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Ileal Adenocarcinoma Presenting with Krukenberg Metastasis to Ovaries- Description of a Rare Case with Review of Literature

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Abstract Adenocarcinoma of the small intestine is one of the most uncommon gastrointestinal malignancies, comprising <5% of all GI cancers. Krukenberg tumors are also uncommon, making up only 3-5% of ovarian malignancies. We are reporting a rare case of a patient with small bowel adenocarcinoma presenting with Krukenberg metastasis. A 79-year-old female initially presented with abdominal pain and diarrhea and was found to have a long segment of irregularly thickened distal ileum suspicious for malignancy. The patient was unable to maintain consistent follow-up for almost a year after which she presented with early satiety, abdominal bloating, palpable abdominal mass and 20 lb weight loss. US and CTAP now revealed a large complex cystic mass in the pelvis with persistent bowel wall thickening and elevated CA- 125 tumor marker. The site of origin could not be determined on FNA biopsy so the patient underwent surgical resection with pathology showing adenocarcinoma of the ileum with metastatic involvement of the right ovary (Krukenberg metastasis). Molecular somatic mutation testing showed microsatellite instability (MSI-High status). She completed 12 cycles of consolidative chemotherapy with FOLFOX and currently remains in remission on pembrolizumab maintenance.This case highlights the rarity of presentation, diagnostic challenges and successful treatment of patients with ileal adenocarcinoma presenting with Krukenberg metastasis.

Keywords: *Ileal adenocarcinoma, Krukenberg metastasis, Debulking surgery, Immune checkpoint inhibitor*

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1. Introduction

Adenocarcinoma of the small intestine is one of the most uncommon gastrointestinal malignancies, comprising <5% of all GI cancers. Small bowel adenocarcinomas most commonly occur in the duodenum with a decreasing frequency distally.[1] Krukenberg tumor refers to metastatic involvement of ovaries from a primary tumor elsewhere, typically from stomach and colon adenocarcinomas. Krukenberg tumors are also uncommon, making up around 3-5% of ovarian malignancies. [2] We are reporting a rare case of a patient with small bowel adenocarcinoma presenting with Krukenberg metastasis.

2. Case Presentation

Our patient is a 79-year-old female with a past medical history of pulmonary embolism, on apixaban, remote history of resected pituitary adenoma, parathyroid adenoma treated with parathyroidectomy, hypertension, diabetes, and hyperlipidemia who initially presented to the hospital with two days of cramping lower abdominal pain and non-bloody loose bowel movements. Before this patient had been in her usual state of health. She denied vomiting, fever, chills, hematochezia, melena, unintentional weight loss, sick contacts, hematuria, or dysuria. Other than asymptomatic diverticulosis, the patient did not have any history of chronic gastrointestinal disorders such as Crohn's disease or celiac disease. There

was no family history of malignancy. The patient denied smoking, alcohol use, or any other toxic habits.

On admission, Computed Tomography of Abdomen and Pelvis (CTAP) was done which showed a long segment of irregularly thickened distal ileum, suspicious for malignancy. The infectious workup was negative. Colonoscopy was done for further evaluation which showed a tubular adenoma in the descending colon and unremarkable distal ileum with difficulty advancing the scope to the area of interest. The patient‘s history of pituitary and parathyroid adenomas with a new mass in the ileum raised the possibility of a neuroendocrine tumor. Initial workup for tumor markers including Chromogranin A, 24-hour urine 5-Hydroxyindoleacetic acid (5-HIAA), alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), lactate dehydrogenase (LDH) and cancer antigen -125 (CA-125) came back negative. An Octreotide scan was done which showed non-specific tracer uptake in the ileocolic region. At this point, the patient was lost to follow-up.

She presented again five months later when repeat CTAP demonstrated persistent proximal ileal mass-like thickening now with exophytic extension into the mesentery. The scan also noted new findings of distorted, lobulated, and enhancing appearance of the right adnexa. A transvaginal ultrasound evaluation was done which showed an enlarged right ovary with solid lesions. The patient was unfortunately again lost to follow-up at this time.

