A Case of Concurrent Gastric and Pancreatic Plasmacytomas in a Patient With Multiple Myeloma: An Extremely Rare Entity

Tagore Sunkara, MD, Santosh R. Sharma, MD, Andrew Ofosu, MD, Vinaya Gaduputi, MD, Madhavi Reddy, MD, and Ghulamullah Shahzad, MD

Abstract
Multiple myeloma (MM), a plasma cell tumor, is primarily a disease of the bone marrow. Extramedullary plasmacytoma, also a plasma cell tumor, is very rare in the gastrointestinal tract and the pancreas, and only a handful cases have been documented till now. Gastric and pancreatic plasmacytomas are usually seen in elderly patients; however, cases in patients as young as 32 years of age have been reported. Commonly, patients with gastric plasmacytoma present with nonspecific symptoms like epigastric pain, abdominal fullness, anorexia, and weight loss, or serious conditions like massive upper gastrointestinal bleeding and gastric outlet obstruction. Patients with pancreatic plasmacytoma commonly present with obstructive jaundice. In this article, we present the case of a 79-year-old man with a history of MM for 3 years, diagnosed with gastric and pancreatic masses, which turned out to be plasmacytomas. To our knowledge, simultaneous occurrence of gastric and pancreatic plasmacytomas is extremely uncommon with less than 5 cases reported in the literature. We also compiled all the individual cases of gastric and pancreatic MM that have been reported in literature till now.

Keywords
multiple myeloma, extramedullary multiple myeloma, gastric plasmacytoma, pancreatic plasmacytoma

Introduction
Multiple myeloma (MM) is primarily the disease of the bone marrow characterized by abnormal proliferation of plasma cells. It is referred to as plasmacytoma when the lesions are sporadic and do not meet the systemic criteria for MM. Most commonly, plasmacytomas arises in the bone; however, it can be seen anywhere in the body. Extramedullary involvement of MM is very rare and most commonly seen in the respiratory tract, and less than 5% of the cases are seen in the gastrointestinal (GI) tract. We present the case of a 79-year-old man who after being treated for MM was found to have a gastric mass and a pancreatic mass, which were diagnosed as plasmacytomas.

Case Report
A 79-year-old man with medical history of hypertension, diabetes mellitus type 2, and MM (phenotype IgA), which was treated with 4 cycles of lenalidomide plus dexamethasone 3 years prior to this presentation and in remission since then, was referred to the gastroenterology clinic for persistent epigastric pain and nausea. Physical examination was significant for liver tenderness on palpation, but otherwise unremarkable. His laboratory test values including liver function tests were within normal limits. The patient underwent esophagogastroduodenoscopy, which revealed a large polypoid mass with central ulceration in the gastric cardia (Figure 1). Subsequently, an endoscopic ultrasound (EUS)
was performed to further evaluate the mass. On EUS, the gastric mass was seen arising from the submucosal gastric layer, measured 29.9 × 19.7 mm in diameter (Figure 2A). In addition, the EUS also revealed an irregular, well-defined, and heterogeneous solid mass with cystic components in the body of the pancreas (Figure 2B). It measured 33.2 × 39.8 mm on its long axis and 39.2 × 33.2 mm on its short axis. The mass was invading the splenic vein abutting the portal vein. There was no invasion of major vessels like hepatic artery, celiac artery, superior mesenteric artery, and superior mesenteric vein. The liver and the kidneys appeared normal. Multiple fine needle aspiration biopsies were taken from both the gastric and pancreatic masses using a 22G cook needle. The gastric biopsy was reported as showing the presence of abundant atypical cells, which had eccentrically placed large nuclei with occasional multinucleation and with few mitotic figures (Figure 3A and B). Immunohistochemically, the cells showed clusters of Kappa-restricted monoclonal plasma cells, positive for CD138 (Figure 4A) and κ (Figure 4B), which was consistent with plasma cell neoplasm. It was negative for Lambda, CK7, CK20, CDX2, synaptophysin, chromogranin, TTF1, CD68, melan-A, S-100, and CD45. Similarly, the biopsy from the pancreatic mass showed atypical cells suggestive for plasma cell neoplasm. The patient was diagnosed with gastric and pancreatic plasmacytomas and was referred to hematology-oncology for possible treatment options. Serum immunofixation was done, and it revealed 2 monoclonal bands present in the gamma region, both demonstrating IgA/Kappa identity. Protein electrophoresis revealed albumin (%) of 35.9%, which is low; gamma globulin (%) of 39.9%, which is elevated, and M-protein (%) of 35.6%, which is elevated. The total M-protein level on protein electrophoresis was 3.3 g/dL, which is elevated. A skeletal survey was performed to assess other sites for the disease. Skeletal survey showed a solitary radiolucent lesion in the left parietal lobe. Patient is started on 4 mg intravenous zoledronic acid once a month. The patient is currently on pomalidomide 2 mg for 21 days/month and 7 days break/month. The patient is clinically improving with guarded prognosis.

