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Case Report

Evan's syndrome- unusual presentation: a case report

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ABSTRACT

Evans syndrome is an extremely rare type of autoimmune (hemolytic) disorder due to development of auto-antibodies against own RBCs, platelets and, at-times, neutrophils; most common presentation being mucosal and cutaneous bleeding with varying degree of anemia with thrombocytopenia. The present case is an unusual presentation of Evans syndrome with massive intra-peritoneal bleeding secondary to ruptured ovarian hemorrhagic cyst, which was managed successfully with timely decision of exploratory laparotomy, steroid, immunosuppressant and transfusion with adequate and appropriate blood and blood products. High index of suspicion and multi-disciplinary approach remained the key factors towards a successful outcome and patient went home in good health on 18th post-operative day.

Keywords: Evans syndrome, Anemia with thrombocytopenia, Hemolysis

INTRODUCTION

Evans syndrome (ES) is an autoimmune condition that presents with two or more cytopenias, which includes autoimmune hemolytic anemia (AIHA) and immune thrombocytopenia (ITP), with or without immune neutropenia (one report reported it in 15% of cases).[1] It predominates in children, mainly due to primary immune-deficiencies or autoimmune lympho-proliferative syndrome. The clinical presentation may include mucosal bleeding, pallor, jaundice, fatigue with remissions and exacerbations during the person's lifetime, and acute manifestations as catastrophic bleeding and massive hemolysis.[2]

The case elaborated here is of a patient of Evans syndrome presenting via acute episode of spontaneous intra-peritoneal bleeding secondary to ruptured ovarian cyst, an extremely rare and catastrophic presentation, managed successfully.

CASE REPORT

A 19 years young, unmarried girl presented to the out-patient department of a tertiary care government hospital (Government Medical College and Hospital, Nagpur) in March 2019 with chief complaints of 3 months of amenorrhea, with profuse menstrual bleeding since 9 days. The bleeding was heavy with soakage of 3-4 sanitary pads per day and with passage of clots and associated dysmenorrhea. Menstrual history was normal prior to the episode, with the patient having attained menarche at 13 years of age with normal menstrual cycles till now. There was no history suggestive of any recent infections, fever or drug intake. There was no history of previous blood transfusions or family history of bleeding disorder, autoimmune or other systemic diseases. She was admitted for further management.

The patient was conscious and oriented at the time of initial assessment. She was stockily built with a calculated body mass index (BMI) of 25.7. She was dyspnoic with a

respiratory rate of 36/min, grade III pallor, pulse rate of 160/min, blood pressure (BP): 120/70 mm of Hg, oxygen saturation was 98% on room air, chest clear with air entry equal on both sides with no significant abdominal findings. No thyroid swelling or lymphadenopathy. On the basis of initial observations, the provisional diagnosis was kept as abnormal uterine bleeding (AUB) with severe anemia.

All basic investigations were done on admission. First complete blood count (CBC) revealed Hb at 5 gm% with total leucocyte count (TLC): 8800/cmm; platelet count: 33,000/cmm; haematocrit (HCT): 16.9, red blood cell (RBC) count: 2.07 l/cmm. The Hb electrophoresis showed AA pattern and ruled out hemoglobinopathies as potential cause. The blood group was B positive. Peripheral smear showed macrocytes + occasional microcytes +, tear drop cells, schistiocytes +, polychromatic RBCs +, platelets depleted and hyper-segmented polymorphs. Ultrasound abdomen revealed mild hepatomegaly and bulky and heterogeneous uterus. She was recently diagnosed (3 months back) with hypothyroidism (TSH 20.43).

