Case Report**Multiple Myeloma as a rare cause of membranoproliferative glomerular nephritis****Albert Nimalan¹, Sivansuthan S¹**¹*Teaching Hospital Jaffna***Abstract**

Multiple myeloma (MM) is a relatively uncommon cancer characterized by the neoplastic proliferation of plasma cells producing a monoclonal immunoglobulin(Ig). Renal failure in multiple myeloma is around 48% and it may be the presenting manifestation of MM.[1] Renal involvement is multifactorial including light chain cast nephropathy amyloidosis, monoclonal Ig deposition disease and less frequently cryoglobulinaemic glomerulonephritis and proliferative glomerulonephritis.[2-5] Hence membranoproliferative glomerulonephritis (MPGN) is a rare form in MM. Here we report a case of multiple myeloma with MPGN in a 60-year-old male who succumbed to death while on chemotherapy.

Keywords

Multiple myeloma, membranoproliferative glomerulonephritis

Introduction

Multiple myeloma accounts for 17 % of all haematological malignancies, and its incidence increases with age.[6] One important organ that commonly gets affected is kidney and the three most common forms of monoclonal Ig-mediated kidney diseases are light chain cast nephropathy, monoclonal Ig deposition disease (MIDD), and AL amyloidosis.[2-4] Beyond these three forms, Glomerular nephritis with active urinary

sediment such as membranoproliferative and cryoglobulinaemic glomerular nephritis are also reported in literature (4-5)

MPGN is a pattern of glomerular injury on light microscopy that characteristically shows mesangial hypercellularity and proliferation of endocapillaries. [4]

Primary pathogenesis described was immune complex deposition leading to activation of complement and dysregulated persistent activation of alternative complement pathway.

MPGN has been classified as type I, II and III based on the microscopic appearances. Type I shows discrete immune deposits in mesangium and sub endothelium, Type II shows continuous dense ribbon like deposits along the basement membrane, tubules and Bowman's capsule, Type III shows similar features like type I in addition to that there are sub epithelial deposits. [4,7-8]

Multiple myeloma with renal impairment should be considered as a treatable medical emergency since the recovery of renal function is associated with survival benefit.

Case report

A 60 years old male diagnosed patient with hypertension for 7 years was on losartan presented with insidious onset of generalized body swelling for 2 months associated with frothy urine. He did not have haematuria, pruritus, loss of appetite,

Corresponding Author: Albert Nimalan A, Email: nimalan1989@gmail.com, <https://orcid.org/0000-0002-2668-6966>

Submitted June 2021 Accepted December 2021

This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License, which permits unrestricted use, distribution and reproduction in any medium provided the original author and source are credited

nausea and vomiting. He denied dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea, jaundice, hematemesis, melena and diarrhoea. Rest of the system enquiry did not reveal any significant findings.

Positive examination findings were pallor and severe generalized oedema with ascites.

His baseline investigations revealed a normocytic normochromic anaemia with Hb of 8.2g/dl with rouleaux formation with normal WBC and platelets. Inflammatory markers were elevated (ESR 66 in 1st hour; CRP 51mg/l). Serum Ca^{2+} - 2.31 mmol/L, Mg^{2+} - 0.85mmol/L, PO_4^{3-} - 1.08 mmol/L and serum uric acid – 361 mmol/L

As the patient had high ESR, normocytic normochromic anaemia with rouleaux formation and reversed albumin globulin ratio, it was decided to proceed with Urine Bence Jones Protein which was negative whereas the serum protein electrophoresis revealed a monoclonal peak in gamma region. Skeletal survey did not show any osteolytic lesions

The renal functions (serum creatinine) worsened from a baseline of 101 $\mu\text{mol/L}$ to 1536 $\mu\text{mol/L}$ within 2 weeks. Urine full report and UPCr showed nephrotic range proteinuria with active sediments and ultrasonically found to have normal size kidneys.

