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Case Report: A Case of Primary Evans Syndrome Involving the Three Lines of Blood Cells

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Abstract Evans Syndrome is a rare autoimmune disorder characterized by the sequential presence of autoimmune hemolytic anemia and thrombocytopenia. Knowing whether an ES is primary or secondary is crucial. The coexistence of ES with other conditions such as hematological malignancies, systemic lupus erythematosus, and infections can affect how it is managed or affect its prognosis. Here we report Evans Syndrome case in a 6 years old female patient who presented with cough, shortness of breath, tachypnea, fever, epistaxis, prolonged bleeding, ecchymosis, and petechia all over the lower jaundice, limbs and trunk, pancytopenia, autoimmune hemolytic anemia (AIHA) and immune thrombocytopenic purpura (ITP), reticulocytosis, and hemolysis of transfused blood, with elevated inflammatory markers. There was no family history of hemolytic diseases. The patient was treated with IV IG, steroids (prednisone) with slight progression for one year, then cyclosporine with better response, and finally mycophenolate mofetil.

Keywords: *Evans syndrome, hemolytic anemia, thrombocytopenia*

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1. Introduction

Evans syndrome is typically characterized by the simultaneous or sequential occurrence of two or more cytopenias. The combination that occurs most frequently is immune thrombocytopenic purpura and autoimmune hemolytic anemia.

This syndrome is primarily linked to certain autoimmune diseases including lymphoproliferative disorders and systemic lupus erythematous [1]. This uncommon condition causes the body to produce antibodies that are directed against one's own platelets, white blood cells, and red blood cells (RBCs) [2].

Signs and symptoms vary according to which type of cells are affected. If red blood cells are targeted, the patient appears with shortness of breath, jaundice, fatigue, and weakness. When platelets are destroyed, there are some clear clinical features that come up with immune thrombocytopenia, like petechiae, purpura, ecchymosis, and prolonged nasal bleeding. In cases when patients become more susceptible to infection and present with fever, white blood cells are considered to be the cells that are affected by the autoantibodies [3].

Complete blood tests which measure the patient's immune function and the absence of any underlying causes are necessary to rule out similar conditions. Furthermore, a direct anti-globulin test, direct or indirect coomb's test that looks for antibodies against red blood cells (AIHA), bone marrow aspiration, and a CT scan for the chest and abdomen, all would help in the diagnosis [2].

Intravenous corticosteroids or intravenous immunoglobulins are the first-line treatments for Evans syndrome, followed by rituximab or splenectomy for patients who are unresponsive to steroids. However, the Recurrence of anemia and thrombocytopenia are common [4].

2. Presentation

A 6-year-old female, known to have immune thrombocytopenia purpura, neutropenia, and anemia, was admitted to the hospital with complaints of yellowish discoloration of skin and sclera with a general weakness for several consecutive months. She also has been infected by herpes zoster and complained of cough due to reduced immunity. She had no history of anorexia, abdominal pain, vomiting, diarrhea, or seizures.

On physical examination, the patient was conscious, alert, and oriented to time, place & person. She looked pale, her temperature was 37.8°C, her respiratory rate was regular 28 breaths per minute, O2 Saturation was 98%, her

blood pressure (BP) was 110/66 mmHg, and her heart rate was 120 beats per minute, regular.

Upon inspection of the upper, and lower limbs and abdomen, it was symmetrical and normal in shape. The patient was noted to have marked small, flat red spots under the skin (petechiae) and red, purple, and brownish-yellow spots (purpura) all over the trunk, upper & lower limbs. Upon palpation, the abdomen was soft and lax, and not tender. No hepatomegaly was found. The spleen was 6 cm below the costal margin No lymphadenopathy was noticed. Upon auscultation, audible bowel gurgling sounds were heard over the abdomen. No bruits were heard over the liver or above and lateral to the umbilicus.

Upon inspection of the head and neck, yellow discoloration in the skin and sclera was observed. A white pharyngeal thrush was seen. Nose bleeding was also noted.

On the patient's last medical exam in the emergency room, the patient appeared pale and in fatigue. Presented overweight with a moon face. She was febrile and tachypneic with 85% SpO2.

The patient developed interstitial pneumonia and urinary tract infection and was given the proper treatment. Additionally, the patient acquired herpes zoster and received the necessary care.

Initial laboratory assessment showed:

Test	Patient results	Normal reference
Hemoglobin g/dl	5.1	12-16
Hematocrit %	15.3	35-47
Mean corpuscular volume fl	80.1	78-98
Mean corpuscular hemoglobin pg	23.8	26-35
Mean corpuscular hemoglobin concentration %	32.3	30-36
Red cell distribution width-CV%	14	11.5-14.5
Red blood cells ×−10^12/l	1.91	3.5-5.5
White blood cells ×10^9/l	6.5	4-10
Lymphocyte	31.6	
Neutrophils (cells\L)	45.1	
Monocyte	0.9	
eosinophils	0.7	
Basophils	5.1	
Platelet count × 10^9/l	23	150-400
Lactate dehydrogenase U/l	590	110-240
Bilirubin total mg/dl	5.99	<1.1
Bilirubin direct mg/dl	1.13	<0.3
Haptoglobin	13	20-300
Aspartate aminotransferase UL	21.8	0-37
Alanine aminotransferase UL	20.3	0-33
Coombs test (indirect)	Positive	
Reticulocyte	2%	

Before suggesting steroid treatment in our situation, a bone marrow aspiration was done to establish the patient's active megakaryopoiesis. The bone marrow aspiration identifies normal numbers of megakaryocytes, confirming that there is peripheral thrombocyte destruction and revealing that the bone marrow is healthy and producing normal amounts of cells, ruling out leukemia.