Discussion

Multiple myeloma is a malignancy of the hematopoietic system characterized by an abnormal proliferation of plasma cells with overproduction of immunoglobulins in the bone marrow.1 Extraskeletal MM in the GI tract is rare,4 and the most common site is the small bowel followed by the stomach, colon, and esophagus. Involvement of the pancreas is even rarer, and only a few cases have been reported. Less than 5 cases of concurrent gastric and pancreatic involvement by MM have been reported in the literature. We compiled all the cases of gastric plasmacytoma (Table 1) and pancreatic plasmacytoma (Table 2) that have been reported in the literature.

From Tables 1 and 2, we can see that most of the patients are more than 60 years old; however, cases as young as 37 years of age for gastric MM and 32 years of age for pancreatic plasmacytoma have also been reported. Most of the patients with gastric plasmacytoma presented with expected symptoms of epigastric pain, anorexia, fullness of the abdomen, and weight loss like our case. Nonetheless, patients also presented with serious complications like massive upper GI bleeding and gastric outlet obstruction.4,5,9,13 There was a case where gastric plasmacytoma was diagnosed on a patient who presented with anemia and vitamin B12 deficiency.14 In contrast, there was relative uniformity in presentation in patients with pancreatic involvement. Most patients presented with features of obstructive jaundice, and one case was diagnosed during autopsy.4,18-30

Involvement of both the stomach and pancreas is very rare. When both organs had been involved, patients had features of both abdominal pain and jaundice. Few patients where both pancreas and stomach were involved had distant metastasis to other organs, and patients have limited survival. In contrast, our patient had only the involvement of the stomach and the pancreas without evidence of metastasis to other organs, and his symptoms were only abdominal pain without jaundice.

Almost half of the patients were diagnosed with MM after gastric plasmacytoma was diagnosed, while the remainder had been diagnosed with MM earlier ranging from a few months to up to 3 years. In case of pancreatic plasmacytoma, only 3 cases were newly diagnosed, and they had longer years of survival with MM before diagnosis of pancreatic plasmacytoma up to 13 years. Our patient was diagnosed with MM 3 years prior to diagnosis of gastric and pancreatic plasmacytoma.

Most of the cases of gastric and pancreatic plasmacytomas have been described as primary extramedullary plasmacytomas without the presence of systemic disease. However,
Figure 2. (A) Endoscopic ultrasound (EUS) showing the gastric mass arising from the submucosal gastric layer, measured 29.9 × 19.7 mm in diameter. (B) EUS showing an irregular, well-defined, and heterogeneous solid mass with cystic components in the body of the pancreas measured 33.2 × 39.8 mm in diameter.

Figure 3. Hematoxylin and eosin staining. (A and B) Histology of the gastric biopsy showing the presence of abundant atypical cells, which had eccentrically placed large nuclei with occasional multinucleation and with few mitotic figures (magnification, ×40 and ×100, respectively).

Figure 4. (A) On immunohistochemistry (IHC), the cells showing clusters of monoclonal plasma cells, stain positive for CD138 (magnification, ×100). (B) On IHC, the cells showing clusters of monoclonal plasma cells, stain positive for Kappa, which was consistent with plasma cell neoplasm (magnification, ×100).
### Table 1. Reported Gastric Multiple Myeloma Cases in the Literature.

