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Management of a newly diagnosed case of myeloma kidney in a recently COVID-19 recovered patient

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ABSTRACT

Multiple myeloma is a malignant monoclonal plasma cell disorder occurring predominantly in the elderly population. Outcomes of coronavirus disease 2019 (COVID-19) are worse in elderly, persons with comorbid conditions such as malignancy and patients who are on immunosuppressive therapy. Here we report a case, in which COVID-19 unravelled the diagnosis of multiple myeloma and myeloma cast nephropathy. Bortezomib-based two drug induction immunosuppression, was given during the peak of second wave of COVID-19, and it resulted in clinical improvement and partial remission of multiple myeloma.

Case Report

Implication for health policy/practice/research/medical education:
Guidelines for induction immunosuppression treatment of hematologic malignancies such as myeloma are not available for a recently recovered patient from COVID-19. Post-COVID status should not discourage clinicians from administering induction immunosuppression for treatment for multiple myeloma.

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Introduction

Multiple myeloma is characterized by malignant proliferation of clonal plasma cells, which secrete monoclonal immunoglobulins detectable in the serum and/or urine. Multiple myeloma leads to organ damage, either from the tumour mass or from its effect on the immune system (1,2).

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has a wide spectrum of clinical presentation ranging from mild, self-limiting respiratory tract illness to severe acute respiratory distress syndrome (ARDS), multiple organ failure, and death. This pandemic has put enormous strain on healthcare delivery system across the world, irrespective of the economic status of the country.

Hematologic malignancies, such as myeloma and immunosuppressive therapy which are used for their treatment could lead to poor outcomes with COVID-19 infection. Clinicians often face therapeutic dilemma in managing such patients regarding the choice and timing of immunosuppressive treatment considering the pandemic situation.

Case Presentation

A 55-year-old female presented with vomiting, loose stools and reduced urine output of two days duration. She was diabetic and was on oral hypoglycemic agents. She was initially treated for COVID-19 infection elsewhere for five days and was subsequently referred to our centre for further management. Physical examination revealed pallor and pedal edema. Relevant baseline investigations were conducted (Table 1). In view of severe renal failure, hemodialysis (HD) was initiated. COVID-19 infection was treated with intravenous steroids and enoxaparin, according to the Institute's protocol.

Ultrasound of abdomen showed normal sized

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Table 1. Baseline investigations

Lab parameter	Value
Complete hemogram	
Hemoglobin	8.1 g/dL
Total count	4370 cells/cu mm
Differential count	78% neutrophils, 18% lymphocytes 1% eosinophils, 3% monocytes
Platelet count	1.52 lakhs/cu mm
Blood biochemistry	
Blood urea	210 mg/dL
Serum creatinine	12 mg/dL
Serum sodium	132 mmol/L
Serum potassium	4.5 mmol/L
Serum chloride	101 mmol/L
Serum bicarbonate	11 mmol/L
Serum calcium	8.2 mg/dL
Liver function tests	
Total bilirubin	0.43 mg/dL
Aspartate transaminase	29 U/L
Alanine transaminase	21 U/L
Serum albumin	3.6 g/dL
Serum globulin	2.2 g/dL
Alkaline phosphatase	85 U/L
Gamma glutamyl transferase	44 U/L
Urinalysis	
Urine routine analysis	3+ protein, no deposit
Spot protein-creatinine ratio	8
Urine Bence-Jones protein	Negative
Investigations done as part of COVID-19 management	
D-dimer	2272 ng/mL
C-reactive protein	48 mg/L
Interleukin-6	196.5 pg/L

kidneys. CT imaging of chest done showed CO-RADS 4 (COVID-19 reporting and data system) changes. There were lytic lesions over right sided seventh rib and eighth thoracic vertebra. Skull radiograph also demonstrated lytic lesions (Figure 1). Serum protein electrophoresis showed hypoalbuminemia and 'M' band and beta 2-microglobulin level was 30500 ng/mL. Serum free light chain assays were conducted. Lambda light chain was 14658 ng/L and kappa light chain was 17.49 ng/L. Bone marrow aspiration showed 11% plasmacytosis.