With the given clinical picture, the patient was immediately transfused 2 pints of whole blood on day 1 of admission itself. Progesterone support (tablet primolut-N 10 mg TDS) was started along with other conservative management for anemia. On third day of admission, her general condition worsened and she developed persistent tachycardia and tachypnea with bleeding from gums and ecchymotic patches on the upper limbs. She had an episode of hematuria on day 3. The repeat CBC was suggestive of low platelet counts and severe anemia. The Hb was now at 4.4 gm%, platelet count 36,000/cmm, hematocrit- 13.8 and TLC- 9600/cmm. The patient was again transfused with 1 pint whole blood and 4 unit platelets. Further investigations revealed ANA as moderately positive, INR-1.5 and Reticulocyte count at 2%. The indirect Coomb's test (ICT) was negative, urine analysis was positive for blood and hemoglobin and the bleeding time was 18 minute and 6 seconds, much prolonged. Physician's opinion was taken at this point to rule out idiopathic thrombocytopenic purpura (ITP) or other bleeding disorder.

Bone marrow aspiration was ordered post physician consultation, which was suggestive of normo- to macrocytic anemia with normochromasia, megakaryocytes +, macroovalocytes ++ (but diagnosis could not be established due to lack of adequate cellularity).

ITP was being considered as the first differential diagnosis at this juncture and she was started on injection methyl prednisolone 1 gm intravenous once a day for next 5 days. Per vaginal bleeding stopped on day 3 of tablet primolute-N. CBC was meanwhile repeated: Hb 4 gm%, platelets 46000/cmm, TLC 18000/cmm and hematocrit- 12.1. Over these first 10 days of admission, she had already been transfused with total 4 pint whole blood and 8 units of platelets.

On day 10, she started developing gradual distension of abdomen with mild tenderness and guarding. The ultrasound abdomen and pelvis was suggestive of 6×8 cm right ovarian hemorrhagic cyst with minimal free fluid in abdomen. Within next 10 hours, the cyst got ruptured leading to gross hemoperitoneum which was confirmed by computed tomography (CT). Simultaneously, general condition of the patient worsened again with rising pulse rate of 160/min and a respiratory rate of 36/min, with persistent hematuria and newly developed ecchymotic patches on flanks. The repeat CBC showed Hb of 2.2 gm% with TLC 17500/cmm, platelet count of 30,000/cmm and hematocrit of 6.8. The patient was immediately taken for exploratory laparotomy under general anesthesia with due procedural risk explained to the relatives. There was evidence of gross hemoperitoneum with 4.5 litre blood mixed fluid along with the ruptured right ovarian cyst. Intraoperative decision of right salpingo-oophorectomy was undertaken and the procedural was completed uneventfully. The patient received 2 pint whole blood, 4 fresh frozen plasma (FFP) and 2 units platelets intra-operatively. The patient was kept on ventilator support for next 3 days post-operatively.

The patient again had a bout of bleeding gums and bleeding from oral cavity post-operatively, for which oral and nasal packing was done. Platelet count was still decreasing and reached 7000/cmm on post-operative day 2. She was again started on injection methyl prednisolone from post-operative day 2 and higher antibiotics were continued; but there was no improvement in counts or clinical status. Hematologist opinion was sought at this point. Investigations were repeated: Hb- 7.4 gm%, TLC: 15410/cmm and platelet count 2000/cmm, reticulocyte count-19% with peripheral smear suggestive of schistiocytes+, polychromasia+, microspherocytes+ and DCT positive. On the basis of the clinical picture along with laboratory parameters, the patient was diagnosed with Evan's syndrome.

Definitive management in the form of intravenous immunoglobulin was started in the dose of 2 mg/kg over 5 days, along with tab azathioprine 50 mg once a day and tab danazol 100 mg BD. Immediate clinical improvement was observed with these medications, as her life support requirement went down, cutaneous/mucosal bleeding stopped, intra peritoneal drain output reduced and the counts started improving. (post-operative day 4 CBC: Hb-6.8, platelet- 32000/cmm). She was extubated on post-operative day 3. She had one episode of generalized tonic clonic seizures on post-operative day 5, for which she was appropriately managed. The CT head was reported to be normal and intracranial bleed was thus ruled out. Higher antibiotics, steroids, immunosuppressant, Progesterone support, and Thyroxine continued. Check dressing was healthy on post-operative day 5. The complete blood counts on post-operative day 6 and day 8 again showed improvement. The abdominal drain was removed on post-operative day 8 and complete suture removal was done on post-operative day 12. After day 15 of oral steroids, the

