Case Report *Open Access*

Journal of Clinical Oncology & Advanced Therapy

DOI: doi.org/10.63721/25JCOAT0115

A Gut Feeling: Mantle Cell Lymphoma Unveiled by Occult Gastrointestinal Bleeding in a 75-Year-Old Woman: A Case Report and Literature Review

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***Citation:** Faizan Sheraz and Mark Hsu (2025) A Gut Feeling: Mantle Cell Lymphoma Unveiled by Occult Gastrointestinal Bleeding in a 75-Year-Old Woman: A Case Report and Literature Review. J of Clin Onco & Adv Thpy 1(4), 01-08. WMJ/JCOAT-115*

Abstract

Background: *Mantle cell lymphoma (MCL) is a rare form of non-Hodgkin lymphoma that frequently involves extranodal sites, particularly the gastrointestinal (GI) tract. While GI involvement is common in MCL, presentation with overt GI bleeding as the primary manifestation is uncommon and poses significant diagnostic challenges.*

Case Presentation: We report a case of a 75-year-old woman with a history of hypothyroidism and hemorrhoids who presented with generalized weakness, dyspnea, and abdominal pain. She denied overt signs of GI bleeding but reported poor appetite and unintentional weight loss over several months. Laboratory studies revealed severe anemia (hemoglobin 5.4 g/dL) and thrombocytopenia. Imaging demonstrated large left pleural effusion, hepatosplenomegaly, splenic lacerations, and lymphadenopathy. Upper endoscopy and colonoscopy revealed multiple gastric ulcers, ulcerated duodenal polypoid lesions, transverse colon polyp, and rectal polypoid lesions. Histopathological examination confirmed mantle cell lymphoma with a characteristic immunohistochemical profile. The patient was initiated on combination therapy with rituximab, bendamustine, and acalabrutinib.

Conclusion: *This case highlights the importance of considering MCL in elderly patients presenting with unexplained anemia and constitutional symptoms, even without overt GI bleeding. Comprehensive endoscopic evaluation with systematic biopsies is crucial for diagnosis, and modern chemoimmunotherapy regimens can improve outcomes in this challenging patient population.*

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Submitted: 18.12.2025 **Accepted:** 29.12.2025 **Published:** 10.01.2026

Keywords: Mantle Cell Lymphoma, Gastrointestinal Bleeding, Hematochezia, Melena, Multiple Lymphomatous Polyposis, Elderly

Introduction

Mantle cell lymphoma (MCL) is an uncommon but typically aggressive B-cell non-Hodgkin lymphoma that accounts for approximately 3-10% of all non-Hodgkin lymphomas [1]. MCL predominantly affects older adults with a median age of approximately 60 years and demonstrates a male predominance [2]. The disease is characterized by the t (11;14) (q13; q32) chromosomal translocation, leading to cyclin D1 overexpression, which serves as a key diagnostic marker [3].

Extranodal involvement is extremely common in MCL, occurring in up to 90% of cases, with the gastrointestinal tract being the most frequent extranodal site [4]. GI involvement is documented in 43.8% of patients in multicenter cohorts, though microscopic involvement may be even more frequent based on autopsy series [5]. The characteristic endoscopic pattern, known as multiple lymphomatous polyposis (MLP), consists of numerous small polyps distributed throughout the GI tract [6].

While GI involvement is common, MCL presenting primarily with gastrointestinal bleeding as the initial manifestation is uncommon and can pose significant diagnostic challenges, particularly in elderly patients with comorbid conditions that may mask or complicate the clinical presentation [7]. This case report describes a 75-year-old woman who presented with occult GI bleeding and constitutional symptoms, ultimately diagnosed with extensive MCL involving multiple sites in the gastrointestinal tract.

Case Presentation

A 75-year-old woman with hypothyroidism presented to the emergency department with a 3-day history of generalized weakness, dyspnea on exertion, and diffuse abdominal pain. She had a recent motor vehicle accident 2 months prior to any significant injuries at the time. Since then, the patient reported having a poor appetite and unintentional weight loss of approximately 15 pounds. The patient denied any overt signs of gastrointestinal bleeding, including hematemesis, melena, or hematochezia. She also denied nausea or vomiting, or constitutional symptoms such as fever, chills, or night sweat.