Routine serology evaluation including Anti-streptolysin O titre (ASOT), human immunodeficiency virus (HIV), VDRL, antinuclear antibody (ANA), hepatitis B and C screening, ANCA studies and Anti glomerular basement membrane antibodies were all negative. Complement studies revealed C3 level of 57 mg/dL (reference range, 90–180 mg/dL) & C4 of 17 mg/dL (reference range 16–47 mg/dL). Echocardiogram showed no vegetations.

Bone marrow biopsy revealed plasma cell infiltration of 40 % was in favour of multiple myeloma.

Renal biopsy and immunofluorescent studies showed features of MPGN. Congo red stain was negative for amyloidosis. He was given methyl prednisolone pulses followed by oral prednisolone

He was found to have MPGN on the background of MM which is very rarely mentioned in the literature.

He was referred to the oncologist as soon as the diagnosis was confirmed. While on chemotherapy he succumbed due to severe pneumonia complicating sepsis and multi organ involvement

Discussion

The international Myeloma Working group criteria for the diagnosis of MM emphasize the importance of end-organ damage in making the diagnosis thus the diagnosis of MM requires Clonal bone marrow plasma cells $\geq 10\%$ or biopsy proven bony or soft tissue plasmacytoma **plus** one of the following

1. Presence of related organ or tissue impairment (end organ damage is suggested by hypercalcaemia, renal insufficiency, anaemia and bone lesion, changes in these factors must be related to the underlying plasma cell proliferative disorder)
2. Presence of a bio marker associated with near inevitable progression to end-organ damage [9]

In this patient there were clonal plasma cells $> 10\%$ with plus renal insufficiency and anaemia were evident for the diagnosis

Most patients with MPGN and a monoclonal gammopathy have no identifiable disease, called as MPGN associated with monoclonal gammopathy of renal significance (MGRS). [10] In contrast our patient found to have multiple myeloma.

Hypocomplementemia is common in all types of MPGN that is supportive in our patient as well. In complement mediated MPGN, there are usually low serum C_3 and normal C_4 complement levels

due to activation of alternate pathway as in this case.[11]

Treatment of these disorders can lead to improvement in the MPGN unfortunately the outcome was not achieved due to the demise of the patient.

References

1. Kyle RA, Gertz MA, Witzig TE, et al. Review of 1027 patients with newly diagnosed multiple myeloma. *Mayo Clin Proc* 2003; 78:21.
2. Jecko Thachil, Walid Sadik, Howida Shawki, Kottarathil A. Abraham, Membranous glomerulonephritis—an under-reported histological finding in multiple myeloma, *Nephrology Dialysis Transplantation*, Volume 24, Issue 5, May 2009, Pages 1695–1696
3. Yu, X., Hu, N., Wang, S. *et al.* Membranoproliferative glomerulonephritis with deposition of monoclonal IgG evolved from polyclonal IgG: a case report with two consecutive renal biopsies. *BMC Nephrol* **20**, 275 (2019)
4. Sethi S, Zand L, Leung N, et al. Membranoproliferative glomerulonephritis secondary to monoclonal gammopathy. *Clin J Am Soc Nephrol*. 2010;5(5):770-782. doi:10.2215/CJN.06760909
5. Okazaki, Masaki et al. “A case of acute renal failure of multiple myeloma due to monoclonal type I cryoglobulinemia with thrombotic microangiopathy.” *CEN case reports* vol. 4,2 (2015): 174-179. doi:10.1007/s13730-014-0162-x
6. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin* 2020; 70:7.
7. Alchi B, Jayne D. Membranoproliferative glomerulonephritis. *Pediatr Nephrol*. 2010;25(8):1409-1418. doi:10.1007/s00467-009-1322-7
8. Sethi S, Fervenza FC. Membranoproliferative glomerulonephritis--a new look at an old entity. *N Engl J Med* 2012; 366:1119.
9. Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *Lancet Oncol* 2014;15:e538.
10. Bridoux F, Leung N, Hutchison CA, et al. Diagnosis of monoclonal gammopathy of renal significance. *Kidney Int* 2015; 87:698.
11. Nasr SH, Valeri AM, Appel GB, et al. Dense deposit disease: clinicopathologic study of 32 pediatric and adult patients. *Clin J Am Soc Nephrol* 2009; 4:22.