

## 1 Evans Syndrome-Rare Cause of Abdominal Pain: A Case Report

2 Md.Wahiduzzaman Mazumder

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5 **Abstract**6 Evan's syndrome is a rare and chronic autoimmune disease characterized by autoimmune  
7 hemolytic anemia and immune thrombocytopenic purpura with a positive Coomb's test in the  
8 absence of an underlying etiology. There is no preferential distribution of Evans syndrome by  
9 age, gender, or ethnic group. The best treatment options for Evans syndrome depend on many  
10 factors, including the severity of the condition; presence of signs and symptoms and person's  
11 response to therapies. We present a case of a 12 year old adolescent girl with abdominal pain,  
12 diagnosed as a case of Evans syndrome based on the clinical features, Coombs test, hemolytic  
13 anemia and thrombocytopenia.14 

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15 *Index terms*— autoimmune hemolytic anemia; immune thrombocytopenic purpura; coomb's test.16 **1 Introduction**

17 II.

18 **2 Case Report**19 Maria, 12 years old adolescent girl, 2 nd issue of non consanguineous parents, admitted into Pediatric Gastro-  
20 enterology and Nutrition department with the complaints of severe, agonizing, epigastric pain without any radiation  
21 and relieved slightly after leaning forward for 5 days, associated with non projectile, non bilious vomiting. She had  
22 no H/O of fever, cough, oral ulceration, joint pain, alopecia, but she had malaise, fatigue for last 15 days. Maria  
23 was severely pale, moderately icteric, no lymphadenopathy, stigmata of chronic liver disease was absent. Maria  
24 had tenderness in epigastric region with just palpable spleen and no other organomegaly or ascites. Laboratory  
25 findings:26 ? CBC: ESR=120 mm, Hct= 23.5%, Hb=7.5gm/dl, MCV=84.5fL, MCH=27 pg, MCHC=31.9gm/dl, RDW-  
27 CV=14.6%, WBC=4500/cmm, N=63%, L=30%, M=05%, E=02%, B=00%, Platelet=80000/ $\mu$ L.28 ? PBF showed features consistent with immune haemolytic anaemia with thrombocytopenia and marked  
29 rouleaux formation. Evans syndrome is an uncommon condition defined by the combination (either simulta-  
30 neously or sequentially) of direct antiglobulin test positive autoimmune haemolytic anaemia (AIHA), immune  
31 thrombocytopenia (ITP) and/or immune neutropenia in the absence of a known underlying etiology. There is  
32 evidence to support abnormalities in both cellular and humoral immunity in Evans syndrome 1 . Its chronic  
33 course is characterized by recurrent relapses and remissions. Evans syndrome is a diagnosis of exclusion. This  
34 means that a diagnosis is made in people with Coombs positive haemolytic anaemia and thrombocytopenia  
35 related to an abnormal immune response, other conditions with similar signs and symptoms have been ruled out.  
36 Various blood tests and in some cases, a bone marrow may be needed to exclude other conditions.

37 ? Bone marrow shows Dimorphic erythroid and megakaryocytic hyperplasia.

38 **3 ? USG of whole abdomen -periportal echogenicity of**39 Liver is increased. Parenchymal echogenicity is decreased. Multiple ill defined hyperechoic areas are noted in  
40 the right lobe of Liver. ? CT scan of whole abdomen with contrast-Hepatosplenomegaly with multiple hepatic  
41 SOLs and irregular heterogenous enhancement of spleen with abdominal lymphadenopathy. She received total 3  
42 bags blood within 10 days for correction of anaemia but her condition was deteriorating. Her general condition  
43 was improved after Injection Methyl Prednisolone 30 mg/kg/day for 5 days followed by oral prednisolone 1.5

44 mg/kg/day continued up to normalization of CBC then slow tapering. Follow up CBC after 7 days showed  
45 increased haemoglobin and platelet level without blood transfusion. CBC: ESR=5 mm, Hct= 24.0%, Hb=12.1  
46 gm/dl, MCV=87.3fL, MCH=27.6 pg, MCHC=31.7 gm/dL, RDW-CV=16.4%, WBC=6000/cmm, N=50%,  
47 L=42%, M=05%, E=03%, B=00%, Platelet= 180000/ $\mu$ L and USG of whole abdomen revealed no mass lesions  
48 in liver but spleen is enlarged in size with altered echotexture in inferior pole. Maria was diagnosed as Evans  
49 syndrome on the basis of clinical picture and laboratory investigations.

