Chronic Hepatitis B atypically presenting as Secondary Evans Syndrome: A Case Report.

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ABSTRACT

Evans Syndrome (ES) is a rare autoimmune disorder defined by Robert Evans in 1951 while studying the association between autoimmune hemolytic anemia (AIHA) and immune thrombocytopenic purpura (ITP)[1]. It is usually associated with an idiopathic etiology, but sometimes, an underlying autoimmune condition may trigger ES.

ES is characterized by the simultaneous or consecutive presence of warm AIHA and ITP, while autoimmune neutropenia is relatively rare. It shows a positive direct anti-human globulin test. This is a type of disorder wherein one's body produces antibodies against RBCs, WBCs, and platelets. The symptoms can, therefore appear in the form of anemia, low platelet counts, or low white blood cells. In the presence of both AIHA and ITP, always rule out thrombotic microangiopathies, anemia from bleeding associated with ITP, vitamin deficiencies, myelodysplastic syndromes, paroxysmal nocturnal hemoglobinuria, and certain conditions like HELLP (Hemolysis, Elevated Liver Enzymes, and Low Platelets) with special attention to pregnant patients as Evans syndrome is a rare diagnosis of exclusion.[4]

ES is a chronic disease that quite often follows a variable clinical course. Spontaneous remissions and exacerbations characterize it. Currently, no conclusive data is available to indicate the worldwide prevalence of the disease; however, certain cohort studies report an incidence of 37%-73% of ES in AIHA. [2,3]

Incidence of ES varies from 0.68 to 1.84 per 1000000 people with a one-year period prevalence ranging from 3.30 to 21.30 per 1000000 people.5 It shows female dominance and is predominantly seen in children.[5]

To make a diagnosis of ES, a high indicator of suspicion and the exclusion of all the differentials are essential. An accurate diagnosis requires the exclusion of Autoimmune lymphoproliferative syndrome (ALPS), Thrombotic thrombocytopenic purpura (TTP), Systemic lupus erythematosus (SLE), antiphospholipid syndrome (APLA), Sjogren syndrome, Common variable immunodeficiency (CVID), IgA deficiency, Lymphomas and Chronic lymphocytic leukemia (CLL)

This case report presents a rare instance of chronic hepatitis B presenting itself as secondary Evans Syndrome.

Keywords: - *Evans Syndrome, Chronic Hepatitis-B, Autoimmune Hemolytic Anemia (AIHA), Immune Thrombocytopenic Purpura (ITP), Epstein Barr Virus (EBV).*

1. CASE

A 67-year-old male presented with generalized weakness for 13 days, breathlessness on exertion for 10 days, petechiae on the arms, and bleeding gums for 9 days. The patient had no significant symptoms before this period. His

breathlessness was not accompanied by cough, fever, chest pain, palpitations, oliguria, or anuria. He also denied any blood in stool or urine, easy or excessive bruising.

Past medical history includes pulmonary tuberculosis 40 years ago, viral meningoencephalitis 3 months ago, and hypertension. The patient underwent bone marrow biopsy in 2017 and 2022 for unknown reasons. He was a chronic tobacco chewer. There was no significant family history.

On examination, vital signs were stable: pulse 92 bpm, BP 156/90 mmHg, respiratory rate 16/min, SpO2 99% on room air, and random blood glucose 146 mg/dl. Pallor was noted on the tongue, nails, and lower palpebral conjunctiva. No icterus, cyanosis, clubbing, lymphadenopathy, or edema was observed. Systemic examination showed normal respiratory and cardiovascular findings. The patient was conscious and well-oriented, with normal abdominal and neurological exams.

2. RADIOLOGICAL FINDINGS

Ultrasonography of the abdomen and pelvis revealed an enlarged spleen and a normal liver.

