Case Report

An interesting and rare presentation of Autoimmune Hemolytic Anemia secondary to Systemic Lupus Erythematosus — A case report

Ronak Jain G[1], G Vijayalakshmi[2], T B Umadevi[3]

Initial Presentation of Systemic Lupus Erythematosus (SLE) in the general population varies among individuals, can be atypical and often very confusing to confirm or even suspect SLE in the early stage of the disease. With low index of clinical suspicion or inadequate follow up, the diagnosis of SLE could be delayed. Sometimes Autoimmune Hemolytic anemia(AIHA) can be the only initial symptom of SLE in a patient which should not be missed and when picked early could drastically improve the outcome and prognosis of the disease. We report an interesting case of SLE initially presenting as AIHA in a 13 year old south Indian girl.

[*J Indian Med Assoc* 2020; **118(9):** 50-2]

Key words **: Autoimmune haemolytic anemia, Thrombocytopenia, Anemia, Childhood, Systemic Lupus Erythematosus.**

Haematological disorders are frequently seen in systemic lupus erythematous (SLE). Anemia is found in 50% of all SLE cases and can be precipitated by multiple elements such as long standing disease, deficiency of iron, chronic kidney dysfunction, myelotoxicity induced by intake of drugs, and even autoimmune Hemolytic Anemia (AIHA)[1]. Much of the literature available on AIHA is from the west.SLE is rare in India. A prevalence analysis carried out in India (in a rural population near Delhi estimated a point prevalence of 3 per 100,000[10].

AIHA is seen in 5–10% of SLE cases[2]. AIHA can appear as an isolated initial manifestation at the onset of SLE diagnosis or during the first year of illness[3]. It is also linked with many forms of SLE manifestations such as lupus nephritis, thrombocytopenia and as well as higher index of disease activity and bad prognosis. With an incidence of 1-3 cases in 100,000[4,5] per year makes AIHA relatively rare and diagnosing AIHA to be secondary to SLE is a rare presentation of the disease itself which has a varied and unusual presentation.

Case Report

A 13 year old female from southern Tamil Nadu came with complaints of easy fatigability, abdominal distension and increased hair fall for the past 4 months. Her past history consisted of recurrent admissions for anemia in the past 4 months for which she was treated symptomatically. Her family and personal history were unremarkable. There was no history stating previous blood transfusions or bleeding manifestations. On examination, patient was thin built and poorly nourished. She was pale, icteric and had bilateral deep cervical lymphadenopathy. Oral cavity was normal with no ulcers. Hepatosplenomegaly was present. Viral markers were negative. Fundus examination showed changes suggestive of anemic retinopathy. Peripheral smear showed anisopoikilocytosis, reticulocytes with spherocytes and a reticulocyte production index of 3.3. USG showed hepatosplenomegaly with normal sized kidneys. We then did serum markers of hemolysis such as serum haptoglobin and serum LDH which was decreased and increased respectively. FNAC of the right cervical node was done which showed reactive lymphadenitis. Bone marrow aspiration showed a reactive erythroid hyperplasia which all pointed towards a haemolytic picture. Direct Coombs test (DCT) was positive. Serum C3 & C4 levels were low. ANA was then done which turned out to be positive and then ENA profile was carried out which was dsDNA positive and a diagnosis of AIHA secondary to SLE was confirmed. Since Proteinuria was present biopsy of the kidney was done which showed Class 4 Lupus Nephritis characteristically showing wire loop lesions (Figs 1-3).

Editor's Comment :

- **The most frequently seen acquired hemolytic anemia is AIHA.**
- **Anemia of Chronic Disease is the most common haematological presentation of SLE seen in 70% of cases[2].**
- **Hemolytic anemia (more commonly warm antibody/ Ig G type) is a rare presentation of of SLE seen only in 10% of cases[2].**
- **Any female patient in the reproductive age group with unexplained anemia should be evaluated for Autoimmune disorders specially SLE.**

Stanley Medical College & Hospital, Chennai 600001
[1]MBBS, MD, Junior Resident
[2]MBBS, MD, Assistant Professor, Corresponding Author
[3]MBBS, MD, Professor
Received on : 14/03/2020
Accepted on : 13/06/2020

Routine investigations		Special investigations	
Haemoglobin	4.1g/dl	Serum LDH	1250 IU/L
Total count	6100/cu.mm	Serum Haptoglobin	10mg/dl
Differential count	N: 50% L:35% M:15%	Direct Coombs test	Positive
Platelets	1,21,000/cu.mm	Urine haemoglobin	Negative
MCV	108fL	Urine PCR	2.4
Serum urea	28mg/dl	Serum C3	50mg/dl
Serum creatinine	1.0mg/dl	Serum C4	15mg/dl
Total Bilirubin	3.1mg/dl	ANA	3+
Direct bilirubin	1.0mg/dl	dsDNA	Positive
Urine albumin	2+	Serum iron studies	Within normal limits
Other routine blood and urine parameters	Within normal limiits	Vitamin B12	500ng/L

