Title

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Authors

Chung, Christina W.
Fares, Charlene M.
Lazarus, Michael E.

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CLINICAL VIGNETTE

High-Grade Undifferentiated Sarcoma Presenting as Duodenal Mass

Christina W. Chung, Charlene M. Fares, MD, Michael E. Lazarus, MD
Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA.

Introduction

Testicular cancer metastasizing to the gastrointestinal (GI) tract is uncommon but has been reported in the small bowel.[1,2] We describe a case of high-grade undifferentiated sarcoma in the duodenum causing gastric outlet obstruction in a patient with history of mixed germ cell tumor. We report this unusual occurrence to alert clinicians to suspect secondary malignancies or recurrence in patients with history of testicular cancer who present with symptoms concerning for GI obstruction.

Case Report

A 43-year-old Hispanic male with history of Stage IIIA mixed germ cell tumor presented with one month of nausea, emesis, and lower back pain. Primary malignancy was initially managed with orchiectomy nine years prior. Two years later, he developed lumbar pain and was found to have a retroperitoneal mass that was consistent with recurrent metastatic testicular cancer on biopsy. Patient completed four cycles of bleomycin, etoposide, cisplatin (BEP) chemotherapy with resolution of disease. In the interim, he had no evidence of disease until developing recurrence of similar lumbar back pain, as well as nausea and emesis.

He was admitted to an outside hospital where he was found to have a duodenal and a retroperitoneal mass. Two of the three biopsies of the duodenal mass done by esophagealgastroduodenoscopy (EGD) as well as a biopsy done during exploratory laparotomy were negative for malignancy. The remaining biopsy by EGD showed atypical cells. Further analysis with FISH was negative for isochromosome 12p although 92% of the analyzed cells demonstrated a gain of chromosome 12. These findings suggested that the mass is consistent with either dedifferentiated liposarcoma or undifferentiated somatic sarcoma arising out of his prior germ cell tumor. A gastrojejunostomy was performed to bypass the duodenal mass although patient continued to have PO intolerance and became TPN dependent for the month-long duration of his hospital stay.

Patient subsequently transferred to UCLA for higher level of care. On presentation, he was hemodynamically stable and physical exam was notable for moderate abdominal distention, chronic pain, and lower extremity pitting edema. Serum levels of α-fetoprotein, β-human chorionic gonadotropin, and lactate dehydrogenase were normal. He was found to have a mass extending from the second through fourth portions of his duodenum causing gastric outlet obstruction. Computed tomography (CT) of abdomen and pelvis showed fluid filled loops of bowel and a nasoenteric tube was maximally advanced past the proximal portion of duodenal mass for decompression. EGD visualized the obstructive, ulcerated mass and a patent gastrojejunostomy. Magnetic resonance cholangiopancreatography (MRCP) revealed a duodenal mass measuring up to 22cm causing aneurysmal dilation, spatially adjacent with previously noted retroperitoneal mass. MRCP also showed a dilated common bile duct with ampullary obstruction in the setting of transaminitis which improved after percutaneous biliary drainage. Abdominal, thoracic, and brain imaging showed no evidence of distant metastasis. Hospital course was complicated by chronic anemia requiring transfusion with exacerbation by acute hematemesis following anticoagulation for newly found pulmonary embolism and inferior vena cava (IVC) thrombosis.

Repeat tissue biopsy was positive for proliferation markers Ki-67 and vimentin. FISH was negative for isochromosome 12 which is classically seen with germ cell tumors. However, negative result does not necessarily exclude sarcomatous transformation of a metastatic germ cell tumor. A gain of chromosome 12 was noted in 82.3% of biopsied tumor, suggestive of a complex underlying hyperdiploid karyotype. The sample was also tested for the murine double minute 2 (MDM2) gene. Its amplification was negative making dedifferentiated liposarcoma less likely. Taken together, these findings could be consistent with a high-grade undifferentiated sarcoma arising from an untreated component from his original germ cell tumor.

The patient was not a candidate for complete resection due to proximity of the tumor to the aorta and IVC, and complete encasement of proximal inferior mesenteric artery. Management of choice was chemotherapy with paclitaxel, ifosfamide, and cisplatin (TIP) to target both sarcoma and germ cell. After undergoing one cycle of salvage TIP, which patient tolerated well despite neutropenic fever, repeat CT showed a

reduction in size of the duodenal mass from 18.3 x 7.0 cm on prior imaging to 13 x 6.8 cm.

Discussion

Germ-cell tumors (GCTs) comprise approximately 1% of malignancies in men in the United States, but are the most common type of cancer in men age 15-35.[1,3] They rarely metastasize to the retroperitoneum and GI tract invasion is reported in less than 5% of GCTs, with rare involvement of the duodenum. Only 53 cases have been reported on review of the English language literature. Metastasis to GI tract occurs more commonly with embryonal carcinomas and choriocarcinomas.[4,5]

The proliferative vascularity and propensity to outgrow its blood supply is commonly seen and can cause tumor necrosis and ulceration. As such, protracted bleeding and perforation of vital structures may cause severe chronic anemia or frank hematemesis or melena.[6] Other presenting symptoms include abdominal masses, abdominal pain, low-back pain, and extremity swelling. Evaluation for concurrent metastases should include extraperitoneal lymph nodes (i.e., inguinal, iliac, para-aortic), lungs, and liver.[6]

In this case, we speculate the mass is a sarcomatous component of his original germ cell tumor. It is possible his prior BEP chemotherapy regimen targeted the germ cell component while the sarcomatous fraction was not eradicated.

