

SLE AND MULTIPLE MYELOMA, A RARE AND UNUSUAL ASSOCIATION

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INTRODUCTION

The increased risk of malignancy especially the Lymphoproliferative disorders in patients with SLE has frequently been reported in the literature^{1,2,3,4}, the association between Multiple Myeloma and SLE has rarely been described. We report this unusual case in which the simultaneous diagnosis of Multiple Myeloma and SLE was made. The case is discussed in the light of a review of the literature. The clinical, laboratory and radiographic findings of this and some of the previously similarly diagnosed patients as well as the subsequent therapeutic approach are discussed.

Case Report

A 35 year old lady who had been treated as PUO for over a year previously, came to the Medical OPD of Khyber Teaching Hospital in April 2014, Peshawar complaining of high grade fever, shortness of breath, joint pains, backache, lethargy and undocumented weight loss. On examination this pale and lean looking lady was running a temperature of 39 degree Celsius, having BP of 105/70 mmHg and O₂ Saturation of 95%. Chest auscultation showed scattered crackles bilaterally. Rest of the examination was unremarkable.

Keeping her pale looks in mind, her blood was sent for a Special Smear which showed Pancytopenia [Hb 6.5 gm/dl with MCV 84fl & MCH 29, TLC 2500/cmm, Platelets 89000/cmm]. Her Mean Platelet Volume (MPV) was 15fl (Normal 7-9fl) with an ESR of 115 at one hour and normal Reticulocyte count. Coomb's test and MP turned out to be negative. As part of workup for her Pancytopenia, Bone Marrow examination was done which showed 30% of Plasma Cells. This was soon followed by Plasma Protein Electrophoresis which showed elevated Gamma Globins of 57.5% (Normal range 11.1-18.8%) mainly IgG type while her Urine for Bence Jones Proteins was negative. Her Serum Calcium was normal and the Skeletal Survey didn't show any Lytic lesion.

Keeping her prolonged history of joint pains, young age and raised ESR and MPV in mind, a decision

was taken to exclude immune mediated disorders especially the SLE and hence ANF was ordered which came out to be positive. Her blood was thus sent for Anti ds-DNA antibodies and while awaiting the results her blood and urine cultures were obtained which did not grow any organism. In the meanwhile a Chest X-ray was done which showed bilateral minimal pleural effusion while her other radiological investigations including the Echocardiography and U/S Abdomen & Pelvis came out to be normal and so was her ECG. Her Urine Examination showed Albumin (++) and 20-25 pus cells. This was soon followed by 24 hour urine examination which showed a proteinuria of 1.2gm/day and a Creatinine Clearance of 50 ml/min. Various biochemical investigations including assessment of the Renal and Liver Function, Serum Electrolytes, Blood Sugar, LDH and Lipid Profile were unremarkable. Her PT/APTT and D-dimers were within normal range as well.

While she was still in the hospital, on the 4th day of admission she developed malar rash typical of SLE. The next day her Anti-ds DNA report became available which showed a high antibody titer of >200U/ml (Ref range <25U/ml). Fundoscopy was done which was normal. Her Serum Complement levels were analyzed which showed C3 of 0.20 g/L (Normal > 0.75) and C4 of 0.1g/L (Normal >0.30). Antiphospholipid antibodies were negative. The final diagnosis of SLE & Multiple Myeloma was made and she was put on Steroids to which she responded dramatically. A Renal Biopsy was planned to stage her Lupus Nephritis but the decision was refused by the patient. In our case we decided to target the acute flare of SLE initially so we discharged our patient on Prednisolone 45mg/ day, Hydroxychloroquine 400mg/day and Mycophenolate Mofetil 1gm/day. On discharge She was not given the drug Melphalan fearing the myelosuppressive side effects of Melphalan as her all Blood Cell Lines were already suppressed (TLC 2500/mm³, Platelets 89000/mm³ and Hb 6.5gm/dl) and a decision was taken to introduce this drug later on during the follow up when her blood cell counts would get normal. When She was reviewed in three weeks' time she was stable and in complete remission. On follow up her joints pains had improved and the malar rash had disappeared. Biochemically her ESR had dropped from an initial value of 115 to 80 at one hour and so was the case with the Mean Platelet Volume (MPV) which was 12fl on follow up in comparison to the initial value of 115fl.

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Table 1: Summarized data of five case reports obtained from “Clinical and Experimental Rheumatology 2008: 26”

Author	Diagnostic Pattern	Ig Type	Main Treatment	Outcome
Pehamberger ⁸	Simultaneous	IgG	Cyclophosphamide + CS	Not known
J.J. Canoso ⁴	MM after SLE	Not Known	Melphalan+ CS	Stable
Vaiopoulos ⁷	Simultaneous	IgG	Azothioprine+CS	Stable
F.C. Powell ⁹	MM after SLE	IgA	Not Precise	Death
E. Solary ¹⁰	SLE after MM	IgG	Melphalan+CS+Chloroquine	Death

CS=Corticosteroids, Ig=Immunoglobulin

On follow up her Complete Blood Count showed TLC of 3900/m3, Hb 9gm/dl and Platelets 115000/mm³. Taking her tremendous symptomatic and biochemical improvement in consideration, Melphalan at dose of 8mg/day for four days to be repeated every 7th week was introduced. She would be reviewed in six weeks' time.

