

A Durable Response of Primary Advanced Colonic Plasmacytoma Using a Combination of Surgical Resection and Adjuvant Bortezomib: A Case Report and Literature Review

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Background: Primary isolated extra-medullary plasmacytoma (EMP) is a rare entity that most commonly involves the nasopharynx or upper respiratory tract. Only 10% of cases involve the gastrointestinal tract, mainly the small intestine and the stomach. Involvement of the colon is extremely rare with less than 40 reported cases worldwide.

Case Presentation: We report a case of a 57-year-old man who was presented with a 3-week history of fresh bleeding from the rectum. Colonoscopy showed a polypoidal mass arising from the ascending colon; biopsy showed clonal plasmacytosis and a primary colonic solitary EMP diagnosis was made after exclusion of multiple myeloma (MM). Accordingly, the patient underwent a right hemicolectomy, followed by 6 cycles of bortezomib, cyclophosphamide, and dexamethasone (VCD). The patient continued to be disease-free 30 months after the completion of his chemotherapy.

Conclusion: To our knowledge, this is the first reported case of primary colonic plasmacytoma managed with surgical resection followed by an adjuvant bortezomib-based regimen with a durable response.

Keywords: primary plasmacytoma, plasmacyte dyscrasia, myeloma, colon, bortezomib

Introduction

Multiple myeloma (MM) and plasmacytoma are the two main plasma cell dyscrasias, which are characterized by monoclonal plasma cell proliferation, but while the former is systemic the latter is localized.¹ Plasmacytoma may occur as a primary disorder or may occur concurrently or following the onset of MM (secondary).² It is also classified based on the sites of involvement: osseous or extramedullary plasmacytoma (EMP), and both have different treatment outcomes and risk of progression to MM.^{3,4}

Plasmacytoma can be diagnosed if all the following criteria are fulfilled: Biopsy-proven solitary lesion of bone or soft tissue with evidence of clonal plasma cells, no evidence of clonal plasma cell in the bone marrow, no skeletal lesions seen in computed tomography (CT), positron emission tomography (PET) scan, or magnetic resonance imaging (MRI) and no evidence of end organ damage including renal dysfunction, hypercalcemia and anemia.⁵ Serum protein electrophoresis (SPEP) showed a monoclonal band in up to 25% of patients with EMP. However, M band and/or Bence-Jones protein in urine does not necessarily preclude the diagnosis and this M protein usually disappears after treatment.⁶

Extramedullary plasmacytoma is less common than osseous plasmacytoma and constitutes less than 5% of all plasma cell neoplasms, with the aerodigestive tract being the most common site and involved in 80% of cases.^{6,7} Gastrointestinal tract primary plasmacytomas are a rare entity (10% of all EMP),⁸ and it most commonly involves stomach⁹ or small

intestine. Given the rarity of such occurrence,¹⁰ in addition to the scarcity of data reporting similar cases worldwide,⁸ there is no knowledge present regarding treatment and/or prognosis of primary colon plasmacytoma.

In this paper, we report a case of colonic plasmacytoma that underwent right hemicolectomy, followed by adjuvant chemotherapy with bortezomib, cyclophosphamide and dexamethasone (VCD).

Case Presentation

A 57-year-old male was presented in July 2019 with a 3-week history of fresh bleeding via the rectum, dizziness, weight loss, and altered bowel. By physical examination, it was evident that the patient looked pale, but the abdominal and rectal examinations were unremarkable. In addition to this, basic laboratory investigations including kidney function test (KFT), liver function test (LFT), coagulation profile, and urine analysis were all within normal range. On the other hand, hemoglobin (Hb) was low at 8.5 gm/dL with low mean corpuscular volume (MCV), and blood film showed microcytic hypochromic anemia with slight neutrophilic leukocytosis and thrombocytosis.

