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EVAN'S SYNDROME- A RARE PRESENTATION WITH DIAGNOSTIC DILEMMA AND TREATMENT CHALLENGES

Medicine

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ABSTRACT

Evan's Syndrome is a very rare and chronic autoimmune disease characterised by autoimmune haemolytic anaemia and immune thrombocytopenia with a positive DAT (direct antihuman globulin test). ES is a rare presentation that represents up to 7 %of AIHA and around 2%of ITP. When AIHA and ITP occur concomitantly , the diagnosis is even more difficult to make as in this case. The clinical presentation can include fatigue , pallor , jaundice and mucosal bleeding and the disease shows remissions and exacerbations. Catastrophic manifestations as acute bleeding is a very rare presentation and in our case it was the only complaint as bleeding per vaginum. Due to its rarity , the treatment is mostly extrapolated and the most reliable treatment is corticosteroids , rituximab , splenectomy and supportive therapies . Despite continuous advancements in diagnostic techniques and treatment modalities , mortality due to ES remains high.

KEYWORDS

Evan' Syndrome , autoimmune haemolytic anaemia

INTRODUCTION—

Evan's syndrome , as described first in 1951 by Robert Evan,s is an autoimmune disorder characterised by the development of autoimmune haemolytic anaemia (AIHA) and immune thrombocytopenia (ITP) along with or without immune neutropenia [1]. Immune disorders are mainly responsible , but that does not preclude further research for genetic predisposition and other immune disorders. The typical characteristic course of the disease shows heterogeneous chronic condition with clinical variability and spontaneous remissions and exacerbations [2]. There are very few cohort studies and case reports in literature that shows the incidence of about 37-70 % . A higher female gender has been reported that makes two thirds of all the cases . ES may be primary or secondary[3]. ES , if presented with other conditions eg SLE , primary immunodeficiencies and lymphoproliferative disorders is called a secondary type and is seen in almost 50% of the cases with ES.

Case Report-

Here , we are presenting a very rare case of Evan's syndrome of a 13 year old female presented to our emergency ward with h/o heavy menstrual bleeding since one week. She also had h/o breathlessness at rest , easy fatigability for two days. On examination she was clinically 3 gm % with pulse rate of 120/ min and BP of 94/58 mm of Hg . She never had her periods before and this was her first presentation with heavy vaginal bleeding, though she had the history of gum bleeding and melena one month ago. Her urine pregnancy test was negative and SARS -Covid testing was also negative , making prognosis in this case slightly better. There have been case reports where patient was SARS – Covid positive also in ES making the diagnosis and treatment even more challenging. Her reported investigations were Hb – 2.3 %, TLC 24,000 and platelets were 2800 / mm3. There was no history of fever or bleeding from any other site present. She was transfused with 3 units of PRP , 4 units of each FFP and PRP. She was immediately sent to the high dependency unit where she was in intubated as she was not maintaining adequate oxygen saturation. She underwent all the investigations that showed – LDH 953,D- Dimer – 104, S. fibrinogen levels- 303, DCT positive, ICT was negative . Her ANA was positive (88), vWF Factor - 1327, vWF Ag – 132 and her anti ds DNA was negative, Her Retic count was 27.88. Lft showed SGOT and SGPT levels were raised and ALP – 141. Coagulation profile showed PT – 15 , APTT – 24 and PT -INR = 1.2. On day 2 of admission, she developed subconjunctival haemorrhage , epistaxis and melena for which blood transfusion was done with3 packed cells. It was clearly a very challenging case in terms of diagnosis and her haematology opinion was done on the day of admission and DAT was sent on Day 1, which was positive. In her ICU stay of ten days , she received total 26 PRP, 5 PC and 5 SDP. She developed multiple spikes of fever on day 3 and started with higher antibiotics in the form of Inj. Meropenem and Inj. Teicoplanin. She also started developing haematuria on day 3 of ICU admission. She was started on oral Prednisolone 1mg/ kg/day. She was also started on second line drugs eg Rituximab weekly injections total of four injections. Patient showed some clinical improvement and was extubated on day 10 after which she suddenly had multiple episodes of epistaxis and haematuria. Her repeat investigations showed Hb- 8.9 gm %, TLC- 11, 500, Platelet count- 8000 , Coagulation profile of 12/21.7/1.02 on which she received 5 more PRP and one SDP. After four days, she became very drowsy and was not maintaining saturation. She was intubated again, but after a very brief clinical improvement she had acute exacerbation of the disease and expired the next day.

