



# Gone to Guts: Osteosarcoma With Metastasis to Small and Large Intestines Presenting as Recurrent Bleeding

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## ABSTRACT

Gastrointestinal involvement in osteosarcoma is uncommon, with colonic spread being particularly rare. Symptoms range from abdominal pain and obstruction to anemia and melena. Chemotherapy for metastatic lesions has not been standardized, and surgery remains the treatment for selective candidates. We describe a rare occurrence of osteosarcoma metastasizing simultaneously to the small and large intestines in a 43-year-old man who presented with recurrent gastrointestinal bleeding causing symptomatic anemia. Endoscopic examination revealed multiple nodules in the jejunum and colon consistent with metastatic osteosarcoma.

**KEYWORDS:** osteosarcoma; gastrointestinal bleed; anemia; metastasis

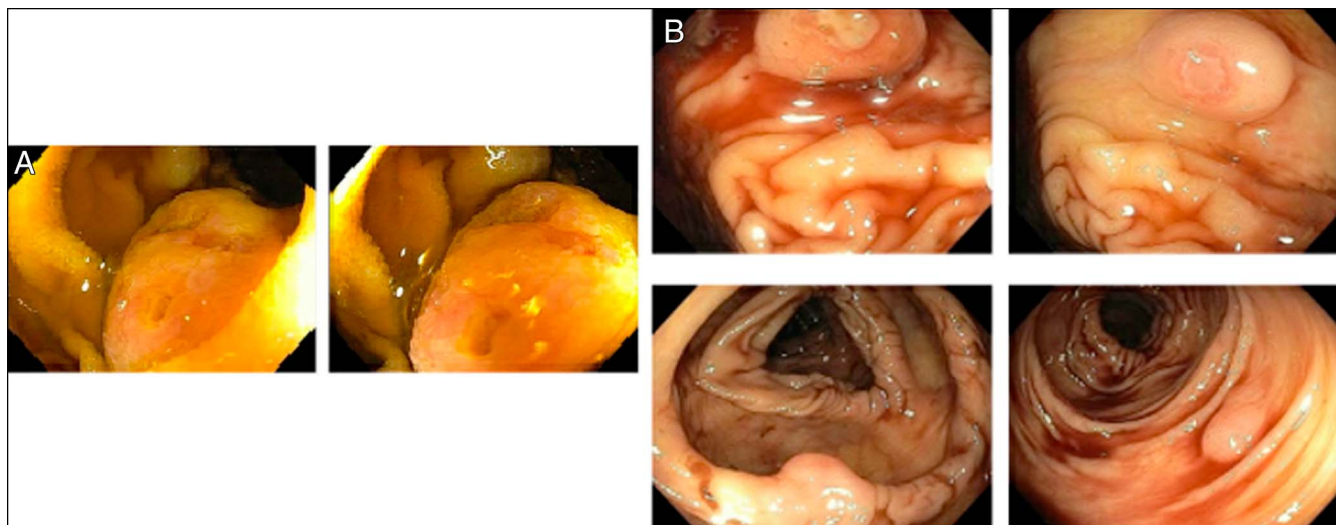
## INTRODUCTION

Osteosarcomas are the most common bone tumors in children and adolescents. Predilection for pulmonary metastasis is the highest with an incidence of 80%–90%.<sup>1,2</sup> Gastrointestinal metastasis remains extremely rare with sparsely reported cases in literature.<sup>2</sup> Manifestations vary depending on the location of lesion within the gastrointestinal tract.<sup>3,4</sup> Investigations for metastases involves computed tomography imaging and Technecium-99 m bone scan to detect visceral and skeletal metastases respectively.<sup>5,6</sup> Chemotherapeutic regimens for metastatic lesions have not been standardized.<sup>7</sup> Consequently, the 5-year survival probability is 44% with pulmonary metastasis and only 19% when extra-pulmonary sites are involved.<sup>6</sup>

We present a case of metastatic osteosarcoma that presented with recurrent bleeding secondary to metastasis to the small and large intestines simultaneously.

## CASE REPORT

A 43-year-old man presented to the hospital with a syncopal episode and intermittent episodes of melena for a month before presentation. His medical history entailed osteosarcoma arising in femur, diagnosed at 20 years of age. The malignancy was complicated by metastases to the lungs and the brain. The chemotherapeutic agents used as adjuncts to surgical modality included ifosfamide, doxorubicin, carboplatin, and etoposide, and he was considered to be in remission for 6 years. On presentation, the patient was tachycardic to 102 and hypotensive to 85/40 mm Hg. On physical examination, he was pale, and the abdomen was soft and nontender. A digital rectal examination was positive for melena. Laboratory investigation was significant for hemoglobin 5.3 g/dL and mean corpuscular volume 80.3 fL consistent with profound microcytic anemia. Chest X-ray revealed multiple pulmonary metastatic nodules. Computed tomographic angiography of the abdomen also showed concerns for questionable nodules in the small and large bowel. To evaluate the gastrointestinal bleed, enteroscopy was performed; it revealed no active bleeding; however, a 2-cm ulcerated jejunal nodule was noted (Figure 1). Colonoscopy with deep cannulation of terminal ileum



