoclonal anti-CD20 antibody), alemtuzumab (humanized monoclonal anti-CD52 antibody).

CASE REPORT

A 15 year old boy was brought with history of bleeding gums since 21 days after he underwent a minor dental procedure. On examination, he was pale and had minimal bleeding from gums at the site of upper left 1st premolar tooth which was removed 21 days ago (Figure 3). Few petechial lesions were seen around the lips, trunk and upper limbs (Figure 2) and a conjunctival hemorrhagic spot (Figure 4). There was no icterus, significant lymphadenopathy or hepatosplenomegaly. Laboratory investigations revealed severe thrombocytopenia (1000 cells/cumm), moderate anemia (7.8 gm%), reticulocytosis - 4.2% (corrected reticulocyte count 2.1), ESR-52 mm/hr with normal PT and APTT. Direct coombs test was

weakly positive and bilirubin levels were normal. There was no history of prior infections nor any family history of bleeding tendencies.

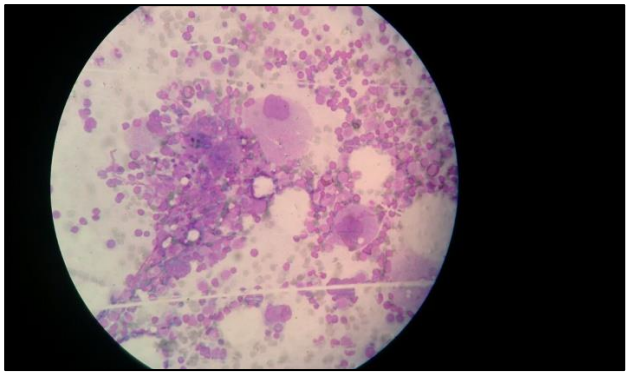

Figure 1: Hypercellular marrow with erythroid hyperplasia and megakaryocytes.

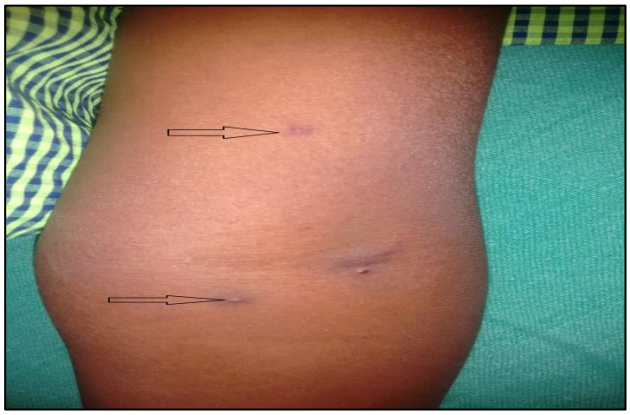

Figure 2: Petechiae over forearm.

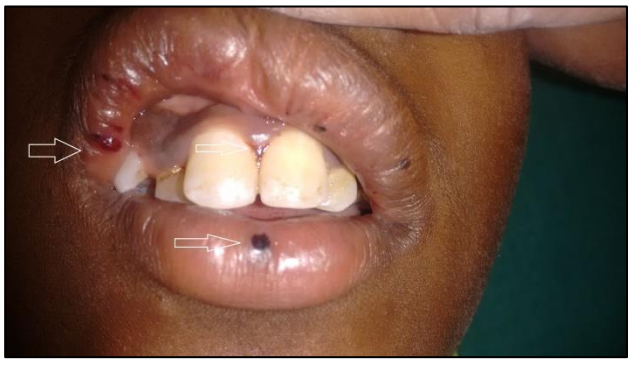

Figure 3: Minor bleeds and petechiae over upper lips and gums.

Peripheral smear showed normocytic normochromic anemia with severe thrombocytopenia. Bone marrow examination showed erythroid hyperplasia, megaloblasts and increased megakaryocytes (Figure 1). Serum IgG, IgM and serum LDH were in normal range. Screening for SLE was negative. As the bone marrow showed megaloblasts child was screened for Vit B12 which was also normal.

