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Article Title: A Case Series of MGUS and COVID-19

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Letter:

Monoclonal Gammopathy of Undetermined Significance (MGUS) is a pre-malignant clonal plasma cell disorder, with 25 to 30% life-long risk of progression to multiple myeloma (MM). It is usually asymptomatic, but infrequently associated with several serious conditions, such as neuropathies, glomerulonephritis, and
acquired angioedema. Moreover, a higher risk of infection and deep venous thrombosis has been reported in patients with MGUS.

In recent studies of SARS-CoV-2 infection (COVID-19) in cancer, a higher fatality rate was found, especially in hematologic malignancies. While not an overt hematologic malignancy, MGUS falls within the spectrum of plasma cell dyscrasias, and has the potential to disrupt immunity and coagulation. Therefore, MGUS could affect the course and outcome of COVID-19, however such association remains unknown.

We describe 7 patients diagnosed with MGUS who tested positive for COVID-19 from March 18th through April 8th, 2020, at Montefiore Health System, that was the epicenter of the COVID-19 pandemic in the Bronx, NY (Table 1). All cases were positive by real-time reverse-transcriptase polymerase chain reaction of nasopharyngeal swabs.

Case 1: 59-year-old Hispanic man with low-intermediate-risk IgG-kappa MGUS, diabetes mellitus (DM) and hypertension (HTN), presented to the Emergency Department (ED) with three days of dry cough, subjective fever, and myalgias. He was normotensive, afebrile, with room-air oxygen saturation (SpO2) of 98%. He did not require hospital admission, was followed-up one month later and his symptoms had resolved.

Case 2: 66-year-old Caucasian woman with low-risk IgG-lambda MGUS, HTN, and bronchiectasis, presented to the ED with one week of productive cough, subjective fever, wheezing, and diarrhea. She was normotensive, febrile to 102F, with a room-air SpO2 of 98%. Chest X-Ray (CXR) showed chronic changes. She was hospitalized, started on broad-spectrum antibiotics for presumed superimposed pneumonia, and a course of hydroxychloroquine and Lopinavir/Ritonavir per institutional protocol. Her hospitalization was complicated by non-infectious diarrhea, which eventually improved, and was discharged to a rehabilitation facility after a 16-day hospitalization.

Case 3: 83-year-old African American (AA) man with high-intermediate-risk IgA-kappa MGUS, HTN, DM, and chronic kidney disease (CKD), presented with altered mental status (AMS) and lethargy noticed few hours prior; and six days of dry cough and malaise. He was normotensive, afebrile, with room-air SpO2 of 80%, which corrected to 96% on nasal canula (NC) (4L/min). His CXR revealed multifocal bilateral infiltrates. Serum glucose was 884mg/dL. He was started on intravenous fluids and insulin for hyperosmolar hyperglycemic...
state. D-dimers peaked at 20ug/mL. Received broad-spectrum antibiotics for potential bacterial superinfection. His confusion gradually resolved, oxygen requirements improved, and was discharged home on hospital day eight.

Case 4: 71-year-old man with low-intermediate-risk IgM-lambda MGUS, and HTN presented to his general practitioner’s office with dry cough. He was instructed to self-isolate at home, was followed-up one month later and noted his symptoms had resolved.

Case 5: 81-year-old AA woman with low-risk IgG-Lambda MGUS, HTN, DM, CKD, congestive heart failure, and pulmonary sarcoidosis presented to the ED with ten days of dry cough and dyspnea. She was hypotensive (90/53), afebrile, with room-air SpO2 of 89%, that improved to 99% on non-rebreather mask (NRB). CXR showed left lung base atelectasis. Acute kidney injury (AKI) was noted. She was hospitalized, started on intravenous fluids with resolution of hypotension, and treated with hydroxychloroquine per institutional protocol. She was transitioned to NC on hospital day two. Her renal function and oxygenation gradually improved, and she was discharged to a rehabilitation facility after an 11-day hospitalization.

Case 6: 76-year-old Hispanic man with low-intermediate-risk IgA-Lambda MGUS, HTN, DM and CKD, presented to the ED with five days of dry cough, and dyspnea. He was hypertensive (181/78 mmHg), febrile (101F), with room-air SpO2 of 96%. CXR showed bibasilar infiltrates. AKI with hyperkalemia was noted. He was hospitalized and later developed non-ST-elevation myocardial infarction, managed conservatively. His renal function deteriorated and on hospital day 6 hemodialysis was initiated. His renal function gradually improved and was discharged home on hospital day 25.