Laboratory studies on presentation were notable for hemoglobin of 5.4 g/dL and thrombocytopenia with a platelet count of 89,000/µL. White blood cell count was within normal limits at 6,800/µL. Computed tomography (CT) imaging of the chest, abdomen, and pelvis with contrast was notable for left pleural effusion, hepatosplenomegaly, splenic lacerations, and axillary and abdominal lymphadenopathy. Endoscopic evaluation was pursued given severe anemia. Upper endoscopy (Figure 1A) revealed superficial gastric ulcers and ulcerated polypoid lesion in the duodenal bulb. Colonoscopy (Figure 1B) revealed multiple polyps in the transverse colon and rectum, as well as diverticulosis and internal hemorrhoids. Biopsies were obtained from gastric ulcers, duodenal polypoid lesion, transverse colon polyp, and rectal polypoid lesions for histopathological examination. Pathological findings were consistent with mantel cell lymphoma, with an immunohistochemical profile confirming the diagnosis. Patient was positive for CD5, CD20, and cyclin D1 markers, and fluorescence in situ hybridization (FISH) analysis revealed the presence of t (11;14) (q13; q32) translocation, a hallmark genetic abnormality in MCL.

Given the patient's endoscopic findings, the patient proceeded to undergo bone marrow biopsy which was positive for MCL involvement (15% infiltration). Flow cytometry confirmed clonal B-cell population consistent with MCL.

Due to this constellation of findings, the patient was diagnosed with stage IV mantle cell lymphoma. The patient was initiated by chemotherapy.

Discussion

Clinical Significance and Diagnostic Challenges

This case illustrates several important clinical considerations in the diagnosis and management of mantle cell lymphoma presenting with gastrointestinal bleeding. First, it highlights the atypical presentation in elderly patients. Moreover, the absence of overt GI bleeding symptoms in this case demonstrates how MCL can present with occult bleeding leading to severe anemia. The patient's age, comorbidities, and recent trauma history initially diverted attention from

the underlying malignancy. This highlights the importance of maintaining a high index of suspicion for hematologic malignancies in elderly patients with unexplained anemia and constitutional symptoms [8].

The case presented multiple confounding factors including the presence of known hemorrhoids, diverticulosis, and recent trauma created a complex diagnostic picture that could have easily masked the underlying lymphoma. The combination of these benign conditions with the malignant process emphasizes the need for comprehensive evaluation rather than attributing symptoms to known comorbidities [9].

Additionally, this case highlights the importance of systematic endoscopic evaluation as the endoscopic findings of multiple polypoid lesions throughout the GI tract were crucial for diagnosis. The pattern of multiple lymphomatous polyposis (MLP) is characteristic of MCL and should prompt immediate biopsy and histopathological examination [10].

Literature Review and Comparison

MCL is uncommon and defined by distinct epidemiological and clinical features. Typically, it is an aggressive B-cell non-Hodgkin lymphoma that frequently has extranodal involvement and can affect the GI tract, producing symptoms from occult blood loss to massive bleeding and weight loss [1]. In clinical series, endoscopic or radiologic evidence of GI involvement is common (43.8% in one multicenter cohort) though microscopic involvement may be even more frequent in autopsy/series reports [1].

MCL with GI involvement demonstrates several characteristic features based on recent literature. The frequency of GI involvement occurs in 43.8% of MCL patients in multicenter studies, making it the most common extranodal site [5]. The symptoms include common presentations like abdominal pain, diarrhea, obstruction, melena, hematochezia, and weight loss [11]. Past literature shows MCL predominantly affects older adults with male predominance, consistent with our case despite the female patient [2].