Treatment

Patient was then started on 1 mg/kg per day of Prednisone along with Tab Mycophenolate Mofetil (MMF) 500mg OD (combination therapy for lupus nephritis), multivitamin, ferrous sulphate and calcium supplements and within 1 week she showed drastic improvements indicated by increase in haemoglobin and general wellbeing. At the time of discharge she was asymptomatic with lab parameters showing a Haemoglobin of 9.1g/dl and a platelet of 1,35,000/mm^3 She was discharged on T.Prednisone(0.5mg/kg/day), Tab MMF 500mg OD and T Hydroxychloroquine 200 mg OD along with vitamin supplements.

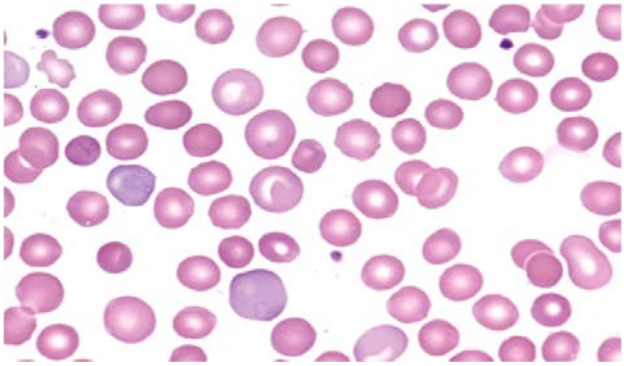

Fig 1 — Spherocytes, reticulocytes and Anisopoikilocytosis in peripheral smear Wright-Giemsa Stain, 200X

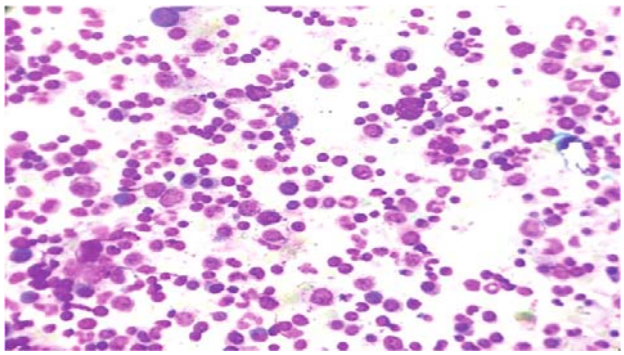

Fig 2 —

- Bone marrow aspiration showing erythroid hyperplasia suggestive of hemolysis. Myeloid to erythroid ratio is 1:3 which is reversed.Erythropoiesis is active and increased with erythroid hyperplasia.Myeloid series shows normal pattern of maturation.
- IMPRESSION: reactive erythroid hyperplasia showing micronormoblastic and normoblastic maturation
- Wright-Giemsa stain, 200x

Discussion

AIHA can be a primary or as in our case secondary to SLE. Autoimmune haemolytic anemia is an acquired disorder due to antibody mediated destruction of the RBCs. The most common type of anemia encountered in SLE is Anemia of Chronic Disease (ACD) which is seen in 60-80% of SLE patients. AIHA has been described in 4-10% of adult SLE which is relatively rare.

AIHA is characterized by elevated counts of reticulocytes, low levels of haptoglobin, increased concentration of indirect bilirubin and a positive direct Coombs' test. Warm/Ig G mediated AIHA accounts for 65-70% of the disease. Onset is sudden. Hepatosplenomegaly is present due to extravascular type of hemolysis. It is a serious condition and if untreated leads to 10% mortality.

The pathogenesis for AIHA in SLE involves erythrocyte damage mediated by antibodies, usually by warm-type IgG antibodies. The band-3 anion, a transporter glycoprotein of membrane erythrocytes, is also seen as a likely target[6]. Healthy people may also exhibit anti band 3 antibodies, and may help in clearing senescent erythrocytes, which when undergo aging reveal band 3 neoantigens. According to some authors, the antigenic neoepitopes, that are seen in these red cells may cause autoimmune mediated hemolysis[7]. Another pathogenic theory is cell lysis by complement activation commonly found in IgM mediated cold type AIHA causing an intravascular hemolysis[8].