**Figure 1.** (A) Esophagogastroduodenoscopy images showing a 2-cm ulcerated jejunal nodule; (B) colonoscopy images showing 2- to 3-cm ulcerated transverse and hepatic colon nodules.

revealed old blood throughout, and similar multiple 2- to 3-cm ulcerated nodules were found in the transverse and hepatic colon, which were biopsied and sent for histopathological analysis (Figure 1). Pathology revealed spindle-shaped cells with marked nuclear atypia with poor immunoreactions indicating poorly differentiated sarcoma. Eventually, the bleeding stopped with supportive care, and he was discharged on palliative chemotherapy.

## DISCUSSION

Metastases are discovered synchronously at the time of diagnosis of osteosarcoma, in about 10%–30% of patients, and literature on metastatic activity of osteosarcoma favors pulmonary involvement.<sup>1,2,8</sup> Other commonly involved sites include brain, pleura, and axial skeleton.<sup>3</sup> When gastrointestinal involvement is observed, it is preceded by pulmonary metastases, with a very few reports highlighting concomitant spread or pulmonary metastasis appearing after gastrointestinal spread, shedding light on late-stage involvement of the gastrointestinal tract in this condition.<sup>3,9,10</sup> Although gastrointestinal metastasis of osteosarcoma is an uncommon finding, metastasis to colon is a rarer phenomenon with only 2 previous case studies reported.<sup>4,10</sup> These reported cases showed simultaneous gastric and jejunal lesions with colonic metastasis, respectively.

On one end of the clinical spectrum, case studies with jejunal or ileal metastases reported abdominal pain, nausea, vomiting, and anorexia secondary to partial or complete small bowel obstruction or intussusception.<sup>2,11,12</sup> Symptoms of melena, generalized weakness with anemia, and a positive fecal occult blood test have been reported in osteosarcoma with gastric involvement.<sup>3,4,9,10</sup> Our case presented with a syncopal episode secondary to profound anemia from gastrointestinal losses from jejunal and colonic metastasis. Only one other report, by Costa et al, had similar findings as

ours, in addition to a palpable right iliac fossa mass because of right colonic involvement.<sup>13</sup> Varied involvement of gastrointestinal tract secondary to osteosarcoma has been summarized in Figure 2.<sup>2-4,10-20</sup>

Typically, computed tomography scan is the modality of choice to delineate the extent of spread once the diagnosis is established and endoscopy is reserved for gastrointestinal bleeding.<sup>11</sup> Jejunal involvement is associated with poorer outcome when compared with gastric and duodenal involvement.<sup>4,10,14</sup> Costa et al's study showed metastatic disease involving the colon and ileum with omental involvement and underwent hemicolectomy and omentectomy and remained in remission at the 12-month follow-up as compared to our case, who because of multiorgan involvement was favored toward palliative chemotherapy.<sup>13</sup>

On our review of literature, this case served as one of the first reports of simultaneous metastasis of osteosarcoma involving the small and large intestines to result in symptomatic anemia from gastrointestinal losses. We believe our case helps educate clinicians to suspect gastrointestinal metastasis in patients presenting with severe hemodynamically unstable gastrointestinal bleeding and having a history of advanced stage osteosarcoma to help arrive promptly at the diagnosis, to aid in directed therapy and improve outcomes.

## DISCLOSURES

**Author contributions:** All authors made substantial contributions to the work, were involved in the final approval of the version to be published, and agree to be held accountable for all aspects of the work. PS Harne is the article guarantor.

