Systemic Lupus Erythematosus associated refractory pancytopenia responding only to intravenous immunoglobulins

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ABSTRACT

Background: We, here, describe the case of Systemic Lupus Erythematosus (SLE) with pancytopenia, refractory to steroids, immunosuppressive therapy, and plasmapharesis that ultimately responded to intravenous immunoglobulins (IVIG). To the best of our knowledge, very few cases of this type have been reported in literature.

Case presentation: A 40-year-old female presented with complaints of hematemesis, hematochezia, gum bleed, epistaxis, menorrhagia, and fever. After careful examination and investigation she was diagnosed with SLE associated with pancytopenia refractory to conventional means of treatment. Pancytopenia responds normally to steroids and immunosuppressive agents in these patients however our patient responded only to IVIG.

Conclusion: This case report highlights the fact that early use of Intravenous immunoglobulins in patients of SLE with severe and refractory pancytopenia can prevent morbidity and mortality.

Keywords: SLE, pancytopenia, intravenous immunoglobulins, case report.

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Background

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder of unknown etiology and the pathophysiological understanding is attributed to several factors [1,2]. The disease is characterized by the production of antibodies by the body against its own nuclear and cytoplasmic antigens. The prevalence of disease is 130 cases per 100,000 population in US [1].The risk is higher among women and individuals with a family history of autoimmune diseases [1,3]. It is a multi-system inflammatory disorder involving almost all the systems of the body commonly skin, joints, kidneys, brain, and bone marrow. Various complications of disease include renal impairment, pancytopenia, Pericarditis, Atrioventricular block, and stroke [4]. The diagnosis is based on clinical symptoms and presence of specific antibodies. Treatment options include hydroxychloroquine, glucocorticoids, immunosuppressive agents, and monoclonal antibodies [5]. The use of intra venous immunoglobulins (IVIG) has been approved for the treatment of complicated SLE but not a common practice [5] Few cases regarding use of IVIG for treatment of SLE associated pancytopenia are reported in literature, but this case is unique because our patient with SLE had pancytopenia refractory to conventional means of treatment responding only to intravenous immunoglobulins.

Case Presentation

A 40-year-old female presented to the OPD of a tertiary care setting with complaints of hematemesis, hematochezia, gum bleed, epistaxis, menorrhagia, and fever for last 10 days associated with weight loss and a past history of abortions and blood transfusions. The review of systems revealed shortness of breath and palpitations with walking, abdominal pain, decreased appetite, joint pains, and irregular menstrual cycles. On examination the blood pressure 110/70 mm Hg, temperature 101ºF, pulse 120/minute, and respiratory rate 20 breaths/minute. The patient had generalized pallor with malar rash, petechiae on extremities, and bruises on multiple areas on the body. There was a suspicion of Pancytopenia, viral haemorrhagic fever, complicated malaria, autoimmune systemic disorder, and hematological malignancy. Initial investigations revealed pancytopenia, and the patient was admitted for further evaluation and management.

The investigations are given in Table 1. Lab Investigations showed low haematological parameters, i.e., low white blood cell and red blood cell count along with anaemia (Hb = 6.9 g/dl). Hematocrit was also below the normal value (19.8%). Tests for non-structural protein 1 Dengue antigen and Immunochromatographic test for malarial parasite for malaria were negative._Serological test for antibodies to

Table 1. *Complete blood count.*

TESTS	BEFORE IVIG	AFTER IVIG	NORMAL RANGE
WBC total	2,300	11,100	4,000–11,000µL
RBC Total	2.40	2.99	3.8–5.8 m/µl
Haemoglobin	6.90	9.5	11.6–16.5 g/dl
HCT	19.8	25.9	40%–54%
MCV	82.5	86	80–90 fl
MCH	28.8	28	27–32 pg
MCHC	34.8	33	32–38 g/dl
Platelet count	8,000	156,000	150,000–400,000/µL
RDW	21.0	22.4	11.5%–13.6%
C3	0.5		0.8–1.6 g/dl
C4	0.09		0.16–0.48 g/dl
ANA	Strongly positive 3+		Negative ≤ 5
Anti ds DNA Ab	≤0.1		Negative ≤ 5
Anti Histone Ab	21 (Positive)		Negative ≤ 5

