soho2023
ELEVENTH ANNUAL MEETING

Characterization of Patients with Coexisting Clonal Myeloid and Plasma Cell Disorders: A Single Center Descriptive Case Series

M. Hochman, MD[1,2], G. Gerber, MD[2], P. Imus, MD[1], S. Ali, MBBS[1], A. DeZern, MD MHS[1].

1. Division of Hematologic Malignancies, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, MD
2. Division of Hematology, Department of Medicine, Johns Hopkins University, Baltimore, MD

JOHNS HOPKINS MEDICINE
THE SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER
1973–2023

BACKGROUND

- Hematologic malignancies often develop from asymptomatic premalignant precursor states:
  - Plasma cell dyscrasias: monoclonal gammopathy of undetermined significance (**MGUS**) ► smoldering multiple myeloma (**SMM**) ► multiple myeloma (**MM**)
  - Clonal myeloid disorders: clonal hematopoiesis of indeterminant potential (**CHIP**) ► clonal cytopenia of undetermined significance (**CCUS**) ► myelodysplastic neoplasms (**MDS**) or acute myeloid leukemia (**AML**)
- Both **c**lonal **p**lasma **c**ell and **m**yeloid **d**isorders (**CPCMD**) have **increased prevalence with age.**
- Co-occurrent CPCMD can **create clinical challenges for therapeutic decisions**
  - When cytopenias (e.g., anemia) develop, the choice of myeloid- or plasma cell- directed therapy is nuanced

AIM

To describe the clinical characteristics, natural history, and treatment outcomes of patients with co-occurrent CPCMD.

METHODS

- **Study design:** retrospective case series of patients with co-existing CPCMD identified by ICD codes or clinical survey
- **Inclusion criteria:** Age ≥18 years-old, seen from 2017-2022 in a single center, myeloid disorders only with <5% blasts
- **Exclusion criteria:** therapy-related myeloid neoplasm after treatment of established MM, cases in which treatment is needed but there is no clinical equipoise between treatment of myeloid and plasma cell disorders
- **Methodology:** Demographic and clinical data abstracted, clinical themes drawn

RESULTS

- A cohort of **18 patients with co-existing CPCMD** was identified (**Figure 1**).
- Seven patients (39%) were female.
- Eight patients (44%) had history of autoimmune disease.
- **Fifteen (83%) had a significant carcinogen exposure history**, most often tobacco (9/15).
- Three patients had therapy-related myeloid neoplasms and two had therapy-related CCUS.
- **Most patients had low-risk classification for both myeloid and plasma cell disorders.** Additional demographic and clinical characteristics are summarized in **Table 1**.
- **Six patients (33%) underwent active surveillance** without clone-directed therapies.
- Four patients (22%) received erythropoiesis-stimulating agents (ESAs) without adverse effects.
- Two patients received lenalidomide, 4 received only anti-plasma cell therapy, 4 received only anti-myeloid therapy, and 3 received therapy targeted against both clones (**Table 2**).

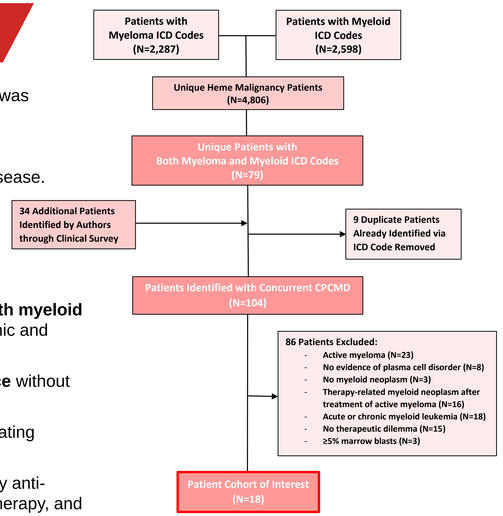


Figure 1. CONSORT diagram demonstrating how the patient population of interest was determined for this case series.

		Plasma Cell Disorder		Myeloid Disorder	
Age at Diagnosis (Years)		65 (33-82)		69 (51-85)	
Disease Type	MGUS	12	CCUS	2	
	SMM	5	MDS	13	
	LCDD	1	MDS/MPN	3	
Risk	**MGUS by IMWG**		**MDS or MDS/MPN by IPSS-M**		
	Low or Low-Intermed	9/13	Very Low	0/14	
	High-Intermed or High	3/13	Low	7/14	
	SMM by IMWG		Moderate Low	3/14	
	Low	3/5	Moderate High	1/14	
	Int	2/5	High	3/14	
	High	0/5	Very High	0/14	

Table 1. Demographic and clinical characteristics of patients with co-occurrent CPCMD. Age presented as "median (range)." LCDD = Light Chain Deposition Disease, MDS/MPN = myelodysplastic/myeloproliferative overlap neoplasms, IMWG = International Myeloma Working Group, Intermed = Intermediate, IPPS-M = Molecular International Prognostic Scoring System. Note LCDD is grouped with MGUS in risk assessment.