The correlation between thrombocytopenia and AIHA has been documented in the past[3] and is also seen in our case. While the correlation between AIHA and the autoimmune thrombocytopenia called as Evan's syndrome might occur with other autoimmune diseases, it is identified more frequently in SLE[9]. This association proposes a

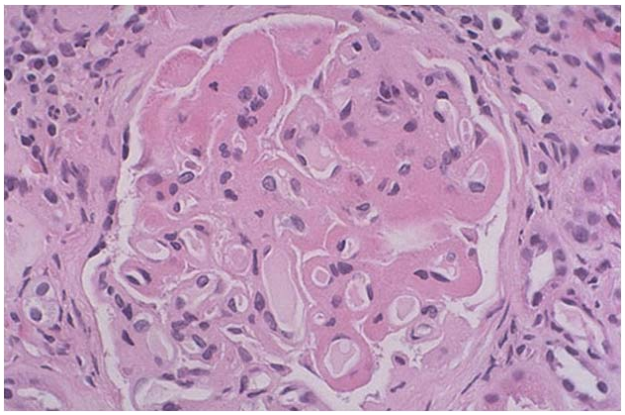

Fig 3 — Wire loop lesions in kidney biopsy characteristic of class 4 Lupus Nephritis, H & E stain, 400X

shared pathogenesis for these two manifestations, presumably involving antibody induced destruction of red blood cells, mostly mediated by warm antibodies of IgG type.

AIHA is treated with steroids as first line agents and second line treatment is with immunomodulators namely rituximab. Determining the cause of anemia is critical to treat the underlying disorder and preventing the progression of the disease to fatal complications such as renal failure. Anemia should never be overlooked because sometimes it can be the only symptom pointing towards a major underlying disorder such as in our case which turned out to be SLE. Whenever AIHA is diagnosed in a patient ,a full screen for autoimmune diseases (especially SLE) is imperative.

Lupus nephritis is a frequent and fatal complication of SLE. 30 to 50 percent of affected individuals will have clinical manifestations of kidney disease when the diagnosis of SLE is confirmed, and 60% of adults and 80% of children show renal defects at some stage during their illness[2]. Lupus nephritis develops from deposition of circulating immune complexes that activate the complement cascade resulting in complement mediated damage, infiltration of leucocytes, activation of procoagulant factors, and release of different cytokines.

Class IV defines universal, diffuse proliferative lesions involving the huge majority of glomeruli. Patients having class IV lesions usually have increased antiDNA antibody titers, serum complements are low, hematuria, red blood cell casts, hypertension, proteinuria and decreased renal function. Latest evidence recommends inducing remission by giving high dose steroids and either cyclophosphamide or MMF for 2–6 months, followed by maintenance therapy with lower dose of steroids, which balances the probability of successful remission with the side effects that may be seen with therapy.

Conflict of Interest : The author declares that they have no conflict of interest with respect to the authorship and/or publication of this article.

Limitations of Study : None

References

1 Giannouli S, Voulgarelis M, Ziakas PD, Tzioufas AG — Anaemia in systemic lupus erythematosus: from pathophysiology to clinical assessment. *Ann Rheum Dis* 2006; **65:** 144-8.

2 Harrisons Principles of Internal Medicine 20th edition Pg no:2520

3 Kokori SI, Ioannidis JP, Voulgarelis M, Tzioufas AG, Moutsopoulos HM — Autoimmune hemolytic anemia in patients with systemic lupus erythematosus. *Am J Med* **108:**198-204.

4 Gehrs BC, Friedberg RC — Autoimmune haemolytic anemia. *Am J Hematol* 2002; **69:** 258-71.

5 Petz LD, Garraty G — Immune Haemolytic Anemias, 2nd Ed. Philadelphia, PA: Churchill Livingstone; 2004

6 Victoria EJ, Pierce SW, Branks MJ, Masouredis SP — IgG red blood cell autoantibodies in autoimmune hemolytic anemia bind to epitopes on red blood cell membrane band 3 glycoprotein. *J Lab Clin Med* 1990; **115:** 74-88.

7 Kay MM, Marchalonis JJ, Hughes J, Watanabe K, Schluter SF — Definition of a physiologic aging autoantigen by using synthetic peptides of membrane protein band 3: localization of the active antigenic sites. *Proc Natl Acad Sci USA* 1990; **87:** 5734-8 21.

8 Richaud-Patin Y, Perez-Romano B, Carrillo-Maravilla E, Rodriguez AB, Simon AJ, Cabiedes J, Jakez-Ocampo J, Llorente L, Ruiz-Argüelles A — Deficiency of red cell bound CD55 and CD59 in patients with systemic lupus erythematosus. *Immunol Lett* 2003; **88:** 95-9.

9 Sultan SM, Begum S, Isenberg DA — Prevalence, patterns of disease and outcome in patients with systemic lupus erythematosus who develop severe haematological problems. *Rheumatology (Oxford)* 2003; **42:** 230-4.

10 Malaviya AN, Singh RR, Singh YN, Kapoor SK, Kumar A — Prevalence of systemic lupus erythematosus in India. *Lupus* 1993; **2:** 115-18.