After clinical improvement, renal biopsy was conducted. Immunofluorescence showed lambda light chains intensely positive on tubular casts (Figure 2). Light microscopy demonstrated normal glomeruli. Periodic Acid-Schiff (PAS) negative casts were seen in some of the tubules. Giant cell reaction was seen surrounding some of the casts. There was tubular epithelial cell injury. Interstitial fibrosis and tubular atrophy (IFTA) were not present. Congo- red stain for amyloid turned negative. The patient had all the features required to fulfil the diagnostic criteria for multiple myeloma and myeloma kidney (1,2).

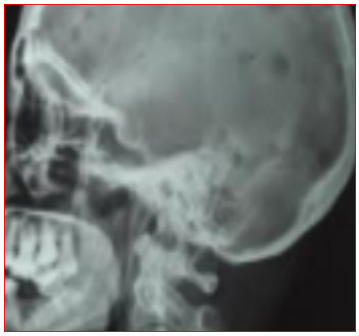

Figure 1. Imaging Studies Showing 'Lytic' Lesions in Skull.

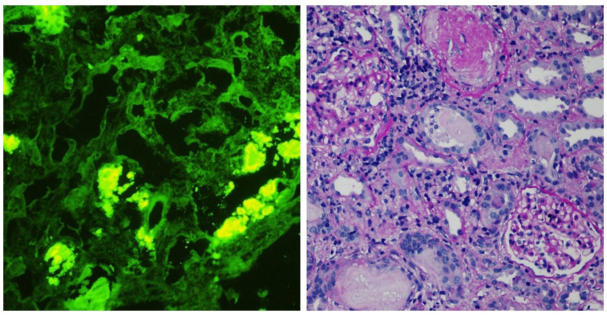

Figure 2. Immunofluorescence showing lambda light chains intensely positive on tubular casts. Light microscopy shoes normal glomeruli. Periodic Acid-Schiff (PAS) negative casts are seen in some of the tubules. Giant cell reaction is seen surrounding some of the casts. There is tubular epithelial cell injury. Interstitial fibrosis and tubular atrophy (IFTA) are not present.

She was managed with intermittent HD and supportive measures. Chemotherapy was not planned immediately because the patient was in convalescent phase of COVID-19. After counselling the patient about the benefits of chemotherapy and the risks associated with it, she was started on bortezomib-based regimen for multiple myeloma. The regimen was planned in consultation with a medical oncologist. Weekly subcutaneous injections of bortezomib along with high dose oral dexamethasone (40 mg) were given. Her general condition improved, and renal failure recovered partially. At the end of four doses of bortezomib, there was partial remission of multiple myeloma. The serum free lambda light chain level was reduced to 360 ng/L. The patient is currently non-oliguric and HD requirement was reduced. She was planned for a permanent vascular access and maintenance immunosuppression with a lenalidomide based regimen.

Discussion

Multiple myeloma is a malignant monoclonal plasma cell disorder and accounts for 10% of all hematologic malignancies (3). The median age at diagnosis is approximately 65 years. Around 20%-30% of myeloma patients present with renal failure. The most common cause of renal failure in myeloma is light chain cast

nephropathy. Other factors such as vomiting, sepsis, hypovolemia and hypercalcemia also contribute to acute kidney injury (AKI). Cast nephropathy occurs when the free light chains in urine bind with the Tamm- Horsfall protein in distal tubule leading to casts and obstruction of tubules. The risk of cast nephropathy is high when the serum free light chain load is high (4).

Treatment of multiple myeloma during this COVID-19 pandemic is challenging (5). The healthcare system is overwhelmed with caring of patients infected with COVID-19. Access to a hospital facility for patients suffering from malignancies has become difficult especially during the intermittent 'lockdown' restrictions, which are announced worldwide as a containment measure to prevent the spread of COVID-19. Patients suffering from hematologic malignancies such as multiple myeloma are immunosuppressed and are prone to infections. Malignancy per se is a risk factor for poor outcomes with COVID-19 and the immunosuppressive regimen for treating the malignancy aggravates that risk manifold.

Several hematologic associations have issued recommendations for management of multiple myeloma patients during this pandemic era (6-8). Notable recommendations include the following; universal use of masks, social distancing measures and personal hygienic practices should be adopted. Patients should be tested for SARS-CoV-2 with polymerase chain reaction (PCR) of nasopharyngeal swab prior to admission and continuous surveillance for the same should be done while the patient is admitted to a facility. Therapeutic immunosuppression regimen should be individualized for a given patient. Treatment initiation should not be postponed for patients with end-organ damage, myeloma emergencies and aggressive relapses. Telemedicine consultation should be encouraged and oral drugs-based regimens should be considered, whenever feasible. Although most of these recommendations are not backed by scientific evidence, these are helpful to clinicians involved in management of such cases. Guidelines are not available yet for management of newly diagnosed cases of myeloma kidney in a COVID-19 recovered patient.