**Financial disclosure:** None to report

AUTHOR(S)	TITLE	PRIMARY TUMOR AND GI INVOLVEMENT	CLINICAL PRESENTATION	ENDOSCOPIC/IMAGING	IMAGE 1	IMAGE 2
Kubo T et al.	<i>Long-term survival after sporadic and delayed metastases of conventional osteosarcoma?</i> <sup>1</sup>	Osteoblastic osteosarcoma in proximal tibia - August, 2002, recurrent pulmonary metastases events since 2004. Multiple GI metastatic (stomach, jejunum, peritoneum) events in 2011, 2012 and 2015.	Tarry stools (Stomach), Abdominal pain and vomiting, CT revealed intussusception caused by a tumor (Jejunum), Peritoneal dissemination lead to death (Peritoneum)	1: Abdominal CT demonstrates jejunojejunal intussusception; 2: Gross specimen of resected intraluminal jejunal tumor with dimensions 2 cm x 2 cm x 2 cm		
Horiuchi A et al.	<i>Metastatic Osteosarcoma in the Jejunum with Intussusception: Report of a Case?</i> <sup>2</sup>	Osteosarcoma of right femur, complicated with bilateral pulmonary metastases (jejunal metastasis)	Progressive abdominal pain since 3 months, sudden-onset vomiting; CT revealed intussusception	1: CT abdomen showing mesenteric fat drawing into small bowel lumen; 2: Gross specimen of resected jejunal segment with mesenteric side tumor with dimensions 4.7 cm x 3.5 cm x 1.8 cm; tumor base was in the submucosa involving vessels		
Moses J et al.	<i>Metastatic osteosarcoma to the stomach and ascending colon in a pediatric patient causing gastrointestinal hemorrhage?</i> <sup>3</sup>	Osteosarcoma of proximal fibular shaft complicated with new pulmonary metastatic nodules 6 months later. GI metastasis (stomach and colon) discovered 8 months after pulmonary metastasectomies	3 episodes of anemia requiring transfusions, melena, no other GI complaints, CT revealed new masses, 1 in the gastric fundus, 1 in the ascending colon	1: CT image showing exophytic soft tissue mass arising from gastric fundus measuring 2.3 cm in craniocaudal dimension (white circle). 2: CT image showing eccentric soft tissue mass at the medial wall of ascending colon measuring 3.6 cm in craniocaudal dimension (white arrow).		
Urakawa H et al.	<i>Metastasis of osteosarcoma to stomach made clinically evident by hematemesis: a case report?</i> <sup>4</sup>	Osteosarcoma of the sternum, complicated with malignant pleural effusion post tumor resection. 11 months post-surgery GI involvement (stomach) noted. 12 months post-surgery, isolated lung metastasis.	Decrease in hemoglobin from 8.6 to 7.8 g/dL in one week and one episode of hematemesis	Endoscopy revealed gastric body tumor with ulcerated surface and fresh bleeding. Suctioning procedure done. Images of 1: finding and 2: procedure present.		
Costa A et al.	<i>Metastatic Osteosarcoma involving the Colon and Ileum</i> <sup>5</sup>	Osteogenic sarcoma of the tibia with multiple pulmonary metastasis. GI spread (colon) 7 years after primary.	Fatigue, anemia, fecal occult blood test positive and serum Alkaline Phosphatase raised. CT revealed 10-cm irregular right colonic mass.	Colonoscopy done, semipedunculated submucosal tumor of diameter 3 cm in ascending colon with ulcerated, white, firm, granular, necrotic mucosa overlying the mass. Image present.		
Chandramohan K et al.	<i>Metastatic osteosarcoma causing intussusception?</i> <sup>6</sup>	Osteogenic sarcoma of distal left femur diagnosed in December 1999. Bony metastasis to left scapula in March 2002. GI metastasis (jejunum) identified shortly after the bony metastatic lesion.	Abdominal pain, distension and vomiting. Distended abdomen and epigastric tenderness on examination. Dilated small bowel loops on erect abdominal X-ray and Ultrasonography suggested small bowel obstruction. Conservative management provided temporary relief, with recurrence of symptoms few days later. This time sonography revealed ileocolic intussusception	Resected specimen on being cut-open showed gangrenous intussusception and mucosal polyp at its apex.		
Panizo-Santos A et al.	<i>Metastatic osteosarcoma presenting as a small-bowel polyp. A case report and review of the literature</i> <sup>7</sup>	Osteosarcoma of right tibia (September 1994) complicated with pulmonary metastases (March and December 1996). GI mets to jejunum and ileum.	Abdominal pain, nausea, vomiting and anorexia, CT revealed a mass attached to the distal jejunum and proximal ileum and 3 nodules in the liver; resected specimen revealed 2 masses in the bowel, liver masses were 2 to 5 cm in size	Gross specimen of resected jejunum showing largest nodule involving the entire thickness of the wall, of dimensions 8 x 4.5 x 4.5 cm, and the second, an ulcerated polliculated mass in the mucosa of jejunum with dimensions 3 x 2.5 x 1.5 cm		