patient landed in steroid-induced psychosis and depression. The psychiatrist opinion was sought and antidepressant and tranquilizers started, to which she responded well. Steroid were continued with tapering doses. Complete blood count one day prior to discharge showed normalization with an Hb of 11 gm%, platelet counts of 1.73 l/cmm and TLC at 6800/cmm and the patient had recovered completely clinically (Table 1).

Table 1: Complete blood count parameters during hospitalization.

Parameters	2 months prior	D1	D4	D6	D9	D3 (PO)	D4 (PO)	D6 (PO)	D8 (PO)	D13 (PO)
Hb	11.8	5.1	4.4	4.0	2.0	5.2	7.4	10.7	10.4	11
TLC	10800	8,800	9,600	18000	17,500	13,800	15,410	-	-	-
Plt	219000	33,000	36,000	46000	30,000	7000	2000	64,000	99000	1.73
HCT	-	16.9	13.8	12.1	6.8	5.2	-	-	-	-
RBC count ($\times10^{12}$/l)	-	2.07	1.61	1.43	0.75	2.00	2.50	-	-	-
Retic. count (%)	-	-	2	-	-	-	16	-	-	-

Finally, the patient was discharged on immunosuppressants, tapering steroids, Progesterone and antidepressants with advice for regular follow-up.

DISCUSSION

Evans syndrome is a very rare autoimmune disorder wherein immune system produces autoantibodies against self RBCs, platelets and sometimes neutrophils. This leads to destruction of RBCs, called as autoimmune hemolytic anemia (AIHA) producing varying degrees of anemia. Low platelet count is due to destruction of platelets also referred as ITP. Neutropenia is not a usual finding. Thus, Evans syndrome is combination of AIHA and ITP (according to National Organization for Rare Diseases, NORD) with positive direct Coombs test, in absence of any known underlying pathology.[3] The disorder was first described by Robert Evan in 1951. He had postulated the diagnostic criteria as presence of anemia, reticulocytosis, hyper-billirubinemia, fecal urobillinogen, no family history of hemolytic disease, antibodies against RBCs at 37°C, lysis of transfused erythrocytes, thrombocytopenia, purpura, prolonged bleeding time, bone marrow aspiration showing normal or increased number of megakaryocytes; in absence of other baseline disease.[4]

It is said that Evans syndrome could be simultaneous, with features of AIHA and ITP occurring together (destruction of RBCs and platelets at the same time); but in majority of cases the destruction is sequential, one (AIHA/ITP) followed by the other, as was seen in our patient. The present case had the initial picture of ITP but it was soon followed by that of hemolytic anemia.

Evans syndrome could be primary or secondary. Secondary Evans syndrome can be associated with other autoimmune disorders like autoimmune lympho-proliferative syndrome (ALPS), SLE, antiphospholipid syndrome, certain lymphomas and CLL. The exact incidence is unknown. It is known to be more common in children and in females (M: F ratio 1:44).[5,6] The presenting features could be easy fatigability, weakness, jaundice, palpitations, pallor, tachycardia attributed to anemia and petechial hemorrhages, ecchymosis, mucocutaneus, gingival, vaginal bleeding or epistaxis secondary to thrombocytopenia.[5-7] Remission and exacerbations are seen during their life where life threatening bleeding can be catastrophic. In the current case the presentation was of similar kind and the clinical picture was suggestive of ITP for it to be considered as the first differential diagnosis.

CONCLUSION

A case of Evans syndrome presenting via acute episode of spontaneous intra-peritoneal bleeding secondary to ruptured ovarian cyst is very rare. High degree of suspicion, timely diagnosis and multidisciplinary approach helped in the eventually successfully managing the case with clinically acceptable outcome.

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