The child was given platelet transfusions along with oral prednisolone (2mg/kg/day) and his condition improved clinically and hematologically within 3 days. He was advised to continue for 2 weeks and tapered off over a period of 2 weeks. Though the child went for remission and he was advised to be under follow up as a relapsing course is expected.

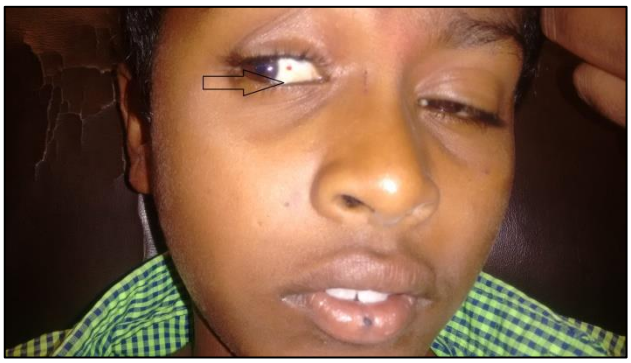

Figure 4: Minute conjunctival hemorrhagic spot.

DISCUSSION

Evans syndrome is defined as the simultaneous or sequential association of autoimmune hemolytic anemia (AIHA) and immune thrombocytopenic purpura (ITP).[1,2] There is no preferential distribution of this disease by age, gender, or ethnic group. Its chronic course is characterized by recurrent relapses and remissions.[2]

The etiology is unknown and immune dysregulation may be involved in the pathogenesis of the disease. Constitutive increase in production of interleukin-10 and Interferon-Gamma may lead to activation of autoreactive antibody-producing B cells which inturn produces antibodies against different lineages of blood cells.[3,4] Evans syndrome is deemed secondary if associated with a primitive immunodeficiency or systemic lupus erythematosus and it remained primary in 30% of cases.[5,6]

Most of the cases of evans syndrome presents primarily with severe AIHA and mild thrombocytopenia. Clinical phenotype includes symptoms of hemolysis (fever, pallor, jaundice, lethargy) and thrombocytopenia (petechiae, bruising and mucocutaneous bleeding). Physical examination may reveal lymphadenopathy, hepatomegaly and/or splenomegaly. These signs may be chronic or intermittent and in same case may occur during acute exacerbations.[2]

The appearance of the second cytopenia may occur months to years after the first immune cytopenia and may delay diagnosis. Neutropenia may be present in 55% of the cases.[2,6] Total serum immunoglobulin levels IgG, IgM levels may be decreased. Auto antibodies against RBC is diagnostic of this syndrome but presence of antiplatelet antibodies may be inconsistent. DCT may be positive

even in patients with absent haemolytic anemia.[2] First-line therapy is usually corticosteroids and/or intravenous immunoglobulin, to which most patients respond. Neverthless relapse is frequent. Second-line therapy include immunosuppressive drugs, especially cyclosporin or mycophenolate mofetil, vincristine, danazol or a combination of these agents.[7-10] Splenectomy can be done in cases of resistance to second line treatment.[8,9] More recently a small number of patients have been treated with rituximab, which induces remission in the majority although such responses are often sustained for <12 months.[7] SCT (stem cell transplantation) is the only curative option for evans syndrome. Studies suggests allogeneic HSCT may be superior to autologous HSCT but both carry risks of severe morbidity and of transplant-related mortality. Cure following reduced-intensity conditioning has now been reported and should be considered for younger patient.[10] Unrelated umbilical cord blood can be used for transplant after conditioning with busulfan, thiotepa, etoposide and antithymocyte globulin.

Five-year relapse-free survival of ITP component and AIHA component is 25 and 61%, respectively. 69% of children required one or more second-line immune treatments, 10% mortality by the age of 14.3 years.[6]

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Kamalamma R, Siddaraju ML, Badam S, Mahankali N. Evans syndrome with severe thrombocytopenia: a rare presentation. Int J Contemp Pediatr 2016;3:1474-6.