The literature describes several characteristic endoscopic patterns in MCL including multiple lymphomatous polyposis (MLP). This is the most characteristic pattern, featuring numerous small polyps distributed throughout the GI tract, particularly in the ileocecal region extending to colon, small bowel, and stomach [6,12]. Other patterns include infiltrative mucosal thickening, ulcerative lesions, fungating masses, and solitary polypoid masses that may mimic adenocarcinoma [13]. Our case demonstrated a mixed pattern with both ulcerative (gastric ulcers) and polypoid lesions (duodenal, colonic, and rectal polyps), which is consistent with the heterogeneous endoscopic appearances described in the literature.

Previous literature shows various diagnostic strategies for MCL. Current literature emphasizes the importance of multiple biopsies sampling suspicious lesions and adjacent normal mucosa due to patchy involvement [14]. Immunohistochemistry is emphasized to look for the characteristic CD5+/CD20+/cyclin D1+ profile with negative CD10 and CD23 [15]. Finally, molecular confirmation utilizing the FISH analysis for t (11;14) translocation is suggested [3].

Regarding staging and prognosis, it should be noted that GI involvement in MCL is associated with advanced staging where most patients present with stage III/IV disease [16]. Additionally, there appears to be poor prognosis due to a higher recurrence rate and frequent GI tract relapses compared to non-GI MCL [5]. Also, based on MIPI scores, age, performance status, LDH, and WBC count, stratify risk and correlate with survival [17].

Treatment Considerations

Modern therapeutic approaches adopt treatment regimens, like those used in this case, and reflect current evidence-based approaches for elderly patients with MCL. These approaches include rituximab-based chemoimmunotherapy, which is a standard of care for MCL with proven efficacy [18]. It also includes bendamustine which is a well-tolerated alkylating agent particularly suitable for elderly patients [19], and bTK inhibitors like acalabrutinib which represents a second-generation BTK inhibitor with improved safety profile compared to ibrutinib [20].

Special considerations should be taken for GI bleeding. The use of BTK inhibitors in patients with gastrointestinal involvement requires careful consideration due to increased bleeding risk as BTK inhibitors impair platelet aggregation as a class effect [21]. Monitoring and close surveillance for bleeding complications are needed, particularly in patients with active

GI lesions [22]. Timing is important as it may require delay in BTK inhibitor initiation until acute bleeding is controlled [23] Considerations for elderly patients must be taken. Prognostic factors mentioned in table 1. Treatment of elderly MCL patients requires individualized approaches like fitness assessments to determine treatment intensity [24]. Comorbidity management for this population is important, and careful attention to cardiovascular and other comorbidities [25] should be kept. Lastly, quality of life should be considered to balance between treatment efficacy and maintaining functional status [26].

Table 1: Prognostic Factors in Mantle Cell Lymphoma (MCL) with GI Involvement

Poor Prognostic Factors	Favorable Factors
Advanced age (>65 years)	Good performance status
High MIPI score	Early treatment response
Blastoid or pleomorphic variant	Absence of CNS involvement
TP53 mutations	Successful achievement of complete remission
High Ki-67 proliferation index	

Future Directions and Novel Therapies

Recent novel therapies and advances in MCL treatment have come to light. These include CAR-T cell therapy which has promising results in relapsed/refractory disease [27]. Novel BTK inhibitors like zanubrutinib and other agents have come out and show improved safety profiles [28]. BCL-2 inhibitors like venetoclax have recently demonstrated activity in combination regimens [29]. Finally, minimal residual disease monitoring is now guiding treatment duration and intensity [30].

Clinical Implications and Recommendations

Based on this case and literature review, several clinical recommendations emerge. One is to maintain a high index of suspicion and to consider MCL in elderly patients with unexplained anemia and constitutional symptoms. Comprehensive endoscopy should be considered for systematic evaluation of entire GI tract with multiple biopsies, and a multidisciplinary approach involving gastroenterology, hematology-oncology, and pathology teams should be strongly considered. Individualized treatment that considers age, comorbidities, and disease characteristics in treatment selection is important. Finally, providers should consider bleeding precautions with careful monitoring when using BTK inhibitors in patients with GI involvement.