3. Discussion

Robert Evans originally described Evans Syndrome 1951 [5], which is a rare illness characterized by the coexistence (either concurrently or sequentially) of immune thrombocytopenia (ITP) that is characterized by active IgG autoantibodies against platelet-derived membrane glycoproteins, GPIIb/IIIa glycoprotein (fibrinogen-binding site) which cause platelets to be eliminated prematurely and have a shorter lifetime[6] and autoimmune hemolytic anemia (AIHA) with a positive direct antiglobulin test (DAT) in the absence of a known underlying cause.

Symptoms may present with similar symptoms of leukemia or lymphoma as a result these illnesses must be ruled out before a diagnosis may be confirmed. Dark brown urine, pale skin, jaundice, tiredness, exhaustion, and shortness of breath are all symptoms of a low RBC count, as for the symptoms of decreased platelet count include petechial rash, Increased bruising, (little red dots under the skin caused by extremely little bleeds into the skin), and increased bleeding signs such as a bloody nose or heavy menstruation [7], in addition to Fever, mouth sores, and recurrent bacterial infections are all symptoms of a low neutrophil count, organomegaly (hepatomegaly and/or splenomegaly) and Lymphadenopathy can present persistently but are sometimes only noticeable during severe exacerbations [8].

In general, the absolute instance of Evans syndrome in clinical practice may reveal a variety of underlying diseases or syndromes that may have an impact on both outcome and care. As a result, detailed history, physical exam, and further investigations should be done to rule out any underlying conditions that may be misdiagnosed with idiopathic state [6].

Our patient presented with ecchymosis, oral petechial rash then noticed in her upper and lower limbs and trunk, epistaxis, and weakness without symptoms of infections or lethal complications at first. In long-term admissions, the patient had symptoms and signs of recurrent infections presented by fever, cough, shortness of breath, and oral thrush. She also developed yellowish discoloration of the skin and sclera, and an important finding on the exam reveal splenomegaly (palpable 6 cm below costal margins). These symptoms and signs were comparable with those published in previous case reports. Because the diagnosis of this syndrome is by exclusion, full blood count, direct and indirect coombs test, liver enzymes, indirect and total bilirubin, blood smear, bone marrow aspiration, and biopsy were done in our case, the results showed pancytopenia (anemia, thrombocytopenia, and neutropenia), hemolytic anemia (high ESR, high TSB (total serum bilirubin), low haptoglobin, high lactate dehydrogenase, positive direct and indirect coombs test), [9] peripheral blood smear with atypical lymphocytes, hypersegmented granulocytes, and WBCs with many immature cells bone marrow aspiration with tri lineage hematopoiesis within the adequate number of megakaryocytes confirming adequate megakaryopoiesis [6] and diagnosis of peripheral platelet destruction, bone marrow biopsy was free.

Therefore, our case results strongly suggested Evan Syndrome.

All data worldwide suggest that steroid therapy such as prednisone, prednisolone, and IVIG are the first-line therapy for severe cytopenias in addition to blood products if necessary, second-line therapy either a single agent or multiple agents form of immune suppressant according to the patient state and severity [6], a therapeutic study of cyclosporine as the best second-line treatment for the majority of patients [5], followed by MMF (mycophenolate mofetil) and multi-agent therapy or rituximab for those who do not react. Some cases may undergo splenectomy to reduce using immunosuppressive agents [5]. In cases that don't respond to immunosuppressive agents, hematopoietic stem cell transplantation may be effective with potential adverse effects [6].

Our patient had blood and platelet transfusions, as well as prednisolone, neubogen, and intravenous immunoglobins, and our therapy was similar to the therapeutic methods noted in other research but due to the mild response of steroids we switched to MMF and she is well responding to it.

Steroids generally function by eliminating macrophages, which are responsible for the death of one's own red cells and platelets. Despite the fact that concentrated immunoglobulin G from human plasma donors inhibits the FCy receptor of macrophages, it remains a controversial therapy [6], while MMF triggers T and B lymphocyte and inhibit the formation of antibodies, therefore, suppressing the immunity [10], neupogen Enhance the proliferation and maturation of neutrophils progenitors [11].

4. Conclusion

Even with multimodal treatment, ES remains a rare disease with a varied course marked by several relapses over the course of a lifetime. Evans syndrome is challenging to identify and treat.

Typically, corticosteroids and other immunosuppressive medications are used to treat the illness. The response, however, is unpredictable and inconsistent.

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