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Secondary Gastric Plasmacytoma Mimicking Aggressive Gastric Lymphoma in Relapsed Multiple Myeloma: A Case Report

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Abstract

Extramedullary plasmacytoma (EMP) secondary to multiple myeloma (MM) is an aggressive rare manifestation of plasma cell dyscrasia. Plasmacytomas of the stomach are generally misdiagnosed as primary gastric adenocarcinoma and/or lymphoma because of overlapping clinical presentation and endoscopic findings. We report the case of a 73-year-old male with a seven-year history of relapsed λ-light chain multiple myeloma who presented with severe pancytopenia, general weakness, and upper gastrointestinal bleeding (melena). Esophagogastroduodenoscopy (EGD) revealed an ugly-looking, ulcerated, fungating mass with heaped-up edges along the greater curvature of the stomach that bleeds upon contact. The endoscopy report was suggestive of aggressive gastric lymphoma. However, immunohistochemical analysis revealed dense sheets of atypical plasma cells strongly positive for CD138, leukocyte common antigen (LCA), and λ -light chain restriction, with a high Ki-67 proliferation index of 80%, establishing a diagnosis of secondary gastric plasmacytoma. Despite plans for urgent palliative radiotherapy, the patient suffered sudden cardiopulmonary arrest secondary to fulminant gastrointestinal bleeding and passed away. Our case emphasizes the importance of timely immunohistochemical profiling rather than macroscopic endoscopic impressions and demonstrates the rapid course of extramedullary transformation.

Categories: Pathology, Oncology, Gastroenterology
Keywords: case report, extramedullary plasmacytoma (emp), gastrointestinal endoscopy, relapsing multiple myeloma, syndecan-1 (cd138)

Introduction

Multiple myeloma (MM) is a clonal plasma cell malignancy characterized by the neoplastic proliferation of plasma cells within the bone marrow, leading to bone marrow failure, osteolytic skeletal destruction, renal impairment, hypercalcemia, and monoclonal gammopathy [1]. Although most plasma cell neoplasms are systemic, they can also present as localized masses, such as solitary plasmacytoma of bone or primary extraosseous/extramedullary plasmacytoma [2].

Epidemiological evaluations highlight that systemic multiple myeloma represents approximately 1% of all human cancers, with an incidence in the United States of 5.35 per 100,000 person-years [3]. In contrast, solitary plasmacytoma of bone and solitary extramedullary plasmacytoma are exceptionally rare, with incidence rates of 0.15 and 0.10 per 100,000 person-years, respectively [3]. Solitary extramedullary plasmacytoma accounts for only 3% to 5% of all plasma cell neoplasms, with an overwhelming predilection (approximately 80% to 90% of cases) for the submucosa of the upper aerodigestive tract, particularly the nasal cavity, paranasal sinuses, and nasopharynx [4]. Primary gastrointestinal tract involvement is extremely uncommon, representing less than 5% of all extramedullary plasmacytoma cases, with the stomach being the second most frequent site within the abdominal cavity after the small intestine [5].

Crucially, a clinical and biological distinction must be made between primary solitary extramedullary plasmacytomas and secondary EMD occurring in the context of relapsed multiple myeloma. Secondary EMD represents a highly aggressive, dedifferentiated phase of multiple myeloma characterized by the hematogenous dissemination of clonal plasma cells to soft tissues, enabling them to proliferate independently of the bone marrow microenvironment [6]. While primary EMD can be present at initial diagnosis, secondary EMD typically emerges later in the disease course, occurring in up to 20% of patients during disease relapse [7]. Recent literature highlights that the incidence of secondary EMD is rising, paradoxically driven by the prolonged overall survival afforded by novel therapeutics (such as proteasome inhibitors and immunomodulatory drugs), which allows time for clonal evolution and the selection of treatment-resistant, high-risk cytogenetic subclones [6]. Pathophysiologically, this disseminated recurrence is associated with altered expression of adhesion molecules, such as the downregulation of CD56 and CXCR4, facilitating the escape of plasma cells from the marrow [8].

We present a rare, highly aggressive, and fatal case of a 73-year-old male with a seven-year history of

relapsed λ-restricted MM, highlighting the importance of rapid tissue diagnosis in patients with a history of plasma cell dyscrasias who present with gastrointestinal bleeding.