Computed tomography scans presented soft tissue mass lesion in the lower pole of the cecum associated with multiple enlarged regional lymph nodes only, without any liver or lung lesions (Figure 1). PET scan done and showed hypermetabolic malignant cecal mass with hypermetabolic regional mesenteric lymph nodes (figure 4). In addition, colonoscopy exhibited a large polypoid mass lesion arising from the cecum and extending beyond the hepatic flexure. Also, biopsy showed clonal plasmacytosis (Immunoreactive for CD138, CD56 and negative for CD3 and CD20 and lambda light chain restricted); a picture consistent with plasmacytoma (Figures 2 and 3). Bone marrow aspirate and biopsy showed no evidence of clonal plasma cell disorder. In addition to this, serum free light chain showed a kappa level of 15.5 mg/L (normal: 3.3–19.4) and lambda level of 364 mg/L (normal: 5.7–26.3); ratio 0.042 (normal: 0.26 to 1.65). Urine protein electrophoresis (UPEP) and immunofixation were normal, while a monoclonal band (IgG Lambda) in the gamma area measuring approximately 2.2 gm/dL was evident in serum protein electrophoresis (SPEP) and immunofixation. Further workup showed a β_2 microglobulin 1.8 mg/L (normal 0.8–2.5), immunoglobulin-G (IgG) 2994 mg/L, IgM:

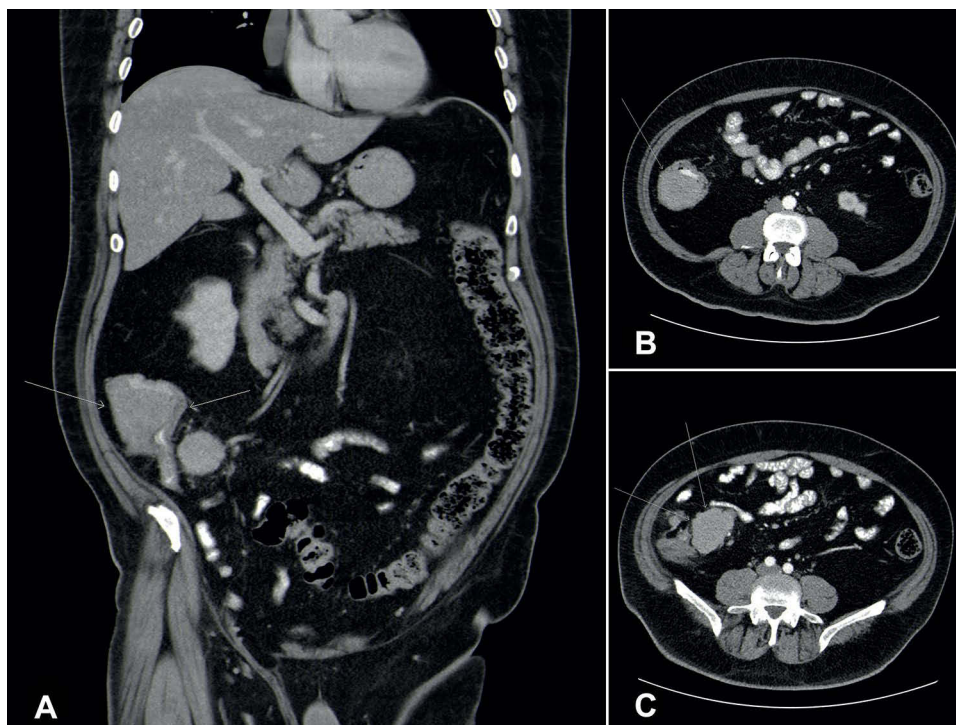


Figure 1 Preoperative computed tomography: (A) coronal CT scan images at presentation showing soft tissue mass in the lower pole of the caecum associated with multiple metastatic regional lymph nodes (B) Axial CT scan images at presentation showing soft tissue mass in the lower pole of the caecum (arrow) (C) Axial CT scan images at presentation showing multiple enlarged lymph nodes located along the course of the ileocolic vessels measures about 4.7*6.4 cm in axial dimension.

