Systemic Lupus Erythematosus Presenting with Fulminant Autoimmune Hemolytic Anemia

Hanan Mothaqab Mashi, Ahmed Ali Jaafari, Zainab Ahmad Jafari, Nourah Ali Homaily, Ahmed Shamakhi
King Fahad Central Hospital

ABSTRACT
We describe a female patient 9-year- old girl with Systemic Lupus Erythematosus (SLE) who developed a fulminant autoimmune hemolytic anemia (AIHA) as an isolated symptom of her underlying disease. On admission, laboratory investigations were conducted and revealed high ESR 150 mm\h, severe anemia Hb was 3.4 g/dl with reticulocytosis 9%, low platelet count 74 \ 10^3\uL and positive direct Coombs tests. Upon further examinations, a diagnosis of SLE complicated by AIHA was reached, and methylprednisolone IVIG therapy was prescribed, and remission was approached.
Keywords: systemic lupus erythematosus, children, Coombs test, mixed-type, autoimmune hemolytic anemia, reticulocytosis.

INTRODUCTION

SLE is a chronic autoimmune disease with a highly variable clinical course. It causes systemic inflammation which affects multiple organs (American College of Rheumatology Committee).

The diagnosis of SLE can be achieved using the revised criteria of the American College of Rheumatology (ACR) which includes: Malar rash, Hematologic disorders, Discoid rash, Renal disorders, Arthritis, Serositis, Oral ulcers, Immunologic Disorders, Neurologic disorders, Photosensitivity and the Antinuclear antibody which is diagnostic per se.

The pediatric-onset SLE (pSLE) is usually associated with a higher disease severity than the adult-onset SLE [1].

AIHA is the most common hematological disorder in pediatric SLE [2]. In some cases, it develops throughout the disease course, while in other cases it might be the first manifested symptom. The warm antibody AIHA (warm AIHA) is detected in the majority of cases [3]. There are reports of adult-onset SLE cases who developed AIHA secondary to the SLE with the involvement of not only warm antibodies but also cold antibodies, known as the mixed-type AIHA (mixed AIHA). The clinical course of this mixed type is not entirely understood. Also, it is scarce in children [3].

The study was done after approval of the ethical board of King Fahad King Fahad Central Hospital.

Table 1: Immunological laboratory parameters at admission

Test	Result	Unit	Reference range
Anti ds DNA Abs	2618.1	H IU\ml	**Negative< 27**
			Indeterminate 27 – 35
			Positive >= 35
Anti-smith Abs	272.9	H CU	**Negative< 20**
			Positive >= 20
Anti nuclear Ab (ANA)	>200.0	CU	**Negative< 20**
			Positive >= 20
Anti ds DNA Abs IFA	Positive 1:1280		**<1:10 negative**
ANA IFA on hep2 cell	Positive 1: 640		**< 1 ; 40 negative**
Florescence pattern			
	Homogenous		

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Table 2: Laboratory parameters

WBC	5.94	**10^3\uL**
RBC	0.68	**10^6\uL**
HGB	3.4	**g\dL**
MCV	123.5	**fL**
MCHC	40.5	**g\dL**
MCH	50.0	**pg**
PLT	74	**10^3\uL**
PDW	18.2	**fL**
MPV	13	**fL**
NEUT	4.11	**10^3\uL**
LYMPH	1.68	**10^3\uL**
MONO	0.07	**10^3\uL**
EO	0.07	**10^3\uL**
BASO	0.01	**10^3\uL**
IG	0.18	**10^3\uL**

CASE REPORT

A previously healthy seven years old, Saudi girl was admitted to our hospital complaining of generalized bone pain and tenderness, decreased appetite, weight loss, and easy fatigability of one-week duration. She had a history of multiple neck swellings two years ago, and she underwent a tonsillectomy four years ago with no postoperative complications.

Her parents are consanguineous, and she had a positive family history of lupus nephritis (Her sister) and SLE (Her paternal grandmother and maternal uncle).

On examination

She was conscious but looked ill. She had marked pallor of skin and conjunctiva.

Her weight was 15 kg, and her height was 102 cm (both were on the 25th percentile), Vital signs were: Temperature 36 ˚C, pulse rate 112 per minute, respiratory rate 25 per minute, blood pressure was normal for age, spO2 99 % in room air. Palpable lymph nodes were detected in the cervical region (anterior and posterior groups) measuring 1.5x1x1 cm3, with firm consistency and the smooth surface was mobile, not tender and not inflamed. Another set of small palpable lymph nodes were detected in the submandibular and submental areas.

Investigations

Upon collection of the blood sample, it coagulated immediately. This was avoided by warming the next collected sample.

Blood tests revealed severe anemia Hb 3.4 g/dL, Thrombocytopenia platelets' count 74\ 10^3\uL WBC 5.94 10^3\uL, Reticulocyte 9%. Also, peripheral blood film revealed hemolytic anemia, reactive neutrophilia, and agglutination of the red blood cells were detected. ESR was also highly elevated > 150 mm\h.