She then presented one year later with early satiety, abdominal bloating, incomplete bladder emptying, and 20 lb weight loss. Abdominal exam was notable for a firm palpable, ill-defined mass in the lower quadrant. Pelvic ultrasound revealed a large complex cystic mass in the pelvis (16.9 cm x 10.6 cm) appearing to displace the uterus anteriorly suggesting the possibility of ovarian origin (**Figure 1**). The same mass was demonstrated on CTAP along with circumferential bowel wall thickening involving the cecum, ascending colon, and proximal transverse colon. CA-125 level was elevated at 456U/ml, CA 19-9 and CEA were within normal limits. Fine needle aspiration (FNA) of the pelvic mass was attempted which revealed atypical glandular cell neoplasm with immunohistochemical stain positive for CDX2 indicative of mucinous neoplasm of Mullerian or GI origin. The site of origin could not be delineated further given the limited biopsy specimen from FNA.

The patient eventually underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, small bowel (ileal) resection and partial sigmoidectomy. Histopathologic evaluation (Figure 2, Figure 3) showed invasive well to moderately differentiated adenocarcinoma of the ileum with metastatic involvement of 1/14 lymph nodes and right ovary (Krukenberg metastasis). Immunohistochemical stains revealed CDX2 and CK 20 positivity favoring adenocarcinoma of intestinal origin. Based on TNM criteria she was diagnosed with Stage IV malignancy (T4N1M1). Molecular somatic mutation testing showed loss of nuclear expression at MLH1 and PMS 2 loci, consistent with microsatellite instability (MSI-High status). The patient also had a high tumor mutation burden (TMB) >10. Germline mutation testing was unremarkable and Lynch syndrome was ruled out.

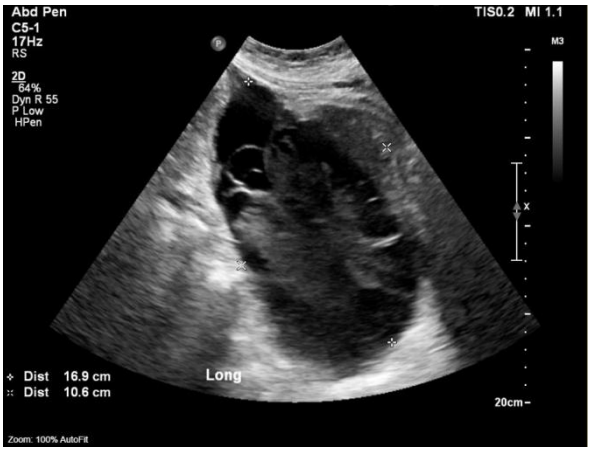

Figure 1. Pelvic ultrasound (prior to surgery) demonstrating a large complex cystic mass in the pelvis (16.9 cm x 10.6 cm)

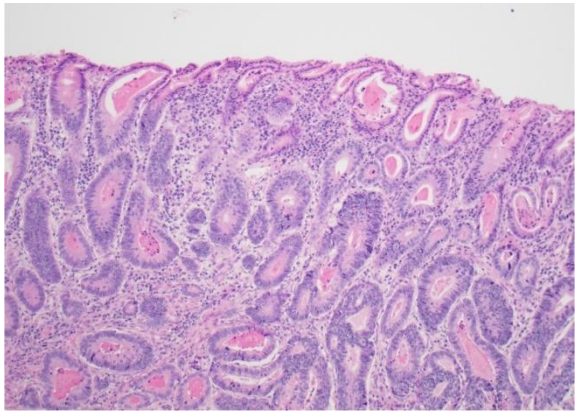

Figure 2. Hematoxylin and Eosin (H&E) stained slide of ileal resection specimen, 100x

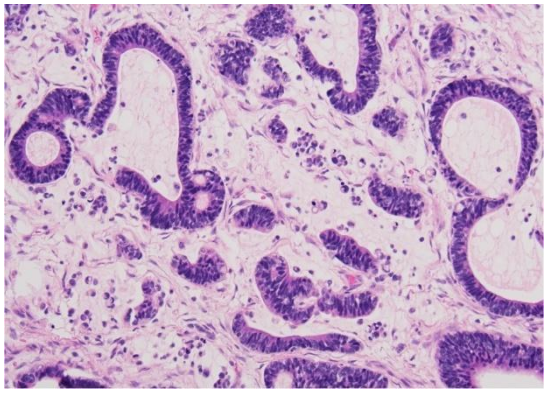

Figure 3. Hematoxylin and Eosin (H&E) stained slide of right ovary specimen, 100x