Aarvold A et al.	<i>Osteosarcoma metastasizing to the duodenum and pancreas</i> <sup>8</sup>	Osteosarcoma of the distal femur (1999); solitary pulmonary metastasis (2004). GI metastasis to duodenum and pancreas.	Acute anemia and melena, Hemoglobin at presentation = 3.8 g/dL, further imaging revealed 2 masses, in the pancreas and wall of second part of duodenum respectively	Gross specimen of duodenum and head of the pancreas prior to fixation. The proximal duodenum is laid open to reveal the tumour (arrow). The two masses in the pancreas and second part of duodenum, which measured 10 cm x 4 cm and 5 cm x 3 cm x 3 cm, were in continuity and shaped like a dumb-bell.		
Akpinar B et al.	<i>Unusual presentation of a pancreatic cyst resulting from osteosarcoma metastasis?</i> <sup>9</sup>	Left distal femur high-grade giant cell rich osteosarcoma, pulmonary metastases 3 years later, GI metastasis (pancreas) 4 years later	Abdominal pain, nausea, vomiting and early satiety, CT significant for cystic mass anterior to pancreas, rehospitalised with similar complaints a few days after discharge, epigastric fullness present, no rebound on palpation	2: (A) Post-contrast venous phase abdominal computed tomography demonstrating a large (20 cm x 6 cm x 12 cm) abdominal mass with peripheral rim enhancement as well as some areas of thickened nodular enhancement in the periphery. (C) Giant cystic-predominant mass (arrows) extends from the hepatic hilum into the pelvis.		
Fujino S et al.	<i>Primary osteosarcoma of the heart with long-term survival: A case report of laparoscopic resection of a metastatic sarcoma in the intestine?</i> <sup>10</sup>	Cardiac osteosarcoma (September 2008). Recurrence in both atria (May 2010). Multiple bone metastases on PET-CT (July 2011) thoracic vertebral metastases on MRI (December 2012). GI metastasis (rectum) discovered in 2013	Anemia with FOBT positive, CECT showed tumor in rectum, PET-CT revealed high fluorodeoxyglucose uptake like other bone metastases	1: Preoperative colonoscopy revealed rectosigmoid tumor with red colored surface; 2: Indigo carmine staining on colonoscopy revealed irregular pit-pattern that was not typical of rectal adenocarcinoma.		
Hung GY et al.	<i>Intestinal metastasis causing intussusception in a patient treated for osteosarcoma with history of multiple metastases: a case report?</i> <sup>11</sup>	High grade Osteosarcoma over right distal femur (October 1995), bilateral multiple pulmonary metastases, multiple intracranial and GI metastasis (jejunum)	Recurrent episodes of abdominal pain before and after autologous peripheral blood stem cell infusion; intussusception suspected in abdominal ultrasonography; abdominal CT showed jejunojejunal intussusception with suspected tumor and enlarged bilateral adrenals. Progressed to develop fever and bilious emesis.	Computed tomographic scan performed before laparotomy reveals jejunojejunal intussusception in the left abdomen with marked swelling of the wall and a leading point about 1.5-2 cm in length.		
Kuwabara H et al.	<i>Cytokeratin + positive rib osteosarcoma metastasizing to the small intestine?</i> <sup>12</sup>	Cytokeratin positive osteosarcoma of the chest wall and metastasis to neck wall and jejunum and ileum	Abdominal pain, nausea, vomiting. On examination abdominal distension present and bowel sounds absent. FOBT positive. CT scan showed intussusception of terminal ileum due to tumor and polyps in small intestine.	Small intestinal tumor. 1: (a) An abdominal computed tomography scan with contrast showed an intussusception of the terminal ileum (red arrows: terminal ileum tumor; a yellow arrow: a tumor as a polyp); 2: (b) Polypoid lesions in the jejunum. (c) A 6-cm tumor, 2 cm distal from the terminal ileum.		
Lasithiotakis K et al.	<i>Pancreatic resection for metastasis to the pancreas from colon and lung cancer, and osteosarcoma?</i> <sup>13</sup>	Osteosarcoma of the left fibula. Bilateral pulmonary metastatic lesions 1 year after diagnosis. GI metastasis 14 months after primary (pancreas and duodenum)	Pyloric stenosis syndrome, abdominal CT showed mass in the head of the pancreas and adjacent duodenum; during abdominal exploration post surgical excision of the mass, another lesion invading liver segment VII was found. 3 months later new mass discovered via ultrasound in right liver lobe extending to the right iliac fossa	Intra-operative specimen of metastatic lesion to the head of pancreas, measuring 6 x 4 x 3 cm		
Strong VE et al.	<i>Osteosarcoma with delayed metastasis to the stomach?</i> <sup>14</sup>	High grade osteosarcoma of distal right femur, bilateral pulmonary metastases present at the time of diagnosis with buttock and GI metastasis (stomach)	Black, tarry stools, vomiting, syncope. Hemoglobin at presentation 5 g/dL.	EGD revealed an ulcerated, and clotted 3 cm diameter lesion on the gastric antrum (Image not available). Intraoperative picture of gastric antral lesion. Invaginated lesion is highlighted with purple ink.		

Figure 2. Summary of gastrointestinal involvement secondary to osteosarcoma.

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Informed consent was obtained for this case report.

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