Direct Coombs test was performed four times with positive result each time. However, subsequent tests reported the following results: IgG 17 g\L, IgM 1.3 g\L, and IgA 0.95 g\L. Also, indicated the disappearance of the cold agglutination reaction.

Immunological tests were conducted to determine whether this sever mixed AIHA was secondary to an autoimmune disease or not. Test results showed ANA > 200 CU which is considered positive. The anti-double-stranded DNA antibodies test (anti-dsDNA), which is regarded as a specific marker for SLE, was also done and yielded a positive result of 2618.1 IU\ml. Also, the Anti-smith test was positive 272.9 CU, the C3 was low recorded 0.244 g\L, and the C4 was 0.06 g\L.Serology tests were conducted and were positive for anti-CMV IgM and anti-CMV IgG, and negative for all hepatitis viruses, HIV, Brucella, RF, CMV-DNA, and CRP.

Lymph node biopsy was done and revealed reactive lymphadenitis as shown in figure (1)

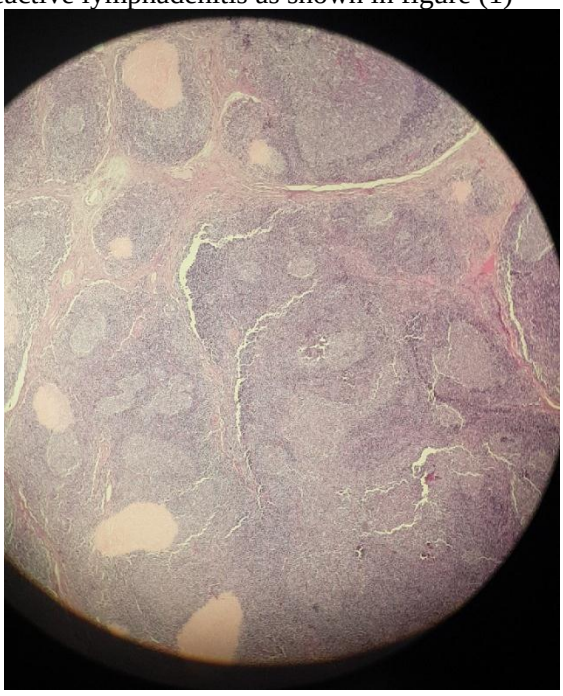

Figure 1

Also, abdominal US was performed, and para-aortic LN measures 5.3 mm were reported. No more abnormal data was detected.

This case was confirmed, based on the laboratory findings and the clinical presentation, as a case of Pediatric-Onset SLE initially presented with a life-threatening mixed fulminant hemolytic anemia. The patient was admitted to the PICU and managed by an immediate transfusion of 150 ml of PRBC over 4 hours, Methylprednisolone 2 mg\kg\day, and IVIG 1 gm\kg iv infusion over 12 hours (just for two days).

The improvement in the condition was first detected in the laboratory results as an elevation of the platelet's count 153 10^3\uL and an increase of the HB 8.2 g/dL followed by more increase 8.8 g/dL one week later.

The clinical improvement followed then the patient was transferred to a pediatric ward then discharged on oral prednisolone.

DISCUSSION

Systemic lupus erythematosus is one of the causes of the secondary AIHA that affects both children and adults. In children, the incidence peaks at the age of 4 years [1]. Most pediatric cases involve the warm type [4]. The pediatric-onset mixed AIHA is very rare; only a few cases have been reported in the literature [3,6,7,8].

Usually, the warm AIHA adopts a slower course than the mixed AIHA, which is considered critical and often presents with acute hemolysis. It is onset with HB ranging between 2.1 - 4.5 g/dL[5], as in our case, the patient who was presented to the ER with a life-threatening progressive anemia and extremely low HB 3.2 g/ dL. The detection of the cold antibodies, the marked hypergammaglobulinemia, and the agglutinative reaction, which was improved after five days of prednisolone therapy, suggested the mixed AIHA diagnosis. AIHA is the initial manifestation of SLE in 21 % of pSLE cases. However, it develops throughout the course of the disease in up to 50 % of pSLE cases [9].It could be initiated by an infectious trigger as viral infections [3].

The role of the viral infection in the pathogenesis of SLE has been a significant interest in many studies over the last decades [10,11,12].

Some studies have suggested that CMV pp65 subfragment peptide elicits the production of pathogenic antibodies that cross-react with nuclear proteins in genetically susceptible individuals [10,11,12].

However, this is not proven yet as It is It is difficult to determine whether CMV is the triggering infection or not, as the primary CMV infection might pass without a diagnosis because it only causes nonspecific symptoms (e.g., mild catarrh) [12].

It was reported that some cases were presented with clinical manifestations of CMV infection exacerbated by an undiagnosed SLE. However, the pathogenesis of this condition has not been fully understood [12]. There is a previously reported case which showed elevated anti-CMV IgG antibodies at the time of the SLE diagnosis [12], similar to our case condition.

CONCLUSION

The life-threatening fulminant AIHA is a rare complication of the pediatric-onset SLE, but remission was successfully achieved using Methylprednisolone and IVIG. So, this case report will be a valuable resource of a new and unusual information that may lead to massive advances in the clinical practice to improve patient outcomes.

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