| Study                | Age/Sex   | Number of Cases | Concomitant Involvement of Pancreas | Clinical Manifestation                                                                 |
|----------------------|-----------|-----------------|-------------------------------------|---------------------------------------------------------------------------------------|
| Talamo et al⁴        | Not documented | 4              | Yes/2 cases                        | 1 case of nausea/vomiting with obstructive jaundice                                   |
|                      |           |                 |                                     | 1 case of upper Gl bleeding                                                             |
|                      |           |                 |                                     | 1 case of gastric outlet obstruction/ascites/MM cells found in ascetic fluid            |
|                      |           |                 |                                     | 1 case of an incidental finding                                                        |
| Griffiths et al⁵      | 68/Male   | 1               | No                                  | Recurrent bouts of hematemesis and melena                                              |
| Goeggel-Lamping and Kahn⁶ | 71/Female | 1               | Yes                                 | Diffuse abdominal pain, nausea, vomiting, intermittent diarrhea, and constipation      |
| Sakai et al⁷          | 37/Male   | 1               | No                                  | No preceding history of multiple myeloma                                               |
| Kusano⁸               | 64/Male   | 1               | No                                  | Has history of gastric cancer and multiple myeloma                                      |
| Yasar et al⁹          | 69/Male   | 1               | No                                  | Massive upper Gl bleeding                                                              |
| Sousos¹⁰              | 64/Male   | 1               | No                                  | Epigastric pain                                                                      |
| Katzenberger¹¹        | 79/?      | 1               | No                                  | Intractable vomiting                                                                  |
| Elbaum et al¹²        | 68/Female | 1               | No                                  | Crampy abdominal pain, fatigue, weight loss                                           |
| Wang et al¹³          | 52/Female | 1               | No                                  | Upper Gl bleeding                                                                     |
| Doberauer et al¹⁴     | 72/Male   | 1               | No                                  | Anemia and B₁₂ deficiency                                                             |
| Kwak et al¹⁵          | 61/Male   | 1               | No                                  | Epigastric pain and weight loss                                                        |
| Birjawi et al¹⁶       | 50/Male   | 1               | Yes                                 | Unknown                                                                               |
| Lu et al¹⁷            | 52/Female | 1               | No                                  | Epigastric pain, anorexia, and fullness of abdomen                                      |
| Kazama et al¹⁸        | 49/Female | 1               | Yes                                 | Painless jaundice, pruritus, and hematuria                                             |

Abbreviations: GI, gastrointestinal; MM, multiple myeloma.

### Table 2. Reported Pancreatic Multiple Myeloma Cases in the Literature.

| Study                | Age/Sex   | Number of Cases | Concomitant Involvement of Stomach | Clinical Presentation                                                                 |
|----------------------|-----------|-----------------|-------------------------------------|---------------------------------------------------------------------------------------|
| Talamo et al⁴        | Not documented | 5              | Yes/2 cases                        | 2 cases of jaundice due to obstruction of CBD                                         |
|                      |           |                 |                                     | 1 case of abdominal pain; nausea and vomiting                                         |
|                      |           |                 |                                     | 1 case of incidental finding in autopsy                                               |
| Goeggel-Lamping and Kahn⁶ | 69/Female | 1               | Yes                                 | Diffuse abdominal pain, nausea, vomiting, intermittent diarrhea, and constipation      |
| Sciancalepore et al¹⁹ | 62/Male   | 1               | No                                  | Obstructive jaundice                                                                 |
| Utsumi et al²⁰       | 83/Male   | 1               | No                                  | Obstructive jaundice                                                                 |
| Smith et al²¹        | 66/Male   | 1               | No                                  | Elevated transaminases and obstructive jaundice                                       |
| Leake et al²²        | 46/Male   | 1               | No                                  | Obstructive jaundice                                                                 |
| Annibali et al²³     | 45/Female | 1               | No                                  | Obstructive jaundice                                                                 |
| Birjawi et al¹⁶      | 64/Male   | 3               | Yes/1 case                          | Unknown                                                                               |
| Kazama et al¹⁸       | 49/Female | 1               | Yes                                 | Painless jaundice, pruritus, and hematuria                                             |
| Balliu et al²⁴       | 32/Female | 1               | No                                  | Jaundice                                                                              |
| Fischer et al²⁵      | 58/Male   | 1               | No                                  | Obstructive jaundice                                                                 |
| Senzaki et al²⁶      | 41/Male   | 1               | No                                  | Was diagnosed by autopsy                                                               |
| Mitchell and Hill²⁷  | Unknown   | 1               | Unknown                             | Jaundice                                                                              |
| Bell et al²⁸         | 88/Male   | 1               | No                                  | Obstructive jaundice                                                                 |
| Matsubayashi et al²⁹ | 51/Male   | 1               | No                                  | Obstructive jaundice                                                                 |
| Simon et al³⁰        | 77/Female | 1               | No                                  | Obstructive jaundice                                                                 |