CTAP done six weeks postoperatively showed a heterogenous inferior pelvic collection with air, up to 7.5 cm with an interval decrease in size (Figure 4). CA-125 levels came down to normal limits. After a multidisciplinary team meeting, a decision was made to start the patient on consolidative chemotherapy. She completed 12 cycles of chemotherapy with FOLFOX (5-fluorouracil, leucovorin, and oxaliplatin) regimen. Oxaliplatin had to be held after cycle 5 due to development of Grade 3 neuropathy. Repeat CTAP was done after completion of the chemotherapy regimen to assess treatment response which showed left hemi-pelvic soft tissue mass (2.4 x 2.1 cm) which was concerning for

recurrent versus residual disease (Figure 5). Given MSI-High status, the patient was started on maintenance therapy with immune checkpoint inhibitor pembrolizumab 200 mg IV every three weeks. She is currently more than two years out from the time of diagnosis and clinically remains asymptomatic on maintenance therapy with excellent functional status. The most recent positron-emission tomography (PET) scan shows no abnormal metabolism in the residual 1.3 x 2 cm mass in the left pelvis. CA-125 levels have consistently been within normal reference range. (Figure 6)

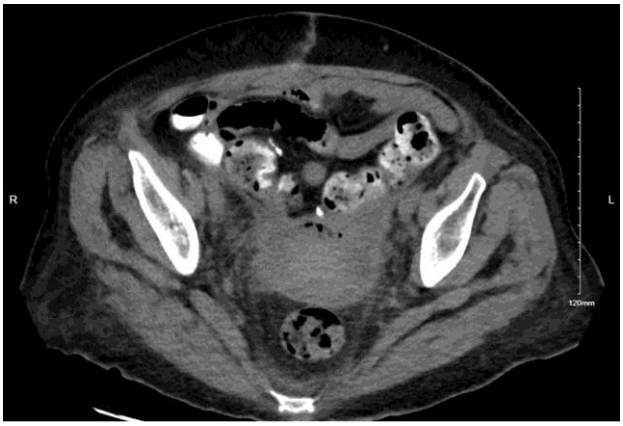

Figure 4. CT Abdomen and Pelvis done after debulking surgery, before the patient received chemotherapy. There is heterogeneous inferior pelvic collection with air 7.5 x 5.2cm

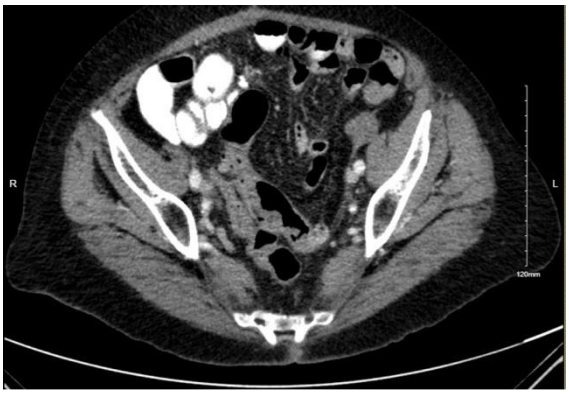

Figure 5. CT abdomen and pelvis with contrast post chemotherapy showing 2.4 x 2.1 cm soft tissue mass in the left hemipelvis posterior to bowel and anterior to the left external iliac vessels

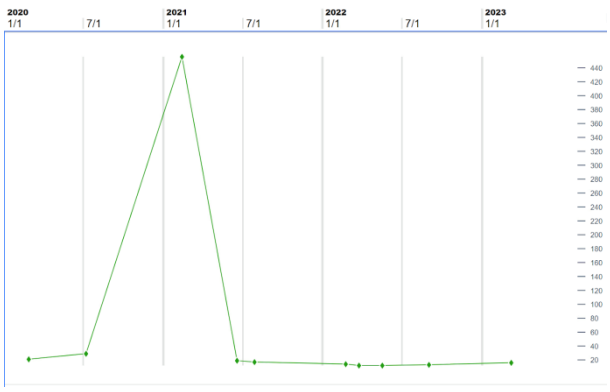

Figure 6. Graph showing CA-125 tumor marker trend. Note sharp drop in CA-125 level from 456 U/ml to 19 U/ml after debulking surgery.