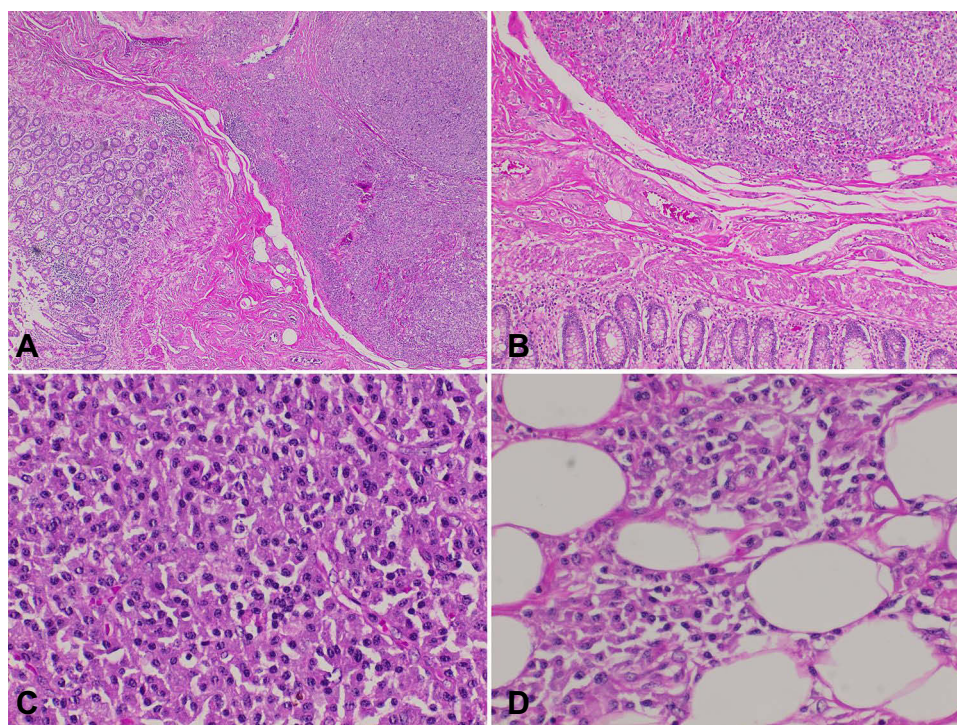


Figure 2 (A) 100X H&E stained section of colonic mass, (B) 200X H&E stained section of colonic mass, (C) 400X H&E stained section of colonic mass, (D) 200X H&E stained section of colonic mass.