## 50 4 III.

## 51 5 Discussion

52 Autoimmune hemolytic anemia (AIHA) is an immune disorder which is characterised by circulating antibodies  
53 against antigens on the red blood cells (RBCs) membrane resulting in shortened life span of the RBC [2].  
54 Robert Evans first described an association between idiopathic thrombocytopenic purpura and autoimmune  
55 hemolytic anemia in 1951. It was characterized by simultaneous destruction of the body's own red blood cells,  
56 white blood cells, platelets, neutrophils which causes Autoimmune Hemolytic Anemia (AIHA) and Idiopathic  
57 Thrombocytopenia Purpura (ITP) or immune neutropenia in absence of any cause 3 .

58 Evans syndrome is predominantly a disease of pediatric age group ?? . There is evidence to support  
59 abnormalities in both cellular and humoral immunity in Evans syndrome. Both CD4 and CD8 lymphocytes were  
60 reduced; increased constitutive production of interleukin-10 and interferon- $\gamma$  caused activation of autoreactive,  
61 antibody-producing B cells. Despite the frequency of haemopoietic cell-specific autoantibodies in patients with  
62 Evans syndrome, there is very little information about the identity of target antigens.

63 Patients may present with AIHA or ITP either separately or concomitantly. Neutropenia occurs in up to  
64 55% of patients at presentation, or pancytopenia (14%). The development of the second cytopenia may occur  
65 months to years after the first immune cytopenia and may delay diagnosis. Usual features of haemolytic anaemia  
66 i.e: pallor, lethargy, jaundice, heart failure in severe cases; and features of thrombocytopenia i.e: petechiae,  
67 bruising, mucocutaneous bleeding may be present. The lymphadenopathy and organomegaly (hepatomegaly  
68 and/or splenomegaly) may be chronic or intermittent and in some cases may only be apparent during episodes  
69 of acute exacerbation [2][3][4][5][6] .

70 A full blood count will confirm the presence of cytopenias and a blood film should be examined for features of  
71 AIHA (polychromasia, spherocytes) and to exclude other underlying diagnoses (malignancies, micro angiopathic  
72 haemolytic anaemia, congenital haemolytic and thrombocytopenic conditions).

73 Features of haemolysis should be sought including a raised reticulocyte count, unconjugated hyperbilirubi-  
74 naemia and decreased haptoglobins. The direct antiglobulin test (DAT) is almost invariably positive (although  
75 often weakly so), even in the absence of haemolytic anaemia, and may be positive for IgG and/or complement  
76 (C3) [3][4][5][6] . The indirect antiglobulin test may also be positive in 52-83% of patients 5,10 .

77 Assays for antiplatelet and antigranulocyte antibodies have shown varied results 11 . In a report of 32 adult  
78 patients with AIHA, showed antiplatelet antibodies in 91% (demonstrated by thromboagglutination and indirect  
79 antiglobulin consumption tests) and leucocyte antibodies in 81% (demonstrated by a cytotoxicity test). Common  
80 variable immunodeficiency (CVID) and IgA deficiency, which have been reported to develop acquired cytopenias  
81 12,13 , and also as a baseline prior to immunomodulatory therapy.