DISCUSSION-

Evan,s syndrome is a rare disorder and is characterized by the sequential or simultaneous development of autoimmune haemolytic anaemia (AIHA), immune thrombocytopenia and/ or immune neutropenia in the absence of any underlying cause in almost 50% of the cases. If this is associated with immune neutropenia, its presentation become even rarer[4]. It was first identified in 1950 and its occurrence is less than0.8% -3.7%.

Diagnosis is based on lab findings like increase lactate dehydrogenase (LDH), low haptoglobin, increased indirect bilirubin, reticulocytosis but gold standard remains the positivity of direct antiglobulin test(DAT) which is found to be present in 99% cases of warm-type AIHA [4,5]. In our patient also similar lab investigations were present. Our patient was ANA+ but had no features of SLE. Evans syndrome may be associated with connective tissue disorders specially in young patients which should be hence ruled out.[3-6]

Pathophysiology of Evans syndrome is not very well understood. It is mainly due to autoantibodies directed to RBCs and platelets. In warm type AIHA IgG antibodies are directed towards RBC surface antigens mostly in spleen leading to splenomegaly and formation of spherocytes in peripheral smear with increased signs of haemolysis such as increased LDH and indirect bilirubin. In ITP autoantibodies are directed towards GPIIb/IIIa on the platelets which in turn leads to thrombocytopenia which is usually severe and can lead to haemorrhage.

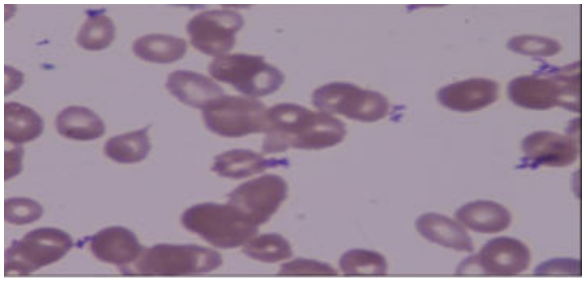

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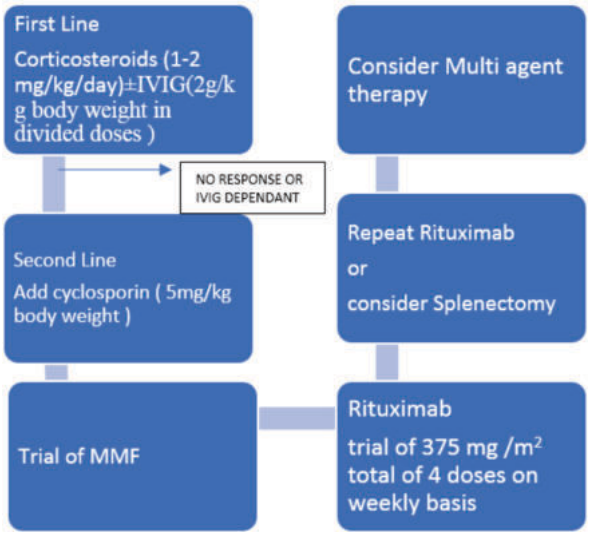
Fig 1 ; shows severe thrombocytopenia with immune neutropenia



Steroids remain the first line management which includes dexamethasone or prednisolone as the choice of drug. Iv immunoglobulins are used for acute episodes however relapses with these first line initial management is quite common.[4,5] Second-line agents include immunosuppressive drugs like, azathioprine, dapsone cyclophosphamide, danazol, mycophenolate mofetil, cyclosporine have been used but success rate with these drugs varies. More recently rituximab has been used, to induce remission in majority of patients however it is not sustained and effect on children and young adults are not known. Splenectomy is considered for long-term remission . For very severe and refractory cases and in those who are not willing for splenectomy stem cell transplantation (SCT) offers the only chance of long-term cure.[6]

CONCLUSION

Evan's syndrome is a life threatening hematological disorder requiring multidisciplinary management. The condition is usually managed with corticosteroids and immunosuppressive agents. splenectomy and bone marrow stem cell transplantation are other options. However, even after aggressive management the response is generally not adequate and associated with relapses. Further studies and research are required for proper diagnosis and management of Evan's syndrome.

Publication type – Case Report

Ethical Clearance—Not Required

Conflict of interest -- None

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