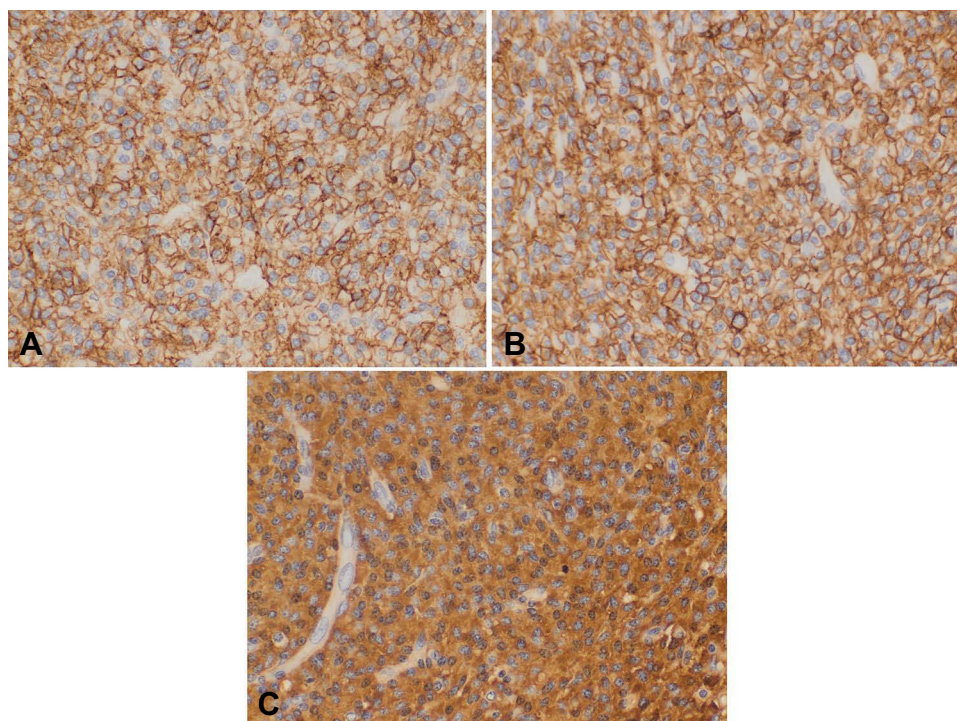


Figure 3 (A) CD138 immunostain (IHC400X) (B) CD56 immunostain (IHC400X) (C) Lambda light chain immunostain (IHC 400X).

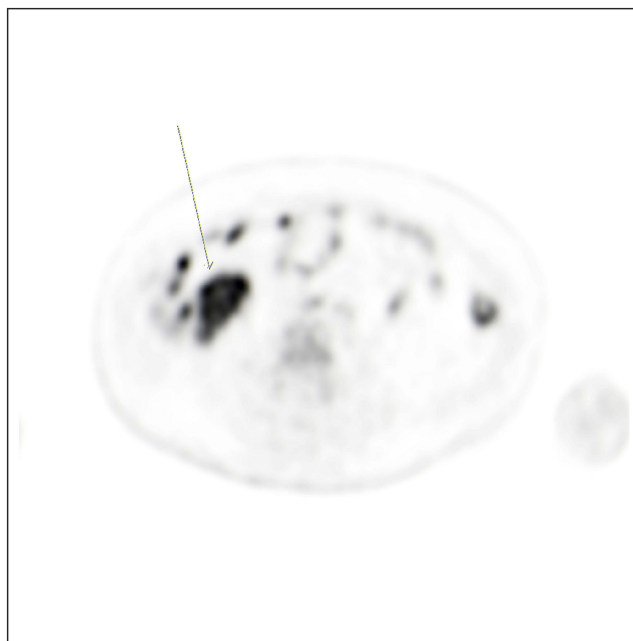


Figure 4 Preoperative PET scan showed: Hypermetabolic malignant right colonic (caecal) mass, which is compatible with known primary tumor and multiple hypermetabolic regional mesenteric lymph nodes metastases.

175 mg/dL and IgA: 203 mg/dL. Moreover, PET scan showed hypermetabolic malignant right colonic (cecal) mass, which is compatible with known primary tumor.

Right hemicolectomy was performed and revealed a cecal exophytic polypoid mass measuring 5.5 cm in maximal dimension. The histopathologic study of the mass revealed a submucosal tumor composed of large oval cells consisting of a round nucleus in eccentric position with coarse chromatin and plenty of cytoplasm. The tumor infiltrates the muscular wall of the intestine and the pericolic fat (Figure 2). Eleven out of fifteen regional lymph nodes were involved, the surgical margins were free and immunohistochemical stains were performed. The tumor cells were immunoreactive for CD138+, CD56+ and showed lambda light chain restriction (Figures 2 and 3). They were negative for CD20 and synaptophysin and CD3. The overall findings are consistent with extramedullary colonic plasmacytoma.

Along with large tumor size, persistent monoclonal band, and regional lymph node involvement, radiotherapy is sought out to have minimal benefits. Moreover, data established from secondary plasmacytoma and primary plasmacytoma of sites other than colon showed favorable outcome with bortezomib adjuvant therapy. Therefore, it is worthy of investigation in primary colonic plasmacytoma.