82 As Evans syndrome is a diagnosis of exclusion so other confounding factors such as malignancies, infections  
83 and rheumatological disorders should be ruled out. A bone marrow examination (aspiration/biopsy) necessary  
84 to rule out causes of aplastic anemia or an infiltrative disorder. Bone marrow aspiration usually shows a mild  
85 to moderate erythroid hyperplasia. Megakaryocytes may be normal to increased in number which indicates an  
86 increased destruction of platelets in the peripheral blood as the cause of thrombocytopenia [6] . F Our patient's  
87 general condition was improved after injection methyl prednisolone 30mg/kg/day for 5 days followed by oral  
88 prednisolone 1.5 mg/kg/day continue upto normalization of CBC then slow tapering. Follow up CBC after 7  
89 days showed increased haemoglobin and platelet level without blood transfusion and USG of whole abdomen  
90 revealed no mass lesions in liver but spleen is enlarged in size with altered echotexture in inferior pole.

91 Evans syndrome is managed by Corticosteroids and/ or intravenous immunoglobulins as the first-line therapy.  
92 Most patients respond to this line of treatment although relapses are quite common. The second line therapy  
93 includes immunosuppressive drug. Recently, some patients have been treated with rituximab. Rituximab is one  
94 such drug that can be tried in cases of refractory Evans syndrome. Rituximab is a chimeric anti-CD20 monoclonal  
95 antibody with human IgG1 and k constant regions and murine variable regions 8,9 . It causes selective depletion  
96 of B cells through complement and antibody-dependent cell-mediated cytotoxicity and induction of apoptosis.

97 In long-term follow-up most authors described more frequent episodes of ITP compared with episodes of  
98 AIHA. Causes of death were mainly related to haemorrhage or sepsis and reassuringly, given the degree of  
99 immune dysregulation seen in many patients, none of the patients described in these long-term studies (mainly  
100 of children) developed malignancy.

101 Splenectomy may also be considered although long-term remissions are less frequent than in uncomplicated  
102 ITP. For severe and refractory cases, stem cell transplantation (SCT) offers the only chance of long-term cure.  
103 A fully developed Evans syndrome should be associated with a Coomb's positive hemolytic anemia which is  
104 essential for definitive diagnosis. Although rare, Evans syndrome should be suspected and investigated for in

105 patients presenting with autoimmune haemolytic anaemia or autoimmune thrombocytopenia concurrently or  
 106 sequentially. Patients of either of these disorders individually should therefore be thoroughly investigated for the  
 107 other so as not to miss a diagnosis of Evans syndrome. Long term follow up is essential in such cases as the  
 108 patient is at a risk of developing other auto immune problems 4 .  
 109 IV.

## 110 6 Conclusion

111 Although a rare disorder, Evans syndrome should always be considered in cases presenting with AIHA or AITP  
 112 occurring simultaneously or in follow up after excluding the causes of unknown etiology. Hence the early diagnosis,  
 knowledge of its presentation and constant follow up is crucial for this syndrome. <sup>1</sup>

? Reticulocyte count was about 4.79%. ? Direct Coomb's test (DAT) was positive, Indirect coomb's test (IAT) was negative. ? LDH-2905 U/L ? Hemoglobin electrophoresis revealed normal finding ? Serum bilirubin was 8.4 mg/dl, serum ALT-23 U/L, ceruloplasmin-44 mg/dl, s.albumin-4.35 g/dl, INR-1.12 ? Serum Lipase-86 U/L, ? Fasting lipid profile , RBS, Serum electrolytes and Creatinine were within normal range ? Viral markers for Hepatitis A, B, C and E were negative ? IgG was 14.3 g/l ? ANA, Anti -ds-DNA, Anti smooth muscle antibody and anti LKM1 were negative ? Flow cytometry for PNH evaluation was not consistent with a diagnosis of PNH  
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[Note: ? S. Iron= 208.98 µgm/dl (raised); S. Ferritin=443.0 ngm/ml (raised); TIBC= 295 µgm/dl (Normal).  
 ? Urine R/M/E showed Color=straw, Albumin=trace, Urobilinogen= 1+, Bilirubin-+++, Pus cell=2-4, RBC=plenty.]

Figure 1:

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141 *USG of whole abdomenperportal echogenicity of Liver was increased. Parenchymal echogenicity was decreased.*  
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143 *contrast showed Hepatosplenomegaly with multiple hepatic SOLs and irregular heterogenous enhancement of*  
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