3. INVESTIGATIONS

TEST NAME	RESULT	REFERENCE VALUE
Hemoglobin	4.50 gm/dL	M: 13-17 gm/dL F: 12-15 gm/dL
RBC	1.58 x 10^6 cells/cu.mm	4.5-5.5 x 10^6 cells/cu.mm
Hematocrit	13.00 %	40-50 %
MCV	108.20 fL	83-101 fL
RDW	15.90%	11.6-14 %
Platelets	26.00 x 10^3 cells/cu.mm	150-410 x 10^3 cells/cu.mm
Total leukocyte count	1260 cells/cu.mm	4000-11000 cells/cu.mm
Neutrophils	40.00%	40-80%
Lymphocytes	53.00%	20-40%
Monocytes	5.00%	2-10%
Eosinophils	2.00%	1-6%
Basophils	0.00%	<1-2%
S. Creatinine	0.66 mg/dL	0.6-1.4 mg/dL
S. Sodium	134.20 mEq/L	136-145 mEq/L
S. Potassium	2.85 mEq/L	3.5-5.1 mEq/L

S. total bilirubin	6.22 mg/dL	0.2-1.2 mg/dL
S. direct bilirubin	1.60 mg/dL	0-0.2 mg/dL
SGPT	42.00 IU/L	0-45 IU/L
aPTT	30.9	26-37.7
S. CPK MB	17.00 IU/L	0-25 IU/L
Reticulocyte count	4.20 %	0.50-2.50%
S. LDH	813 U/L	140-280 U/L
S. TSH	4.29 µIU/mL	0.5-5.0 µIU/mL
Random blood glucose	146 mg/dL	<140 mg/dL

3.1 Other Investigations-1

TEST NAME	**RESULT**
Direct Coomb's test	Positive (Grade 2)
Indirect Coomb's test	Positive (Grade 2)
HBsAg	Positive
HBeAg	Negative
Bone marrow biopsy (Trephine biopsy)	Hypercellular marrow with erythroid hyperplasia
Stool occult blood test	Negative
ANA antibody	Negative
EBV IgM	Positive