Abbreviation: CBD, common bile duct.
finding a gastric or pancreatic plasmacytoma is an indication to rule out MM and surveillance of lesions elsewhere in the body. Treatment of choice for small lesions that can be completely resected is surgery and the role of radiotherapy is not well established. However, for lesions that cannot be completely resected, radiation therapy alone with a dose of 40 to 50 Gyri over a 4-week period is recommended. There are no current recommendations to treat solitary plasmacytoma with chemotherapy; however, the presence of a solitary plasmacytoma anywhere in the body warrants to look for extensive disease (MM), which needs to be treated with chemotherapeutic agents (like bortezomib or lenalidomide), or hematopoietic cell transplantation, or combination of both based on different patient factors.

Acknowledgments

Ratesh Khillan, MD.

Author Contributions

Conception and design: Tagore Sunkara, Ghulamullah Shahzad
Drafting of the article: Tagore Sunkara, Santosh R. Sharma, Andrew Ofosu, Vinaya Gaduputi
Critical revision of the article for important intellectual content: Tagore Sunkara, Vinaya Gaduputi, Madhavi Reddy, Ghulamullah Shahzad
Final approval of the article: Tagore Sunkara, Santosh R. Sharma, Andrew Ofosu, Vinaya Gaduputi, Madhavi Reddy, Ghulamullah Shahzad

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval

Ethical approval to report this case was obtained from the institutional review board.

Informed Consent

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

ORCID iDs

Tagore Sunkara https://orcid.org/0000-0001-9536-9027
Vinaya Gaduputi https://orcid.org/0000-0002-3789-5392

References

1. Oliva S, Gambella M, Boccadoro M, Bringhen S. Systemic virotherapy for multiple myeloma. Expert Opin Biol Ther. 2017;17:1375-1387.
2. Soutar R, Lucraft H, Jackson G, et al. Guidelines on the diagnosis and management of solitary plasmacytoma of bone and solitary extramedullary plasmacytoma. Br J Haematol. 2004;124:717-726.
3. Krishnamoorthy N, Bal MM, Ramadwar M, Deodhar K, Mohandas KM. A rare case of primary gastric plasmacytoma: an unforeseen surprise. J Cancer Res Ther. 2010;6:549-551.
4. Talamo G, Cavallo F, Zangari M, et al. Clinical and biological features of multiple myeloma involving the gastrointestinal system. Haematologica. 2006;91:964-967.
5. Griffiths AP, Shepherd NA, Beddall A, Williams JG. Gastrointestinal tumour masses due to multiple myeloma: a pathological mimic of malignant lymphoma. Histopathology. 1997;31:318-323.
6. Goeggel-Lamping C, Kahn SB. Gastrointestinal polyposis in multiple myeloma. JAMA. 1978;239:1786-1787.
7. Sakai H, Sawamura M, Tamura J, et al. A patient with primary plasma cell leukemia accompanied by an extensive polyloid infiltration of the gastrointestinal tract. J Med. 1991;22:195-199.
8. Kusano Y, Nishimura N, Yokoyama M, Terui Y, Hatake K. Gastric involvement, a rare site for extramedullary myeloma. Ann Hematol. 2016;95:663-666.
9. Yasar B, Gunes P, Guler O, Yagci S, Benek D. Extramedullary relapse of multiple myeloma presenting as massive upper gastrointestinal bleeding: a rare complication. Korean J Intern Med. 2015;30:538-539.
10. Sousos N, Vlachaki E, Anastasiadou K, et al. Diffuse gastric plasmacytoma involvement in multiple myeloma. Endoscopy. 2015;47(suppl 1 UCTN):E197.
11. Katzenberger T, Al-Taie O, Fischbach W, Eck M. Plasma cell myeloma in the stomach? [in German]. Pathol. 2015;36:193-196.
12. Images of the month: a rare etiology of hematochezia. Am J Gastroenterol. 2014;109:1325.
13. Wang CC, Chang MH, Lin CC. A rare cause of gastrointestinal bleeding. Multiple myeloma with extramedullary gastroduodenal plasmacytoma. Gastroenterology. 2013;145:e1-e2.
14. Doberauer C, Sanner B, Henning B. Multiple myeloma involving the stomach with vitamin B12 deficiency. Eur J Gastroenterol Hepatol. 1999;11:205-207.
15. Kwak HS, Jin GY, Lee JM. Radiologic findings of multiple myeloma with gastric involvement: a case report. Korean J Radiol. 2002;3:133-135.
16. Birjawi GA, Jalbout R, Musallam KM, Tawil AN, Taher AT, Khoury NJ. Abdominal manifestations of multiple myeloma: a retrospective radiologic overview. Clin Lymphoma Myeloma. 2008;8:348-351.
17. Lu CH, Hsieh AT, Peng YJ, Yan JC. Multiple myeloma presenting as gastric polyposis. Dig Dis Sci. 2007;52:3340-3342.
18. Kazama T, Noguchi Y, Giralt SA. Multiphasic CT and MRI appearances of extramedullary multiple myeloma involving the stomach, pancreas, and bladder. Clin Imaging. 2005;29:263-265.
19. Sciancalpore D, Musci S, Fracella MR, et al. Extramedullary plasmacytoma mimicking pancreatic cancer: an unusual presentation. Case Rep Oncol Med. 2016;2016:6919210.
20. Utsumi T, Sasajima J, Goto T, et al. The detection of pancreatic and retroperitoneal plasmacytoma helped to diagnose multiple myeloma: a case report. Medicine (Baltimore). 2015;94:e914.
21. Smith A, Hal H, Frauenhoffer E. Extramedullary plasmacytoma of the pancreas: a rare entity. Case Rep Radiol. 2012;2012:798264.
22. Leake PA, Coard KC, Plummer JM. Extramedullary plasma-cytoma of the pancreas as an uncommon cause of obstructive jaundice: a case report. *J Med Case Rep*. 2009;3:8785.