3. Discussion

This case highlights the rarity of presentation and This case highlights the rarity of presentation and challenges associated with the diagnosis and management of a patient with ileal adenocarcinoma and Krukenberg metastasis. Adenocarcinoma of the small intestine is one of the most uncommon gastrointestinal malignancies, comprising <5% of all GI cancers. Out of these, 54% of cases are seen in the duodenum, 28% in the jejunum, and only 18% in the ileum, making ileal adenocarcinoma a rare entity. [1] Krukenberg tumors are also uncommon, making up around 3-5% of ovarian malignancies. [2]. Clinical manifestations of Krukenberg tumors are nonspecific and include abdominal pain, urinary frequency, dysuria, weakness, and weight loss. On seeding of the peritoneum, ascites is also seen. Most patients however are asymptomatic in the early stages, which leads to delayed diagnosis and high morbidity and mortality. On CT scan, Kukenberg tumors appear as bilateral, solid lesions with foci of hemorrhage and necrosis; however cystic lesions may also be seen. [3] This results in difficulty differentiating metastatic tumors from primary ovarian tumors on the basis of imaging alone. Careful radiologic and endoscopic examination of the gastrointestinal tract is required to locate primary malignancy upon diagnosis of Krukenberg tumor; as it may be missed initially. On light microscopy, Krukenberg tumors show signet ring cell morphology with cells arranged in clusters or nests. Large extracellular lakes of mucin are also noted. Immunohistochemistry can be used to confirm metastasis from the intestine; markers for which include CK7, CDX2, and CK20. [4]

In our case, the ovarian primary could not be excluded on imaging due to the predominant involvement of the organ with metastasis and even fine-needle aspiration cytology was not sufficient to make the diagnosis. Hence, debulking surgery was required for accurate diagnosis and staging of ileal adenocarcinoma with Krukenberg metastasis.

After a detailed literature review, only two other similar cases were found.

The first case (Iwata N. et al) is that of a 59-year-old female with Lynch syndrome in whom imaging revealed an ovarian mass. Hysterectomy and salpingo-oophorectomy were performed and an ileal tumor was seen during surgery. Partial ileal resection was performed and post-op capecitabine and oxaliplatin were given. [5]

The second case (Sakpal et al) describes an ovarian metastasis arising from a primary in Meckel's diverticulum in a 56-year-old female. Hysterectomy and bilateral salpingo-oophorectomy were performed. An ulcerative mass was seen in the tip of the Meckel's diverticulum. Right hemicolectomy with the removal of 32cm of small bowel was performed. [6]

Our patient‘s history of pituitary and parathyroid adenomas with a new mass in the ileum was initially concerning for a neuroendocrine tumor. While neuroendocrine tumors commonly present with hepatic metastasis, rare cases of ovarian metastasis have also been described in literature. [7]

As seen in our patient, treatment includes a combination of initial debulking surgery followed by postoperative chemotherapy. Resection of primary intestinal malignancy, bilateral salpingo-oophorectomy, and hysterectomy should be considered for optimal surgical debulking. While surgery is not the standard of care for Stage IV cancers, final diagnosis, and staging in this case was possible only after debulking surgery was performed. Perhaps, metastasectomy could have been a less aggressive mode of diagnosis in such rare cases.

The most commonly used regimen for consolidative chemotherapy is FOLFOX (oxaliplatin, 5-fluorouracil, leucovorin) or CAPEOX (capecitabine, oxaliplatin).[8] Other chemotherapy regimens include paclitaxel + carboplatin or docetaxel + carboplatin. [9] Clinical trials for immunomodulation and anti-EGFRs are currently underway. [10]

The current prognosis of patients with Krukenberg tumors remains poor. The average survival time since diagnosis is less than 10 months. The 2-year survival rate is only 20%. [11] MSI-H status and TMB >10 noted on molecular testing in our patient allowed the opportunity to treat with targeted immune checkpoint inhibitor (ICI) pembrolizumab. [12,13] Patient demonstrated a remarkable response and currently remains in remission on maintenance pembrolizumab therapy. Our current management plan is to continue treatment with pembrolizumab for a total of two years after which the patient will be followed for surveillance per NCCN guidelines.

In conclusion, we present a rare case of Krukenberg metastasis arising from primary ideal adenocarcinoma where the patient demonstrated excellent response to surgery followed by chemotherapy and ICI treatment. Due to the rarity of these malignancies, more such case reports must be published in order to improve the availability of information and patient outcomes.

