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Original Research Paper

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THE DOUBLE CONUNDRUM: APLASTIC ANEMIA WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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ABSTRACT Systemic Lupus Erythematosus is commonly associated with cytopenias. We here present a rare cause of pancytopenia in a patient of SLE. A 48 year old female, known case of SLE presented with fever and severe pancytopenia. Patient was initially managed as a SLE flare, with stepping up of immunosuppression, but since pancytopenia did not improve, a bone marrow study was done which was consistent with aplastic anemia. Patient was managed with cyclosporine and danazol, following which her counts improved.

KEYWORDS : Aplastic , SLE , Azathioprine , Cyclosporine

INTRODUCTION

Isolated cytopenia's are common in patients with SLE, mostly autoimmune in etiology (1). But pancytopenias are not common and usually tend to be secondary to macrophage activation syndrome, drug induced, autoimmune or even nutritional rarely. (2). Here we present a case of refractory pancytopenia in a patient with SLE.

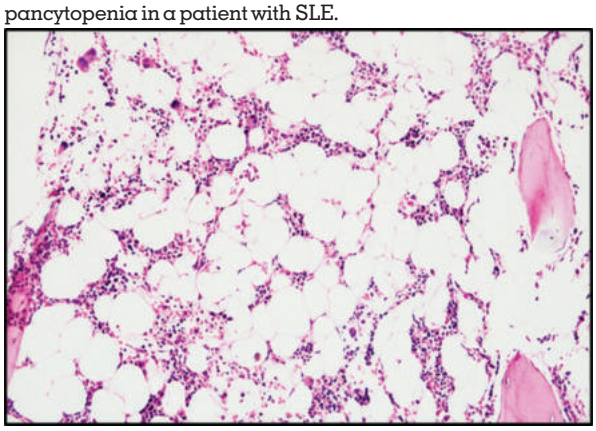

Figure 1: Bone Marrow Trephine Biopsy Showed Hypocellular Marrow For Age With Increase In Stromal Fat Cells. The Hematopoietic Elements Are Significantly Reduced Consistent With Aplastic Anemia.

Case

48 year old female with hypothyroidism and T2DM presented with history of excessive hair fall, photosensitive skin rashes, oral ulcers and arthralgia of 1 year duration. On evaluation she was diagnosed with Systemic Lupus Erythematous (SLE) based on the clinical plus laboratory criteria and SELENA SLEDAI score was 13. She was started on treatment with Prednisone, Hydroxychloroquine, and Azathioprine. After 2 months of regular treatment & follow up, she presented with fever and arthralgia of 1 week duration. No skin rashes, oral ulcers or other constitutional and localising symptoms. On evaluation CBC showed severe pancytopenia with Hb 7.8g/dl, TLC 800 cells/mm^3 (N23 L71 M6) and platelet count 6 x 10^9 cells/L. Tropical fever work up was negative. Blood and urine cultures were sterile. Anti-dsDNA titres were high with hypocomplementemia suggestive of active SLE. Peripheral smear showed normocytic normochromic anemia, leukopenia with lymphocytosis and thrombocytopenia. SELENA SLEDAI was 23 at this admission. Considering a possibility of disease flare patient was started on steroid pulse under antibiotic cover. Patient's fever subsided but the pancytopenia persisted even after steroid pulse. EBV & CMV serology was negative and HLH parameters were also negative. Possibility of Azathioprine induced BM suppression was also considered and bone marrow study was done. Bone marrow aspirate was dilute and biopsy showed hypoplastic marrow (5% cellularity) with significant suppression of all three cell lines and relative increase in lymphocytes. Inspite of stopping Azathioprine for > 4 weeks and using GCSF injections, the pancytopenia persisted. A rare possibility of acquired aplastic anemia was considered and she was started on cyclosporine at 3mg/kg and Danazol. Within few weeks of cyclosporine initiation, patient's pancytopenia improved and recovered in 6 weeks. Last documented cell counts were: Hb 9.2, TC 11000, PLC 1.18L.