DISCUSSION

Although Monoclonal Gammopathy is often detected in SLE patients but the coexistence of multiple myeloma (MM) has rarely been reported. The prevalence of monoclonal gammopathy of undetermined significance (MGUS) in SLE patients varies from 2.2% to 3.3% and the outcome of these patients seems not to differ from the other SLE patients^{5,6}.

Multiple Myeloma may be diagnosed roughly a decade after the diagnosis of SLE is made but it may be diagnosed simultaneously as in our case or even the Multiple Myeloma precedes the diagnosis of SLE. Vaiopoulos and Pehamberger diagnosed SLE and MM simultaneously^{7,8} while Solary and Powel have reported the SLE in previously diagnosed MM patients^{9,10}.

The pathogenesis of the association between these two disorders is mainly speculative. The genetic factors have been claimed to play a role in the pathogenesis¹¹ while some other researchers think that it is the prolonged use of immunosuppressant drugs in previously diagnosed SLE patients¹ which causes Multiple Myeloma to develop. The genes claimed to be responsible include Human Leukocyte Antigen (HLA), activating mutations in Proto-oncogenes including FGFR3, KRAS & NRAS and deletions of Tumor Suppressor Genes like P53. Some authors are of the opinion that it is the Immune System dysregulation involving the defective functioning of the NK and Suppressor T Cells which is responsible for the abnormal clonal proliferation of B lymphocytes which often leads to MGUS or rarely to Multiple Myeloma in SLE patients as in our case¹².

Treating both Multiple Myeloma and SLE in association has been a challenge as no treatment guidelines are available yet due to the rarity of their

coexistence and so was the scenario in our case. From the literature review we came to know that majority of physicians used their own preference of drugs based upon their personal experience in treating such patients although Melphalan plus Prednisolone combination was the most frequently used initial regimen¹³. Thalidomide has been used for both Cutaneous Lupus and Multiple Myeloma with success and may be a good second line drug¹⁴. In our case we decided to target the acute flare of SLE mainly and put our patient on a combination of Steroids, Hydroxychloroquine and Mycophenolate Mofetil initially. We have put our patient on regular follow ups and she was switched to Melphalan on three weeks follow up and would be reviewed again in six weeks' time.

CONCLUSION

Although the association of Multiple Myeloma and SLE is rare, the presence of MGUS in SLE patients is not rare and if present must be investigated for any underlying Multiple Myeloma. In the appropriate clinical context, multiple myeloma should be considered in SLE patients irrespective of young age, race, SLE disease activity, or duration. The association of SLE and MM has rarely been studied so more research needs to be done in this regard so that the definite pathogenetic mechanisms involved can be established and the effective treatment guidelines could be devised. Furthermore SLE is a relatively benign condition with favorable prognosis if treated properly but if its progression to MM takes place, the prognosis usually becomes grave.

REFERENCES

- Bernatsky S, Boivin JF, Joseph L. An International cohort study of cancer in systemic lupus erythematosus. *Arthritis Rheum* 2005; 52: 1481-90.
- Pettersson T, Pukkala E, Teppo L, Friman C. Increased of risk cancer in patients with systemic lupus erythematosus. *Ann Rheum Dis* 1992; 51: 437-39.
- Cibere J, Sibley J, Haga M. Systemic erythematosus and the risk of malignancy. *Lupus* 2001, 10: 394-400.
- Canoso JJ, Cohen AS. Malignancy in a series of 70 patients with systemic lupus erythematosus. *Arthritis*

- Rheum 1974; 17: 383-88.
5. Ali MY, Urowitz MB, Ibanez D, Gladman DD: Monoclonal gammopathy in systemic lupus erythematosus. *Lupus* 2007; 16: 426-29.
 6. Porcel JM, Ordi J, Tolosa C, Selva A, Castro-Salomo A, Vilardell M. Monoclonal gammopathy in systemic lupus erythematosus. *Lupus* 1992; 1: 263-64.
 7. Vaiopoulos G, Konstantopoulos K, Mantzourani M, Kaklamanis P: Multiple myeloma associated with systemic lupus erythematosus. *Leuk Lymphoma* 2003, 44: 893-94.
 8. Pehamberger H, Diem E, Konrad K: Systemic lupus erythematosus with multiple myeloma. *Acta Dermatovener* 1978, 58: 527-30.
 9. Powell FC, Greipp PR, SU WP: Discoid lupus erythematosus and monoclonal gammopathy. *Br J Dermatol* 1983; 109: 355-60.
 10. Solary E, Caillot D, Guy H, Olsson NO, Tanter Y, Chalopin JM: Systemic lupus erythematosus occurring in a patient with multiple myeloma. *Arthritis Rheum* 1986; 29: 933-34.
 11. Landgren O, Linet MS, McMaster ML, Gridley G, Hemminki K, Goldin LR: Familial characteristics of autoimmune and hematologic disorders in 8,406 multiple myeloma patients: A population-based case-control study. *Int J Cancer* 2006; 118: 3095-98.
 12. Renaudineau Y, Pers JO, Bendaoud B, Jamin C, Youniou P. Dysfunctional B cells in systemic lupus erythematosus. *Autoimmun Rev* 2004; 3: 516-23.
 13. M. Maamar, Z. Tazi Mezalek, H. Harmouche, Systemic lupus erythematosus and multiple myeloma: an uncommon association. Two cases and literature review; *Clinical and Experimental Rheumatology* 2008; 26: 667-70.
 14. Coelho A, Souto MI, Cardoso CR et al. Long term thalidomide use in refractory cutaneous lesions of lupus erythematosus: a series of Brazilian patients. *Lupus* 2005; 14: 434-39.

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