References

[1] Chow JS, Chen CC, Ahsan H, et al. A population-based study of the incidence of malignant small bowel tumours: SEER, 1973-1990. Int J Epidemiol 1996;25:722-8.

[2] Holtz F. Hart WR. Krukenbers tumors of the ovary: a clinicopathologic analysis of 27 cases. Cancer 1982; 50: 2438-47.

[3] Bartalena T, Rinaldi M, Alboni C. Giannelli G Leoni C. Rinaldi C. Krukenberg tumor from gastric adenocarcinoma: CT findings. Internet J Radiol 2009;10(1).

[4] Al-Agha Osama M, Nicastri Anthony D. An in-depth look at Krukenberg tumor: an overview. Arch Pathol Lab Med 2006;130(11):1725-30.

[5] Iwata N, Shikama A, Takao W, Hosokawa Y, Itagaki H, Tasaka N, Akiyama A, Ochi H, Minaguchi T, Arita M, Noguchi E, Moriwaki T, Satoh T. Ovarian metastases from ileum cancer in a patient with germline EPCAM gene deletion successfully treated with surgical resection and CAPOX chemotherapy: a case report. BMC Med Genet. 2020 Apr 9;21(1):76.

[6] Sakpal SV, Babel N, Pulinthanathu R, Denehy TR, Chamberlain RS. Krukenberg tumor: metastasis of Meckel's diverticular adenocarcinoma to ovaries. J Nippon Med Sch. 2009 Apr;76(2):96-102

[7] Montoriol PF, Boudinaud C. Ovarian metastases from ileal neuroendocrine tumour: Multimodality imaging. J Med Imaging Radiat Oncol. 2019 Jun;63(3):349-351.

[8] Benson AB, Venook AP, Al-Hawary MM, Arain MA, Chen YJ, Ciombor KK, Cohen SA, Cooper HS, Deming DA, Garrido-Laguna I, Grem JL, Hoffe SE, Hubbard J, Hunt S, Kamel A, Kirilcuk N, Krishnamurthi S, Messersmith WA, Meyerhardt J, Miller ED, Mulcahy MF, Nurkin S, Overman MJ, Parikh A, Patel H, Pedersen KS, Saltz LB, Schneider C, Shibata D, Skibber JM, Sofocleous CT, Stoffel EM, Stotsky-Himelfarb E, Willett CG, Johnson-Chilla A, Gregory KM, Gurski LA. Small Bowel Adenocarcinoma, Version 1.2020, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2019 Sep 1;17(9):1109-1133.

[9] Duerr D, Ellard S, Zhai Y, Taylor M, Rao S. A Retrospective Review of Chemotherapy for Patients with Small Bowel Adenocarcinoma in British Columbia. J Cancer. 2016 Nov 25;7(15):2290-2295.

[10] Zaaimi Y, Aparicio T, Laurent-Puig P, et al. Advanced small bowel adenocarcinoma: Molecular characteristics and therapeutic perspectives. Clin Res Hepatol Gastroenterol 2015;40:154 60

[11] Yook Jeong H, Oh Sung T, Kim Byung S. Clinical prognostic factors for ovarian metastasis in women with gastric cancer. HeDato Gastroenterology 2006:54(75):955-9.

[12] Marabelle A, Le DT, Ascierto PA, Di Giacomo AM, De Jesus-Acosta A, Delord JP, Geva R, Gottfried M, Penel N, Hansen AR, Piha-Paul SA, Doi T, Gao B, Chung HC, Lopez-Martin J, Bang YJ, Frommer RS, Shah M, Ghori R, Joe AK, Pruitt SK, Diaz LA Jr. Efficacy of Pembrolizumab in Patients With Noncolorectal High Microsatellite Instability/Mismatch Repair-Deficient Cancer: Results From the Phase II KEYNOTE-158 Study. J Clin Oncol. 2020 Jan 1;38(1):1-10.

[13] Marcus L, Fashoyin-Aje LA, Donoghue M, Yuan M, Rodriguez L, Gallagher PS, Philip R, Ghosh S, Theoret MR, Beaver JA, Pazdur R, Lemery SJ. FDA Approval Summary: Pembrolizumab for the Treatment of Tumor Mutational Burden-High Solid Tumors. Clin Cancer Res. 2021 Sep 1;27(17):4685-4689.