Conclusion

This case report demonstrates the diagnostic challenges associated with mantle cell lymphoma presenting as occult gastrointestinal bleeding in an elderly patient. The absence of overt bleeding symptoms, presence of confounding comorbidities, and complex clinical presentation could have easily led to delayed diagnosis. However, systematic evaluation with comprehensive endoscopy and appropriate histopathological examination led to accurate diagnosis and prompt treatment initiation.

Endoscopy plays a pivotal role in the diagnosis of mantle cell lymphoma due to its frequent extranodal involvement of the gastrointestinal tract. Characteristic findings such as multiple lymphomatous polyposis or ulcerated lesions can guide targeted biopsies, enabling early and accurate diagnosis. Given the often subtle or occult presentation, comprehensive endoscopic evaluation is essential in elderly patients with unexplained anemia or constitutional symptoms. The case highlights several important clinical points: (1) MCL should be considered in the differential diagnosis of unexplained anemia and constitutional symptoms in elderly patients, even without overt GI bleeding; (2) comprehensive endoscopic evaluation with systematic biopsies is crucial for diagnosis; (3) modern chemoimmunotherapy regimens including BTK inhibitors can provide meaningful responses, but require careful monitoring for bleeding complications; and (4) individualized treatment approaches considering age, comorbidities, and disease characteristics are essential for optimal outcomes.

As our understanding of MCL biology continues to evolve and novel therapeutic agents become available, early recognition and appropriate treatment of this challenging disease remain crucial for improving patient outcomes. This case contributes to the growing literature on MCL with GI involvement and emphasizes the importance of maintaining clinical vigilance in elderly patients with suggestive presentations.

Mantle Cell Lymphoma: Gastrointestinal Involvement

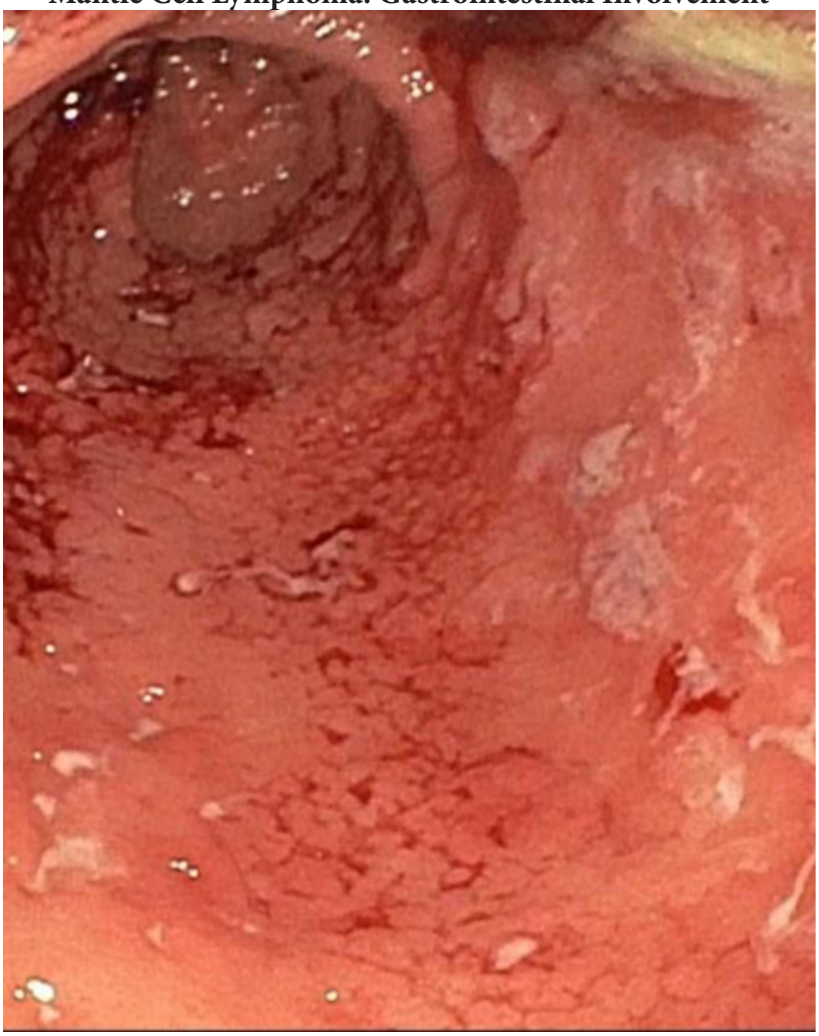

Figure 1A: Upper gastrointestinal tract ulceration from Mantle cell lymphoma.