23. Annibali O, Marchesi F, Petrucci MT, Tirindelli MC, Avvisati G. Relapse of IgA lambda multiple myeloma presenting as obstructive jaundice and abdominal pain. *Onkologie*. 2009;32:119-121.

24. Balliu E, Casas JD, Barluenga E, Guasch I. Multifocal involvement of the pancreas in multiple myeloma: sonographic, CT, and MR imaging findings. *AJR Am J Roentgenol*. 2003;180:545-546.

25. Fischer A, Suhrland MJ, Vogl SE. Myeloma of the head of the pancreas. A case report. *Cancer*. 1991;67:681-683.

26. Senzaki H, Okada H, Izuno Y, et al. An autopsy case of multiple myeloma accompanied by extensive nodular infiltration into the extraskeletal tissue [in Japanese]. *Gan No Rinsho*. 1990;36:2491-2495.

27. Mitchell DG, Hill MC. Obstructive jaundice due to multiple myeloma of the pancreatic head: CT evaluation. *J Comput Assist Tomogr*. 1985;9:1118-1119.

28. Bell HG, David R, Shamsuddin AM. Extrahepatic biliary obstruction and liver failure secondary to myeloma of the pancreas. *Hum Pathol*. 1982;13:940-942.

29. Matsubayashi T, Tanaka T, Furuta M, Nakajima M. Case report 100. Poorly differentiated plasma cell myeloma with widespread involvement of soft tissues and multiple organs. *Skeletal Radiol*. 1979;4:228-232.

30. Simon TL, Rughani IK, Pierson DJ, Hebard DW. Multiple plasmacytomas with thoracic and biliary involvement. *Arch Intern Med*. 1978;138:1165-1167.

31. Tournier-Rangeard L, Lapeyre M, Graff-Caillaud P, et al. Radiotherapy for solitary extramedullary plasmacytoma in the head-and-neck region: a dose greater than 45 Gy to the target volume improves the local control. *Int J Radiat Oncol Biol Phys*. 2006;64:1013-1017.

32. Creach KM, Foote RL, Neben-Wittich MA, Kyle RA. Radiotherapy for extramedullary plasmacytoma of the head and neck. *Int J Radiat Oncol Biol Phys*. 2009;73:789-794.