Few reports on outcomes of COVID-19 in multiple myeloma are available in the literature. From a retrospective analysis and outcome data of COVID-19 infection in 650 patients with plasma cell disorders, Chari et al concluded that old age; 'high-risk' disease, kidney involvement and suboptimal disease control were the predictors of adverse outcomes (9). Wang B et al reported similar findings from their study cohort of 58 myeloma patients. Male gender, older age, patients with cardiovascular risk factors, and patients who were not in complete disease remission were significantly associated with hospitalization (10).

In newly diagnosed multiple myeloma cases, treatment with bortezomib and dexamethasone results in response rates of approximately 70%–90%. The advantages of this regimen are higher remission rates, the lack of any adverse effect on stem cell mobilization and the absence of risk of thrombosis (11). Possible adverse events are life-threatening infections and neurotoxicity. Neurotoxicity associated with bortezomib based regimens could be minimized with weekly injections of this drug. Lenalidomide based regimens pose thrombotic risk, necessitating co-administration of anticoagulants. As part of COVID-19 sequelae, she already possessed an additional risk factor for thrombotic tendencies (12).

This was the rationale behind the treating team's decision to go with two-drug regimen, including bortezomib and dexamethasone and avoiding lenalidomide. Otherwise, we would have considered triple drug regimen. Fortunately, this patient did not develop neurotoxicity or other infective complications secondary to bortezomib therapy.

This patient was admitted with COVID-19 infection and AKI. It was initially presumed that the AKI was secondary to COVID-19. Further workup and renal biopsy suggested that the main etiology of AKI was lambda light chain cast nephropathy. To our knowledge, this is probably the first case where bortezomib-based immunosuppressive regimen has been given for induction treatment of newly diagnosed multiple myeloma patients, who just recovered from COVID-19. The patient achieved partial remission. Renal recovery could have been even better had the immunosuppression been started immediately on diagnosis of myeloma, but we wanted the convalescent phase of COVID-19 infection to pass on. Molecular cytogenic classification for 'risk assessment' of multiple myeloma was not conducted in this case.

The treating team faced several logistic difficulties and therapeutic dilemmas in managing this case. The second wave of COVID-19 pandemic in India started in mid-March 2021 and cases rose rapidly in April and May (13). Daily new cases reported crossed over 400 000 in the first week of May. This case was admitted in April 2021, and when the second wave of COVID-19 reached its peak in the month of May, immunosuppressive drugs were to be administered.

Literature on induction treatment for newly diagnosed multiple myeloma is very scarce. To our knowledge, this is the first case where COVID-19 infection unmasked the diagnosis of multiple myeloma, and anti-myeloma therapy was initiated within two weeks of recovery from COVID-19. Our experience highlights the need for routine care for myeloma with treatment regimen that is individualized for a particular patient. The pandemic should not discourage clinicians from timely treatment of hematologic malignancies like myeloma with standard immunosuppressive medication.

Conclusion

COVID-19 pandemic has posed huge challenges in the delivery of hospital care for non-COVID illnesses like hematologic malignancies. Partial remission of multiple

myeloma was achieved with bortezomib based two-drug regimen in this case. COVID-19 pandemic should not discourage clinicians from administering induction immunosuppression drugs for newly diagnosed myeloma kidney.

Authors' contribution

Conceptualization: Muthukaruppaiah Suganya, Varadharajan Jayaprakash, Vasudevan Manimoliyan Duraimavalavan, Mathew Gerry George.
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Supervision: Varadharajan Jayaprakash.
Validation: Varadharajan Jayaprakash.
Visualization: Varadharajan Jayaprakash.
Writing–original draft: Muthukaruppaiah Suganya, Varadharajan Jayaprakash, Vasudevan Manimoliyan Duraimavalavan, Mathew Gerry George.
Writing–review & editing: Raghavan Padmanabhan, Sailapathy Sreedhar.

Conflicts of interest

The authors declare no conflict of interests.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by authors. Informed consent was obtained from the patient for the publication of this report.

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