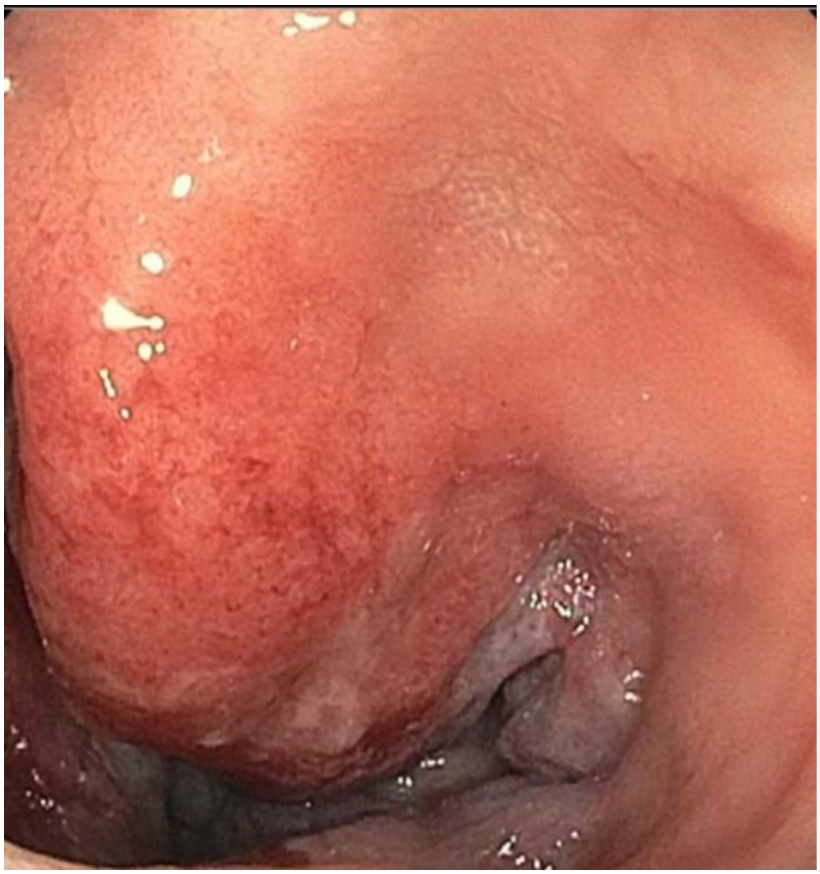

Figure 1B: Rectal polypoid lesion due to Mantle cell lymphoma.

Funding Declaration
This research received no external funding.

Clinical Trial Number
Clinical trial number: Not applicable.
Competing Interest: No competing interests

Revisions
Ethics Approval and Consent to Participate
This case report was reviewed by the Ethics & Compliance Office at HCA Southern Hills Hospital, which determined that formal IRB approval was not required as the report does not constitute research involving human subjects under applicable regulations.

Consent for Publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Name of IRB/Ethics Committee is Ethics & Compliance Office, which is part of the broader HCA Healthcare Ethics & Compliance Program
This case report was reviewed by the Ethics & Compliance Office at HCA Southern Hills Hospital, which determined that formal IRB approval was not required as the report does not constitute research involving human subjects under applicable regulations.

Ethics Approval and Consent to Participate

This case report does not involve research involving human subjects as defined by institutional and federal guidelines. The Ethics & Compliance Office at HCA Southern Hills Hospital, Las Vegas, determined that formal IRB approval was not required. Written informed consent to participate and publish was obtained from the patient.

Data Availability Statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the preparation of this case report.

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