Case 7: 92-year-old AA man, nursing home resident with low-intermediate-risk IgG-Kappa MGUS, HTN, DM, CKD, epilepsy, and dementia presented to the ED with AMS and lethargy noticed few hours prior to presentation. He had dry cough, dyspnea and malaise for 1 week. He was hypertensive (158/88 mmHg), afebrile, with room-air SpO2 of 96%. On examination he was using accessory respiratory muscles. The patient had do-not-resuscitate and do-not-intubate orders and was therefore placed on a NRB. CXR showed left mid-lower lobe infiltrates. He was admitted, started on broad-spectrum antibiotics and additionally treated for decompensated heart failure. D-dimers peaked at 20ug/mL. Finally, his family opted for comfort care and he expired on hospital day 13.
COVID-19 is a heterogeneous disease that ranges from asymptomatic in some patients to fatal in others. Advanced age, male sex, and comorbidities, such as HTN and DM have been identified as risk factors for adverse prognosis. Significant coagulopathy has been observed in severe cases, and elevated D-dimer levels have been shown to have prognostic significance. In a study performed at our institution, patients with hematologic malignancies and COVID-19 had a higher mortality rate than non-cancer patients.

We wanted to investigate the effects that MGUS might have on patients with COVID-19. Our patients were older adults with an age range between 59 and 92 years. They all had underlying conditions, identified as high-risk comorbidities, yet none of the patients required mechanical ventilation or ICU management, and with the exception of one fatality, they all eventually recovered (table 1). The only fatality was a patient with multiple risk factors, including male sex, advanced age, nursing home residency, multiple comorbidities and a very elevated D-dimer.

MGUS represents the earliest stage of plasma cell dyscrasia and is generally an asymptomatic phase of the disease spectrum. Still, some studies suggest MGUS patients manifest increased susceptibility to bacterial and viral infections, as well as coagulation abnormalities. Whether these perturbations of immunity and coagulation have the potential to impact the clinical trajectory of COVID-19 remains to be examined with large-scale data. This small case series seems to suggest that MGUS may not pose additional risks for poor outcomes in COVID-19 infection.

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Authorship:
Contribution: AV, NK, IM conceived the research, AV, VM, RK, LBR, MG, AS, RAS, KG, IB and SJ identified the cases and clinical information, JGL collected the data, JGL, NK, IM, and AV wrote the manuscript. All authors reviewed and approved the final version of the manuscript.

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Table 1: Baseline characteristics, laboratory findings and clinical course of COVID-19 patients with MGUS

| Patient  |  |  |  |  |  |  |  |
|----------|---|---|---|---|---|---|---|
| Patient  |  |  |  |  |  |  |  |
| Age (yr) | 59 | 66 | 83 | 71 | 81 | 76 | 92 |
| Gender   | Male | Female | Male | Male | Female | Male | Male |
| Race/Ethnicity | Hispanic | White | AA | Other | AA | Hispanic | AA |
| Comorbidities | DM HTN | HTN CLD | DM HTN CKD | HTN | DM HTN CLD CKD CHF | DM HTN CKD | DM HTN CKD Dementia |
| Immunoglobulin Subtype | IgG Kappa | IgG Lambda | IgA Kappa | IgM Lambda | IgG Lambda | IgA Lambda | IgG Kappa |
| MGUS Risk Stratification | Low-intermediate | Low | High-intermediate | Low-intermediate | Low | Low-intermediate | Low-intermediate |
| NH Resident | No | No | No | No | No | No | Yes |

Lab Tests

|  |  |  |  |  |  |  |  |
|---|---|---|---|---|---|---|---|
| Hemoglobin, g/dL |  |  |  |  |  |  |  |
| Prior to adm. | 12.5 | 12.7 | 11.8 | 13.5 | 10.4 | 12.5 | 11.2 |
| Minimum | - | 9.9 | 11.5 | - | 8.2 | 10.7 | 8.1 |
| Platelets, x10^9/L |  |  |  |  |  |  |  |
| Prior to adm. | 389 | 317 | 210 | 116 | 282 | 315 | 191 |
| Minimum | - | 156 | 89 | - | 185 | 301 | 141 |
| ANC (x10^9/L) |  |  |  |  |  |  |  |
| Prior to adm. | 6.4 | 6.4 | 2.9 | 1.2 | 4.3 | 2.2 | 1.1 |
| Minimum | - | 1.2 | 5.3 | - | 2.3 | 2.8 | 0.3 |
| Clinical Course | Hospital admission | ICU admission | Intubation | Dialysis | LOS, days | Outcome |
|-----------------|-------------------|--------------|------------|----------|-----------|---------|
|                 | Yes               | No           | No         | No       | -         | Recovered |
|                 | No                | No           | No         | No       | 16        | Recovered |
|                 | No                | No           | No         | No       | 8         | Recovered |
|                 | Yes               | No           | No         | No       | 11        | Recovered |
|                 | Yes               | No           | No         | No       | 25        | Recovered |
|                 | Yes               | No           | No         | No       | 13        | Deceased |

*AA: African American, ALC: Absolute Lymphocyte Count, ANC: Absolute Neutrophil Count, CHF: Congestive Heart Failure, CKD: Chronic Kidney Disease, CLD: Chronic Lung Disease, DM: Diabetes Mellitus, HTN: Hypertension, LOS: Length of stay, MGUS: Monoclonal Gammopathy of Undetermined Significance

**MGUS Risk Stratification per Mayo Clinic Criteria