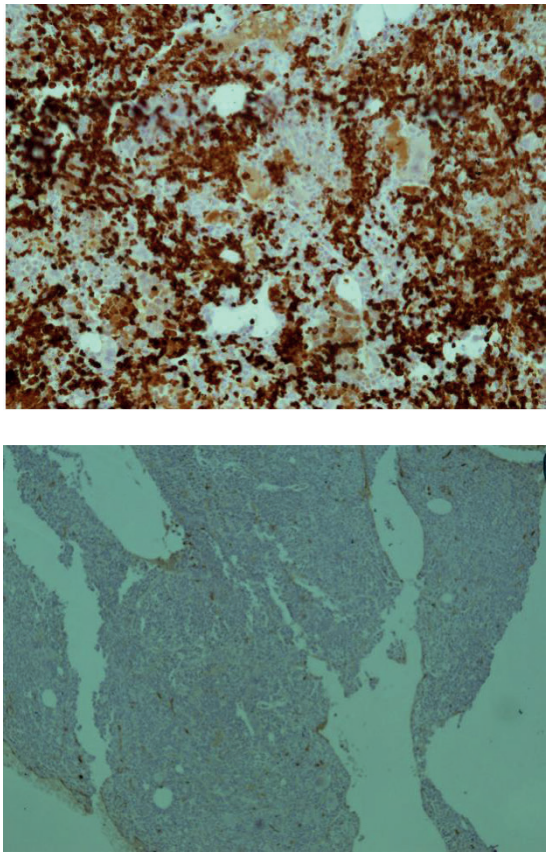

Figure 1. *The bone marrow Trephine biopsy showed a hypercellular specimen showing increased Megakaryocytes (upto 8/HPF) with mild nuclear dysplasia. Granulopoiesis is maturing. HbA immunostain showed hyperplastic and moderately megaloblastic erythropoiesis. No blasts are identified on CD 34 immunostain.*

anti-nuclear antigen (ANA) was positive and Anti-double stranded DNA was negative. Extractable nuclear antigen antibody revealed positive anti-histone antibodies and anti Ro/Sjogren syndrome antibodies (SSA) antibodies. Bone marrow biopsy showed hypercellularity with increased megakaryopoesis as shown in Figure 1 and the findings were suggestive of peripheral destruction or increased consumption of platelets.

The bone marrow aspirate revealed a diluted specimen with predominant mature neutrophils. Megakaryocytes were not seen. Erythropoiesis was moderately megaloblastic with nuclear budding, nuclear lobulation, and karyorrhexis. No atypical cells or blasts were seen. There is no morphological and immunohistochemical evidence of hemato lymphoid malignancy seen in the sections examined. The underlying etiology could have been chronic infection, inflammatory conditions, vitamin B12, folate and iron deficiency, or autoimmune disorders.

After consulatation with Rheumatologist, SLE was diagnosed on the basis of pancytopenia, low complement values, and antibodies against ANA, Histone, Ro/SSA, and clinical features. The treatment was started with IV pulsed steroid therapy without significant improvement in her condition. The patient was then given IV Cyclophosphamide and later plasmapharesis without adequate response. This was followed by administration of IVIG in a dose of 1.5 g/kg and the clinical condition of the patient improved with no observed adverse reactions to therapy. Lab investigations are shown in Table 1.

Discussion

Pancytopenia is a well-recognized complication in patients with Systemic Lupus Erythematosus which is treated in majority of cases with steroids and immunosuppressive therapy [4]. This complication may sometimes prove fatal in these patients and can be very severe leading to life threatening intra cerebral bleed secondary to platelets destruction, hence timely recognition and management is essential to avoid fatal events. IVIG are not commonly used for the management of this complication, and very few cases have been reported in literature in this regard with no study yet

done in Pakistan and South Asia emphasizing the role in severe and refractory pancytopenia [5]. The main reason for limited use of IVIG is cost effectiveness but our case highlights the fact that early use of IVIG can be very helpful and prove life saving in these patients, especially in those cases in which pancytopenia is very severe. Currently, no guidelines are available regarding platelet count at which aggressive treatment with IVIG should be given to these patients and more research is needed in this regard.

Conclusion

SLE with pancytopenia refractory to the conventional modalities of treatment in our patient responded only to intranvenous immunoglobulins. This reflects that prognosis and clinical outcome in such cases can be improved by early use of IVIG, especially in those cases having severe and refractory pancytopenia. Further studies are required to support this fact as very few such cases have been reported.

What is new?

We present a case of SLE associated pancytopenia that was refractory to conventional modes of immunosupression and responded only to intravenous immunoglobulins.Very few such cases have already been reported with no studies yet done in Pakistan and South Asia.

List of Abbreviations

ANA	Anti-nuclear antigen
ICT MP	Immunochromatographic test for Malarial parasite
IV	Intravenous
IVIG	Intravenous immunoglobulins
NS1	Non structural protein 1
SLE	Systemic lupus erythematosus

Consent for publication

A written informed consent to publish/present this case was obtained from the patient.

Ethical approval

The study/Case report was approved by Instituitional Review borard and ethical committee (IRB) of Shifa International Hospital Islamabad,Pakistan. Approval Reference Number IRB#075-0565-2019, Date of Approval March 27 2019.

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Summary of the case

1	**Patient (gender, age)**	Female,40 years old
2	**Final diagnosis**	SLE
3	**Symptoms**	Fever,Menorrhagia,Bleeding gums,epistaxis,hematochezia
4	**Medications**	Methylprednisolone,Cyclophosphamide,Plasmapharesis, IV Immunoglobulins
5	**Clinical procedure**	IV Methylprednisolone for pancytopenia, plasmapharesis and Cyclophosphamide, followed by IV Immunoglobulins
6	**Specialty**	Internal Medicine,Rheumatology