Following surgery, the patient received adjuvant treatment with 6 cycles of VCD, which all were well tolerated. Three months after surgery, monoclonal band was reduced to 0.4 gm/dL, and after finishing all planned adjuvant VCD, no monoclonal band was seen. Currently, with 30 months after surgery, no monoclonal bands were detected and PET scan showed no evidence of disease (complete remission).

Discussion

Multiple myeloma is the most prevalent plasma cell disorder. However, in less than 5% of the cases it may present as localized clonal proliferation of clonal plasma cell called plasmacytoma, which may occur as a solitary or as multiple lesions either in the bone or soft tissue. Due to the high rate of progression to MM, prognosis of osseous extramedullary plasmacytoma is usually worse compared to the one that involves soft tissues.^{11,12}

Extramedullary plasmacytoma of soft tissue is less common than bone EMP, and in 80% of the cases, it involves the upper aerodigestive tract.¹³ Primary gastrointestinal tract EMP is extremely rare and constitutes of around 10% of primary EMP. The gastrointestinal tract, stomach and small bowels¹⁴ are the most commonly involved sites. In Table 1, previously reported cases of colonic plasmacytoma are mentioned. In the literature review, 33 previous cases were

Table I Previously Reported Primary Colonic Plasmacytoma

Author/Year	Sex	Age (Years)	Location	Clinical Features	Therapy
Vasiliu and Popa/1928 ¹⁵	F	47	Sigmoid	Anorexia, epigastric pain, glandular enlargement	Treatment not mentioned
Brown and Liber/1939 ¹⁶	M	57	Colon, rectum	Rectal discomfort	Treatment not mentioned
Hampton and Gandy/1957 ⁴¹	F	43	Rectum	Rectal pain and bleeding	Rectosigmoid resection
Miller/1970 ⁴²	M	35	Cecum	Anemia	Right hemicolectomy
William/1970 ¹⁷	M	84	Cecum	Anemia	Right hemicolectomy
Nielson/1972 ¹⁸	F	82	Sigmoid	Pain	Resection
Wing/1975 ¹⁹	F	82	Ascending colon	Pain	Right hemicolectomy
Shaw/1976 ²⁰	F	47	Cecum	Diarrhea	Resection
Budd/1977 ²¹	M	21	Descending colon	Pain, nausea, vomiting	Left hemicolectomy
Allison/1977 ²²	M	61	Sigmoid	None	Sigmoid colectomy
Adekunle/1978 ²³	M	35	Cecum	Pain	Right hemicolectomy
Gleason/1982 ²⁴	F	20	Transverse colon	Pain, rectal bleeding	Transverse colon resection
Sidani/1985 ²⁵	M	52	Sigmoid	Pain, rectal bleeding	Resection
Sperling/1987 ²⁶	M	77	Cecum	Weight loss, anemia, pain, fecal occult blood	Right hemicolectomy
Saverio Ligato/1996 ²⁷	M	45	Hepatic flexure of the colon	Anemia	Extended right hemicolectomy
Holland/1997 ²⁸	M	62	Sigmoid colon	Pain	Sigmoid colectomy
Lattuneddu/2004 ²⁹	M	86	Sigmoid colon	Pain, rectal bleeding, asthenia	Segmental resection of the left colon
Gupta/2007 ⁸	M	42	Diffuse colon	Diarrhea	Subtotal colectomy
Jones/2008 ³⁰	M	65	Sigmoid colon	Dysuria, abdominal pain	Sigmoid colon resection
Jone/2008 ³⁰	M	57	Sigmoid colon	Fatigue, melena	Hartmann resection
Doki/2008 ³¹	M	64	Ascending colon	Pain	Right hemicolectomy, lymph node dissection, excision of Gerota's fascia, partial resection of the posterior portion of the liver
Collado Pacheco/2009 ³²	M	74	Right colon	Diarrhea, pain, rectal bleeding	Treatment not mentioned
Kodani/2011 ³³	M	42	Sigmoid	Fecal occult blood	Endoscopic submucosal resection
Nakagawa/2011 ³⁴	F	84	Cecum and rectum	Medical examination	Endoscopic submucosal resection
Lee/2013 ³⁵	M	45	Transverse colon	Pain	Extended left hemicolectomy
Zihni/2013 ³⁶	M	54	Descending colon	Pain and weakness	Left hemicolectomy and small intestinal resection