Patient #	Sex	Plasma Cell Diagnosis (Age)	Myeloid Diagnosis (Age)	Anti-Plasma Cell Therapy	Anti-Myeloid Therapy	Brief Synopsis	Relevant to Conclusion #
1	♀	MGUS (59)	MDS-5q (59)	Ø	LEN, LUSP	Obtained treatment-free remission after LEN.	2
2	♂	MGUS (56)	MDS (58)	Vd	AZA	AZA and Vd overlapped, then underwent BMT and in remission.	4
3	♂	SMM (57)	MDS (51)	Ø	AZA	Responded to AZA and after underwent BMT.	Ø
4	♀	MGUS (73)	MDS/ MPN (73)	Ø	AZA	Planned to start AZA with bortezomib. After treatment with AZA first, M-spike and light chains decreased; anti-plasma cell therapy deferred.	1, 4
5	♂	MGUS (81)	MDS (85)	Ø	AZA	No response to ESA, but decreased transfusion needs with AZA.	3
6	♂	MGUS (33)	MDS/ MPN (58)	THAL, Rd, Dara-Vd	AZA	Treated with multiple MM therapies before switching to AZA due to marrow more concerning for MDS/MPN with positive response.	1
7	♀	SMM (76)	MDS (76)	Ø	AZA	AZA improved marrow blast % but progressed to AML and died.	Ø
8	♀	SMM (56)	CCUS (61)	CyBorD, LEN, Pd	Ø	History of chronic neutropenia. Started MM therapies since M-spike increased, but neutropenia did not improve until she began G-CSF after an episode of typhlitis.	3
9	♂	SMM (82)	MDS (82)	Dara-Vd, LEN	Ø	Observed until SMM progressed to MM and started on MM therapy.	Ø
10	♂	LCDD (48)	MDS (46)	Vd	Ø	Responded well to ESA initially. Renal biopsy done for AKI showed LCDD, started MM therapy.	2, 3
11	♂	MGUS (78)	MDS (84)	Rd	Ø	Anemia and ? lytic lesion prompted MM therapy, but anemia only improved with ESA.	3
12	♂	MGUS (56)	MDS (56)	LEN	AZA	Started AZA and LEN together but unable to tolerate latter. After AZA underwent BMT.	Ø

Table 2. Table displaying brief summary of 12 patients with concomitant CPCMD who underwent clone-directed treatment. Diagnosis ages shown in years. LEN = lenalidomide, THAL = thalidomide, LUSP = luspatercept, AZA = azacitidine, BMT = bone marrow transplant, ESA = erythropoiesis stimulating agent, AKI = acute kidney injury. MM therapy abbreviations here are standardly used.

CONCLUSIONS

1. **Serial reassessment of disease status** via serologic testing and bone marrow biopsy **is key in making management decisions** for patients with concurrent CPCMD.
2. Prioritize treating the clone **with an actionable genetic lesion or responsible for clone-specific end-organ complications** in patients with concurrent CPCMD.
3. **Growth factors appear safe** for management of cytopenia in patients with concurrent CPCMD.
4. Patients with **concurrent CPCMD can be safely treated for both clonal disorders simultaneously**, but this should be **done in a stepwise approach.**

REFERENCES

1. **Steensma DP, et al.** Clonal hematopoiesis of indeterminate potential and its distinction from myelodysplastic syndromes. *Blood. 2015 Jul 2;126(1):9–16.*
2. **Kyle RA, et al.** Prevalence of monoclonal gammopathy of undetermined significance. *N Engl J Med. 2006 Mar 30;354(13):1362–9.*
3. **Zeidan AM, et al.** Epidemiology of myelodysplastic syndromes: Why characterizing the beast is a prerequisite to taming it. *Blood Reviews. 2019 Mar;34:1–15.*
4. **Yoshida Y, et al.** Co-occurrence of monoclonal gammopathy and myelodysplasia: a retrospective study of fourteen cases. *Int J Hematol. 2014 Jun;99(6):721–5.*
5. **Fermand JP, et al.** Monoclonal gammopathy of clinical significance: a novel concept with therapeutic implications. *Blood. 2018 Oct 4;132(14):1478–85.*
6. **Bohlius J, et al.** Management of cancer-associated anemia with erythropoiesis-stimulating agents: ASCO/ASH clinical practice guideline update. *Blood Advances. 2019 Apr 10;3(8):1197–210.*

ACKNOWLEDGEMENTS & CONTACT INFO

Dr. Hochman's work was funded by Hopkins Hematology T32 Training Grant NHLBI# T32HL007525.

Email: Michael.Jamie.Hochman@emory.edu

X: @mjhochman