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Monoclonal Gammopathies of Clinical Significance (MGCS), an under recognized entity in the Plasma Cell Disorder World and the significance of an MGUS tumor board.

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INTRODUCTION

The main clinical consequence of monoclonal gammopathy of undetermined significance (MGUS) is the progression to malignant disease with resultant tissue destruction primarily due to direct invasion, tumor burden and the destructive properties of the clone. In 1986 Duggan and Schattner¹ described the unusual manifestations of monoclonal gammopathies, not necessarily due to tumor burden or clone size but due to organ damage caused by the immunogenic properties of the M protein. There is increasing recognition of clinical entities in which the monoclonal protein itself and not the clonal mass is implicated as the causative factor, that is monoclonal gammopathies of clinical significance (MGCS). The challenge in the evaluation of MGUS patients is deciding if there is a truly causative relationship between the condition and the monoclonal gammopathy (MGCS) or whether it is merely associative. The major categories of MGCS include renal, dermatologic, neurologic and monoclonal gammopathies of hematological significance.

Need for a comprehensive and coordinated multi-disciplinary approach has been recognized and recommended². At our large academic medical center that consists of a main campus and several regional sites, we receive > 100 consults annually to evaluate cases of monoclonal gammopathy. Due to the volume of requests, rapid access to specialty evaluation and care remains an additional challenge. To manage the volume, and to systematically review new "MGUS" consults so as not to miss MGCS, we established an advanced practice providers (APPs) MGUS clinic where initial consults are seen by our APPs and then based upon established criteria (lab parameters, clinical findings and an organized review of systems), concerning cases will be reviewed at an MGUS Tumor Board. This tumor board is run by three of our main campus myeloma focused hematologists and our myeloma dedicated APRN-PhD. We meet twice a month. This tumor board offers CME credit for both APPs and physicians.

RESULTS

From 2021 to 2023 (2-year period) we reviewed 147 cases and recommended additional work up if necessary. 41 cases (28%) were found to have a clinically significant monoclonal protein necessitating referral to a physician at main campus. The breakdown of these cases is detailed below in Table 1. Sixteen patients (11%) were started on treatment, the other 25 (17%) remained on observation.

Table 1: Breakdown of Cases Presented at "MGUS" Tumor Board

Diagnosis	#Patients (%), total n=147	Location of Patient Care
Low-Risk MGUS ¹	78 (53.0%)	Remained with APP
Paraproteinemia	28 (19.0%)	
High-Risk MGUS ¹	6 (4.1%)	
Low-Risk sMM ²	8 (5.4%)	Referred to physician on main campus
High-Risk sMM ²	3 (2.0%)	
Active Myeloma	5 (3.4%)	
Cryoglobulinemia—monoclonal	2 (1.4%)	
WM/LPL ³	6 (4.1%)	
WM/LPL ³ with anti-MAG Neuropathy	3 (2.0%)	
CLL ⁴	2 (1.4%)	
MGRS ⁵	2 (1.4%)	
TTR amyloidosis	2 (1.4%)	
MDS ⁶	2 (1.4%)	

¹Monoclonal Gammopathy of Undetermined Significance

²Smoldering Multiple Myeloma

³Waldenstroms Macroglobulinemia/Lymphoplasmacytic Lymphoma

⁴Chronic Lymphocytic Leukemia

⁵Monoclonal Gammopathy of Renal Significance

⁶Myelodysplastic Syndrome

CONCLUSION

This data suggests the benefit of some standardization for reviewing and working up "MGUS" referrals. This is especially important at large centers with multiple regional locations. We recommend a tumor board style review as it allows for discussion and education of "MGUS" referrals which often prove to be complex MGCS.

By developing a team of knowledgeable APPs, we have shifted 72% of monoclonal gammopathy referrals to remain under the care of APPs which has improved access to main campus myeloma physician experts for other patients. This allowed the myeloma team at main campus to see more second opinions, open more clinical trials and expand our cell-therapy options for patients. Our referral base has grown, and we have hired more APPs in the region and two additional myeloma physicians at main campus since starting the MGUS tumor board.

REFERENCES

1. David Duggan, Amichai Schattner. American J Medicine 1986 Vol 81 (5): 864-870.
2. Rios-Tamayo et al. Cancers 2022, 14, 5427.

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