(Continued)

Table I (Continued).

Author/Year	Sex	Age (Years)	Location	Clinical Features	Therapy
Han/2014 ³⁷	M	49	Transverse colon	Pain	Left hemicolectomy
Gabriel/2014 ³⁸	M	62	Cecum	Perforation during diagnostic colonoscopy	Right hemicolectomy
Parnell/2015 ³⁹	F	72	Right colon	Fatigue, light-headedness, dyspnea, dark stool	Right hemicolectomy Distal ileal resection
Dalgic/2015 ⁴⁰	M	51	Cecum and the ascending colon	Abdominal pain, changes in bowel habits, bloody diarrhoea, and a 10 kg loss of weight	Right hemicolectomy
M Mjoli 2016 ⁴³	M	42	Sigmoid	Abdominal cramps sigmoid colic intussusception	Sigmoid colectomy
Kitamura2018 ⁴⁴	F	77	Sigmoid	Lower abdominal pain and nausea, perforation	The abdominal mass was removed en bloc, including resection of the sigmoid colon.
Bhangoo 2020 ⁴⁵	M	82	Rectosigmoid	Rectal bleeding	Treatment not mentioned

reported of 9 females and 24 males. The mean age (median) was 56.8 (57), and the most commonly reported symptoms were abdominal pain, lower gastrointestinal bleeding, change in bowel habits, large bowel obstruction, and intussusception.⁴⁶ Only 2 cases were presented with perforation, and surgery was the main modality of treatment; nevertheless, one reported case was treated with EMR.^{33,34,38}

In general, EMPs are considered radiosensitive, with a local control rate of 90–100%,^{47,57} and radiotherapy is the preferred approach for those involving the head, neck, anal⁴⁶ and rectal⁴⁸ regions. When complete surgical resection is feasible, surgery remains the treatment of choice for colonic lesions. Alternatively, endoscopic treatments such as sub-mucosal resection or polypectomy have proven to be sufficient in selected cases.^{33,34,38} In the case of a tumor size greater than 5 cm, response to radiotherapy can be poor and recurrence is potentially high.⁴⁹ Nevertheless, complete resection is not feasible, or in cases of patients with positive regional lymph nodes, adjuvant radiotherapy is recommended.⁵⁰

Chemotherapy has been used in the treatment of disseminated disease and preoperatively to reduce the size of the tumor. Data about using bortezomib in EMP secondary to MM showed significant efficacy in this setting. However, the number of treated patients is small in order to make a proper conclusion. In one case report, 3 out of 4 soft tissue plasmacytomas, complicating multiple myeloma, at time of relapse, had completely disappeared with bortezomib. However, other agents, like thalidomide, were not effective.⁵¹

Another case report displayed complete response of primary extramedullary gastric plasmacytoma with bortezomib and dexamethasone.⁵² Several other case reports illustrated similar response using bortezomib with cyclophosphamide, and dexamethasone.^{53–56,58}

In conclusion, colonic plasmacytoma is extremely rare. Surgical resection followed by adjuvant bortezomib-based therapy may result in durable response.

Data Sharing Statement

Data will be available upon request. Please email your request to BS.13628@khcc.jo.

Ethical Statement

Written informed consent was provided by the patient to have the case published.

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Disclosure

The authors declare no conflicts of interest in this work.

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