While biopsies for GCTs are not recommended given the concern for seeding, soft tissue sarcoma biopsies are evaluated by light microscopy, immunohistochemistry, and molecular studies.[7] Undifferentiated sarcoma can vary in histologic morphology such as spindled, epithelioid, pleomorphic, or round cell. But per 2013 WHO guidelines, this diagnosis of exclusion is made when immunohistochemistry and molecular studies are not further revealing of presumptive tissue of origin and cannot fit any alternative classification.[7] Grading is based on tumor differentiation, necrosis, and mitotic activity.

Salvage TIP chemotherapy usually consists of four cycles.[8] This patient already noted some reduction in size after the first cycle. The hope is that this regimen will continue to decrease the tumor burden away from vital structures enough for safe resection. Sarcomas are unlikely to be cured by chemotherapy alone and often require surgical debulking.[9,10]

Conclusion

We report this unusual occurrence to alert clinicians of secondary malignancies in patients with history of testicular cancer who present with symptoms concerning for GI obstruction or bleeding. Given the advanced disease with poor prognosis, our management was chemotherapy targeting both sarcoma and germ cell, with future reevaluation for resection. We recommend a multidisciplinary approach at a tertiary care center for such patients.

Figures

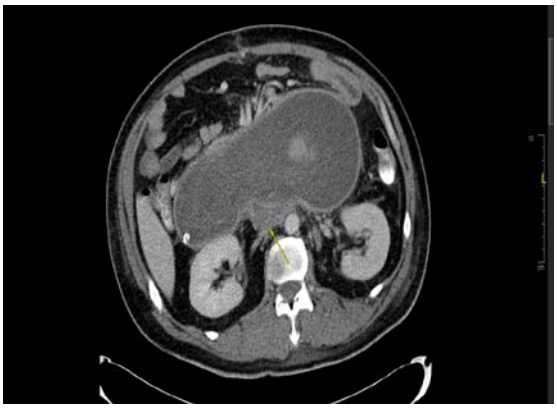

Figure 1. CT scan of the abdomen shows an 18.3cm intraluminal ulcerated mass with mucinous and fibrous elements causing aneurysmal dilation of second and third portions of duodenum, as well as infiltrative tissue (arrow) anterior to aorta and inferior vena cava.

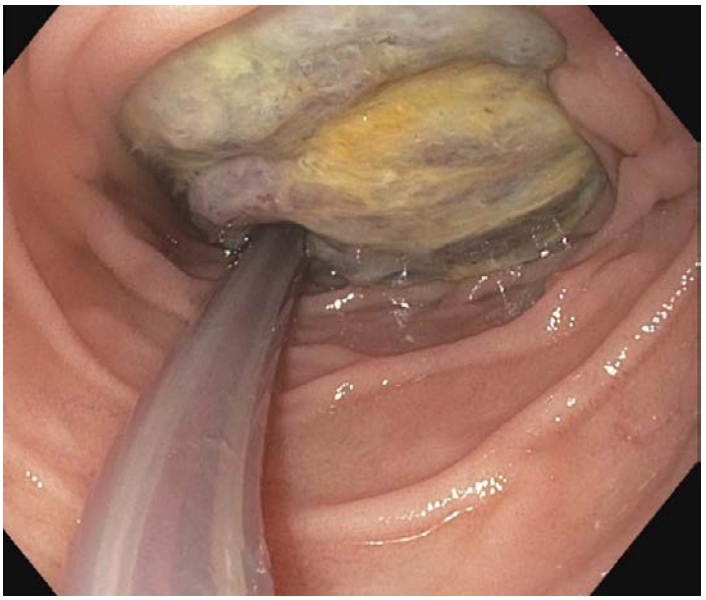

Figure 2. Endoscopy of duodenum shows the proximal portion of complex mass at the level of the second duodenum, and nasoenteric tube.

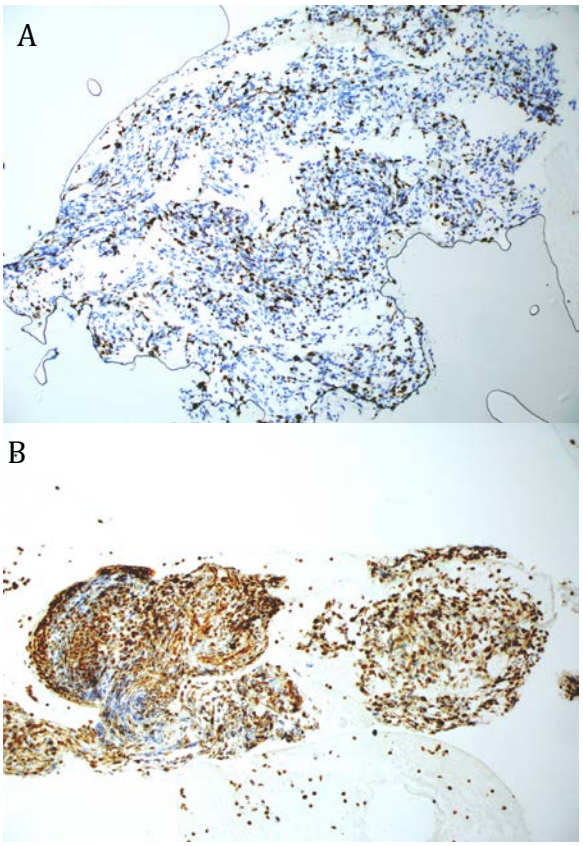

Figure 3. Pathology of duodenal mass biopsy. A shows proliferation of short spindle cells that exhibit high nuclear-to-cytoplasmic ratio and mild to moderate nuclear pleomorphism (H&E, 20x magnification). B shows Ki-67 stain with positive proliferative index in ~40% of tumor cells, suggesting a high grade neoplasm.

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