Case Presentation

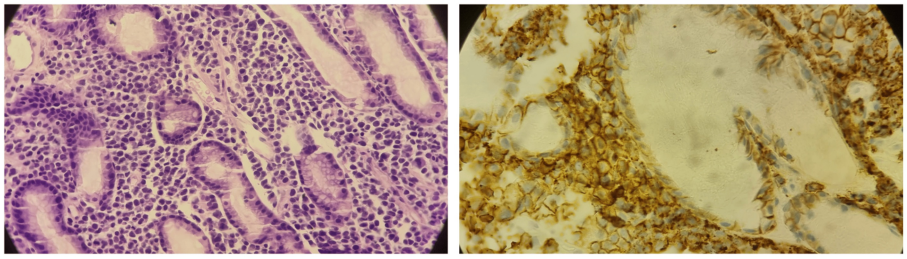
We present the case of a 73-year-old male patient with a medical history of type 2 diabetes mellitus (T2DM), hypertension, and ischemic heart disease (IHD). He has a history of multiple myeloma diagnosed seven years ago, and since then he has been monitored closely by our hematology-oncology clinic.

An initial diagnosis of multiple myeloma was made by a bone marrow aspirate (BMA) and core biopsy, which demonstrated a hypercellular marrow with 40% to 65% atypical plasma cells exhibiting light-chain restriction via CD138 immunohistochemistry. An 18F-FDG-PET/CT scan revealed extensive hypermetabolic lytic malignant bone lesions and a mostly benign right adrenal lesion. A serum protein electrophoresis (SPEP) confirmed a distinct biconal M-band. The patient was initially managed with zoledronic acid, external beam radiotherapy (EBRT) to multiple painful skeletal sites, and a melphalan-prednisone (MP) regimen, later switched to a thalidomide-dexamethasone (TD) protocol, and was placed on observation after achieving remission.

This initial remission was maintained for over a year when the patient experienced a relapse presenting with severe axial back pain, multiple pathological vertebral fractures (C7, T12), and progressive, hypermetabolic skeletal lesions on 18F-FDG-PET/CT scan. Second-line salvage therapy with the VCD protocol (bortezomib, cyclophosphamide, dexamethasone) successfully induced a second clinical remission a year later and showed a complete resolution of the serum monoclonal bands, with a bone marrow biopsy showing only 1% to 2% plasma cell infiltration.

Six years after his initial diagnosis with MM, the patient presented to the emergency department (ED) complaining of general weakness and dizziness lasting three days, and an episode of upper gastrointestinal bleeding with dark, tarry stools. Physical examination revealed a soft, non-tender abdomen with no palpable masses or active signs of macroscopic bleeding. Digital rectal exam was positive for melena. He had pancytopenia with a hemoglobin level of 5.6 g/dl. A bone marrow biopsy showed a normocellular marrow with megaloblastic erythroid hyperplasia and only 1% to 2% plasma cells via CD138 staining.

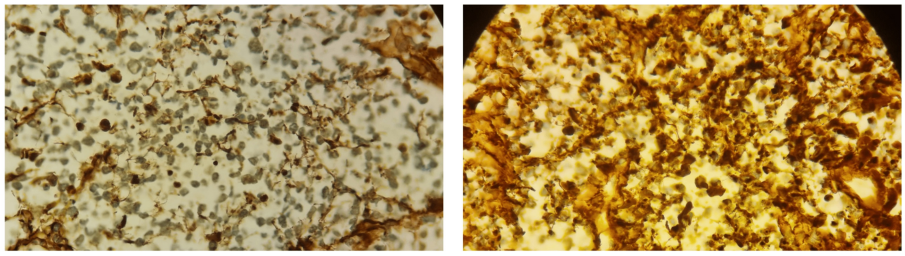
An urgent esophagogastroduodenoscopy (EGD) was performed, revealing a large gastric mass that was macroscopically "ugly-looking", ulcerated, fungating, mass-like lesion with prominent, heaped-up edges along the gastric mucosa that bled upon contact. The endoscopy report was suggestive of aggressive gastric lymphoma. Thereafter, a biopsy was performed and sent for immunohistochemical profiling. Plasma cells exhibited classic malignant plasmacytoid features, including eccentric, hyperchromatic nuclei, conspicuous nucleoli, and abundant basophilic cytoplasm, punctuated by brisk apoptotic bodies and prominent geographical zones of tumor necrosis (Figure *1*). Immunohistochemical profiling revealed diffuse immunoreactivity for CD138 and leukocyte common antigen (LCA), and monoclonal λ-light chain restriction (with a negative κ-light chain) and focal CD79a positivity (Figure *2*). The cells were negative for CD56, CD3, CD20, cytokeratins (CK), and CD10, excluding epithelial carcinomas and alternative lymphoma subtypes. The Ki-67 proliferation index was elevated at 80%, indicating an aggressive, proliferative plasmablastic phenotype. Based on these histopathological and molecular findings, the definitive diagnosis was revised from gastric lymphoma to secondary gastric plasmacytoma (plasma cell neoplasm with light-chain restriction). An 18F-FDG-PET/CT scan showed widespread progression of extramedullary disease. Findings included an intensely hypermetabolic mass along the gastric greater curvature (SUVmax = 15.58) with gastrohepatic lymphadenopathy and carcinomatosis-like omental-peritoneal seeding (SUVmax = 16.4). Additionally, extensive hypermetabolic involvement was noted in the mediastinum (SUVmax = 15.6), pericardium, left maxillary sinus (SUVmax = 24.2), subcutaneous tissues, skeletal muscles (predominantly the right lower limb), and across the axial and peripheral skeletons, with a focal spinal cord lesion at T12.