DISCUSSION

Patients with SLE, when they present with pancytopenia the most common differential diagnosis are 1) Disease related autoimmune cytopenias 2) hemophagocytic lymphohistiocytosis 3) drug induced and rarely haematological disorders like MDS, acquired aplastic anemia etc. French Lupus registry data published by chalayar et.al in thirty patients who underwent BM biopsy for panyctopenia from 19 centres showed central hematologic manifestations mainly comprised of bone marrow fibrosis (n=17; 57%), pure red cell aplasia (n=8; 27%), myelodysplastic syndrome (n=3; 10%), aplastic anemia and agranulocytosis (n=1; 3% each (3).

Aplastic anemia is a rare manifestation of SLE and often difficult to diagnose due to overlapping features but easier to treat as compared to classical aplastic anemia (4). It is important to differentiate between azathioprine induced BM suppression and other causes in patients with SLE. Usually drug induced BM suppression, recovers in 4-6 weeks following withdrawal of the offending drug. Azathioprine is more commonly linked to leucopenia rather pancytopenia (5). In our patient, azathioprine was stopped 1 weeks before admission when falling platelet counts were discovered and diagnosis of aplastic anemia was made after 4 weeks from stopping azathioprine. TPMT or NUDT mutation analysis were not available in our hospital, hence couldn't be done. Here we had a patient of SLE on immunosuppression who presented with acute onset pancytopenia associated with fever and arthralgias. The available infective work up, HLH parameters were negative and Azathioprine induced pancytopenia was also ruled out as the counts didn't improve post stopping the drug. BM showed a picture of aplastic anemia and the patient responded to cyclosporine and danazol. The treatment

guidelines for aplastic anemia suggest medical management with triple immunosuppression – Cyclosporine, Eltrombopag and Anti-thymocyte globulin (horse) versus Allogeneic Hematopoietic Stem Cell Transplant. The Later is preferred in young patients below 20 years of age. In our patient, she responded to Cyclosporine and Danazol (still commonly used in LMIC countries for aplastic anemia). Our patient did not need the full repertoire of immunosuppression suggesting that the aplastic anemia was more likely to be secondary to SLE, rather than a separate entity. There have been case reports of Allogeneic HSCT used to treat refractory aplastic anemia in a patient with SLE. Our patient needs close follow –up with a repeat Bone Marrow study at 6 months to document bone marrow recovery.

CONCLUSIONS

Bone marrow study are important for evaluation of cytopenias in SLE and aplastic anemia is a rare but treatable complication of the disease.

REFERENCES

1. Teke HÜ, Cansu DÜ, Korkmaz C. Detailed features of hematological involvement and medication-induced cytopenia in systemic lupus erythematosus patients: single center results of 221 patients. Eur J Rheumatol. 2017 Jun; 4(2):87-92. doi: 10.5152/eurjrheum.2017.160086. Epub 2017 Apr 11. PMID: 28638678; PMCID: PMC5473461.
2. Santacruz JC, Mantilla MJ, Rueda I, Pulido S, Rodriguez-Salas G, Londono J. A Practical Perspective of the Hematologic Manifestations of Systemic Lupus Erythematosus. Cureus. 2022 Mar 7; 14(3):e22938. doi: 10.7759/cureus.22938. PMID: 35399432; PMCID: PMC8986464.
3. E Chalayer and others, Bone marrow involvement in systemic lupus erythematosus, QJM: An International Journal of Medicine, Volume 110, Issue 11, November 2017, Pages 701–711, https://doi.org/10.1093/qjmed/hcx102
4. Tagoe C, Shah A, Yee H, Belmont HM. Aplastic anemia in systemic lupus erythematosus: a distinct presentation of acquired aplastic anemia? J Clin Rheumatol. 2001 Dec; 7(6):377-83. doi: 10.1097/00124743-200112000-00006. PMID: 17039179.
5. Connell WR, Kamm MA, Ritchie JK, Lennard-Jones JE. Bone marrow toxicity caused by azathioprine in inflammatory bowel disease: 27 years of experience. Gut. 1993 Aug; 34(8):1081-5. doi: 10.1136/gut.34.8.1081. PMID: 8174958; PMCID: PMC1374358.