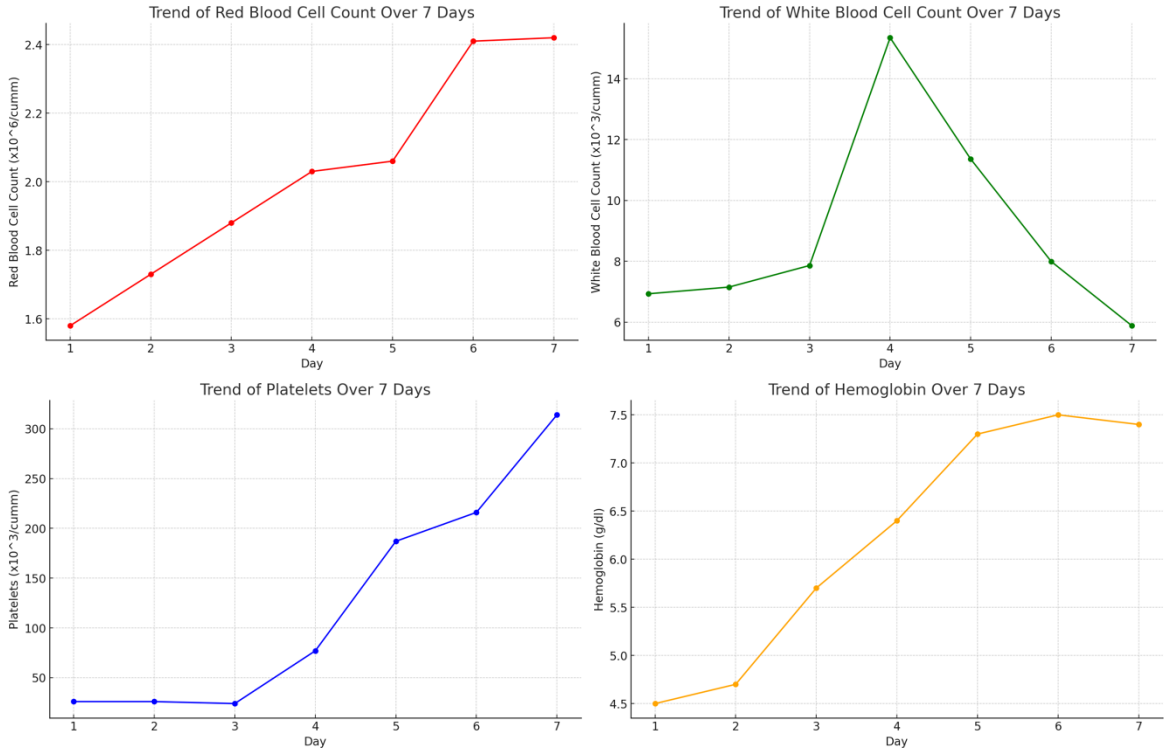
4. TREATMENT

On admission, the patient was immediately started on intravenous administration of 1 unit of Packed Red Cells and IV Furosemide 40 mg q6h for correction of severe anemia. The patient underwent 3 packed cell transfusions. After the diagnosis was established, the patient was started on pulse steroid therapy consisting of Injection Dexamethasone 8 mg once a day. As HBeAg was negative, the patient was not started on anti-viral therapy for chronic hepatitis B infection.

5. OUTCOME

By day 7 of admission, symptoms had diminished. Platelet and Hemoglobin levels demonstrated a positive change after timely diagnosis and prompt administration of steroids. The patient was discharged on the 9th day with the advice to continue 2 tablets of oral prednisolone 10 mg for 3 days, tapering to 1 tablet of oral prednisolone 10 mg for the following 15 days.

On follow-up after 1 month, the patient's symptoms were almost negligible with normal blood investigations.



6. DISCUSSION

The case of a 67-year-old male with chronic hepatitis B (grade 4) and Epstein Barr Virus (EBV) infection presenting atypically with secondary Evans Syndrome and trilineage cytopenia underscores the importance of carefully ruling out other potential causes of such symptoms.

Once secondary Evans Syndrome was diagnosed, identifying the underlying cause, which in this case was chronic hepatitis B, became paramount. The patient was previously undiagnosed with hepatitis B, and the investigations revealed it as the precipitating factor for Evans Syndrome, making symptomatic treatment alone insufficient.

Typically, the diagnosis of Evans Syndrome is supported by at least two cytopenias along with a positive Direct Coomb test. Management requires a tailored approach, often involving corticosteroids. In this case, the decision to maintain the patient on oral prednisolone with a gradual taper aimed to prevent future relapses and exacerbations, which are common in Evans Syndrome. Treating the underlying cause, such as chronic hepatitis B in this patient, is equally critical, necessitating a personalized drug regimen for each patient.

This case highlights the need for clinicians to maintain a vigilant approach towards conditions like chronic hepatitis B, which may present atypically as Evans Syndrome, thereby reinforcing the importance of comprehensive diagnostic evaluations.

7. CONCLUSION

Evan's syndrome is characterized by AIHA (autoimmune hemolytic anemia) and ITP (Immune thrombocytopenic purpura), which can be idiopathic or secondary to underlying autoimmune conditions like SLE (systemic lupus erythematosus), Sjogren syndrome and infections like EBV (Epstein Barr virus), HIV(human immunodeficiency virus), HCV (Hepatitis C virus). So, a physician should be vigilant in the search for the etiology underlying this disease.

Abbreviations:

ES - Evans Syndrome
AIHA - Autoimmune Hemolytic Anemia
ITP - Immune thrombocytopenic purpura
RBC - Red Blood Cells
WBC - White Blood Cells
HELLP - Hemolysis, Elevated Liver Enzymes, and Low Platelets
ALPS - Autoimmune Lymphoproliferative Syndrome
TTP - Thrombotic Thrombocytopenic Purpura
SLE - Systemic Lupus Erythematosus
APLA - Antiphospholipid Syndrome
CVID - Common Variable Immunodeficiency
CLL - Chronic Lymphocytic Leukemia
EBV - Epstein Barr Virus
HCV - Hepatitis C Virus
HIV - Human Immunodeficiency Virus

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