(a) (b)

FIGURE 1: Immunohistochemical profiling

(a) Gastric mucosa revealing sheets of poorly differentiated, discohesive neoplastic plasma cells characterized by eccentric nuclei, conspicuous nucleoli, and abundant cytoplasm; (b) Immunohistochemical staining showing membranous positivity for CD138 (40x)



(a) (b)

FIGURE 2: Immunohistochemical staining

(a) Kappa-light chain (20x) showing a completely negative result; (b) cytoplasmic positivity for lambda-light chain (40x)

Following a recurrent episode of melena, the patient was stabilized with blood products and urgently referred to radiation oncology for emergency palliative gastric radiotherapy to control the hemorrhage. However, before treatment initiation, the patient suffered a massive upper gastrointestinal hemorrhage leading to immediate hemodynamic collapse, and the patient could not be resuscitated and was pronounced dead.

Discussion

The pathogenesis of secondary extramedullary disease in multiple myeloma involves a complex biological transformation whereby malignant plasma cell clones acquire "bone marrow escape" characteristics, enabling them to survive and proliferate independently of the protective medullary microenvironment [9]. In the present patient, the atypical plasma cells obtained from the gastric mass demonstrated a complete loss of CD56 expression, which is highly consistent with the established literature linking CD56-negativity to aggressive extramedullary dissemination, plasmablastic morphology, and secondary plasma cell leukemia [10]. Notably, in our case, there was a clinical discordance between the medullary compartment and the extramedullary space. While the concurrent bone marrow biopsy demonstrated medullary control, with only 1% to 2% plasma cell infiltration, the patient experienced multi-organ extramedullary escape across the stomach, omentum, peritoneum, maxillary sinus, skeletal muscles, and subcutaneous tissues [11]. Prolonged multi-regimen therapy suppressed medullary-dependent clones in the bone marrow, while promoting the expansion and distal vascular colonization of microenvironment-independent subclones [12].

Endoscopically, secondary gastric plasmacytomas lack pathognomonic macroscopic features. They typically appear as subepithelial nodules, large, ulcerated plaques, or, as observed in our case, "highly invasive, ugly-looking, ulcerated, and fungating masses with prominent, heaped-up edges that easily bleed upon contact" [13]. This leads to formulating an initial diagnosis of primary gastric cancer or lymphoma, delaying the recognition of the underlying plasma cell pathology. Histopathological morphology closely overlaps with large-cell lymphomas or signet-ring cell colorectal and gastric adenocarcinomas, making definitive diagnosis dependent entirely on immunohistochemical staining. Neoplastic plasma cells typically express intense membranous CD138 (syndecan-1) and demonstrate monoclonal light-chain restriction (λ or κ) [14]. However, clinicians must exclude rare variants that exhibit a loss of CD138 expression, which can easily be misdiagnosed as MALT lymphoma, necessitating the use of alternative plasma cell-directed markers such as

MUM1 and CD79a [14].

The clinical management of secondary gastrointestinal extramedullary disease remains challenging, and the prognosis is unfavorable, with historical median survival rates ranging between two and five months from the time of gastrointestinal diagnosis [15]. Treatment strategies are largely palliative and require a rapid, multidisciplinary approach. While primary, localized gastrointestinal plasmacytomas are highly radiosensitive and can be managed effectively with localized external beam radiotherapy or surgical resection, secondary extramedullary disease in the relapsed setting is often refractory to standard therapies [15].

Conclusions

This case highlights a rare and lethal presentation of secondary gastric plasmacytoma arising as an extramedullary lesion in a patient with long-standing multiple myeloma. Emphasizing that relying solely on macroscopic findings can lead to initial misdiagnosis, and that a large, ulcerated, fungating gastric mass in an MM patient should immediately raise suspicion for an extramedullary plasma cell neoplasm, regardless of how clear the bone marrow appears or how strongly the gross endoscopic findings point toward a primary gastric lymphoma. Early tissue biopsy and definitive immunohistochemical staining for CD138 and light-chain restriction are essential to avoid diagnostic delays and initiate urgent local therapies like palliative radiotherapy before hemorrhagic complications occur.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Yara Alswaiti

Acquisition, analysis, or interpretation of data: Yara Alswaiti, Muna Al-Khawaldeh

Drafting of the manuscript: Yara Alswaiti

Critical review of the manuscript for important intellectual content: Muna Al-Khawaldeh

Supervision: Muna Al-Khawaldeh

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. The Hashemite University Institutional Review Board issued approval N/A. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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