

Skull Base Metastasis and Krukenberg Tumor in a Pregnant Woman: An Unusual Presentation of Metastatic Gastric Cancer

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ABSTRACT

Gastric cancer is an infrequent cause of vomiting during pregnancy. It is often diagnosed at an advanced stage due to late presentation by patients, mistaking it for gestational symptoms. We report a 24-year-old pregnant woman with gastric cancer with skull base metastasis and Krukenberg tumor on initial diagnosis. She underwent medical termination of pregnancy and best supportive care before dying of her illness.

KEYWORDS: Krukenberg tumor; skull base; stomach neoplasms; pregnancy

INTRODUCTION

Pregnancy-associated gastric cancer complicates 0.026% to 0.1% of all pregnancies.¹ The symptoms during early pregnancy may mimic that of gastric cancer.² Endoscopy is not routinely performed for gastrointestinal symptoms during early pregnancy. Hence, there is a risk of diagnosing gastric cancer at an advanced stage. Krukenberg tumor (KT) occurs in 5% to 10% of female patients with gastric cancer.³ By contrast, skull base metastasis (SBM) is extremely rare in gastric cancer, and to date, only 3 cases have been reported in the literature.^{4–6} We report a pregnant woman with gastric cancer with skull base metastasis and KT on initial diagnosis.

CASE REPORT

A 24-year-old woman, primigravida in 16 weeks gestation, presented with double vision for the past 3 days. She had recurrent vomiting, diffuse abdominal pain, reduced oral intake, and a weight loss of 10 kg over the past 2 months. She did not have fever, headache, blurred vision, weakness of limbs, or seizures. There was no history of trauma. Her medical history was unremarkable. None of her family members had any gastrointestinal disease. On examination, she was ill-nourished and anemic. Her best corrected visual acuity was normal in both eyes. She had a restriction of abduction in the right eye, but the rest of the extraocular movements were normal (Figure 1). Pupillary reaction and corneal sensation were normal in both eyes. Fundus examination did not reveal papilledema. The findings suggest abducent nerve palsy on the right side. Examination of other cranial nerves was normal. Abdominal examination showed a 6 × 6 cm hard mass in the epigastrium and free fluid. Laboratory evaluation revealed microcytic and hypochromic anemia with hemoglobin 71 g/L (120–150 g/L), white cell count $4.8 \times 10^9/L$ ($4.5–11 \times 10^9/L$), platelet count $335 \times 10^9/L$ ($150–450 \times 10^9/L$), and decreased serum total protein and albumin levels 54 g/L (60–80 g/L) and 21 g/L (35–50 g/L), respectively.

An abdominal ultrasound scan showed a gravid uterus and thickening of the antropyloric region of the stomach, enlarged ovaries, and ascites. Abdominal paracentesis was performed, which revealed malignancy cells on cytology. The patient and her family members were not willing to continue the pregnancy; hence, medical termination was performed because of advanced malignancy.



Figure 1. Restriction of abduction in the right eye.

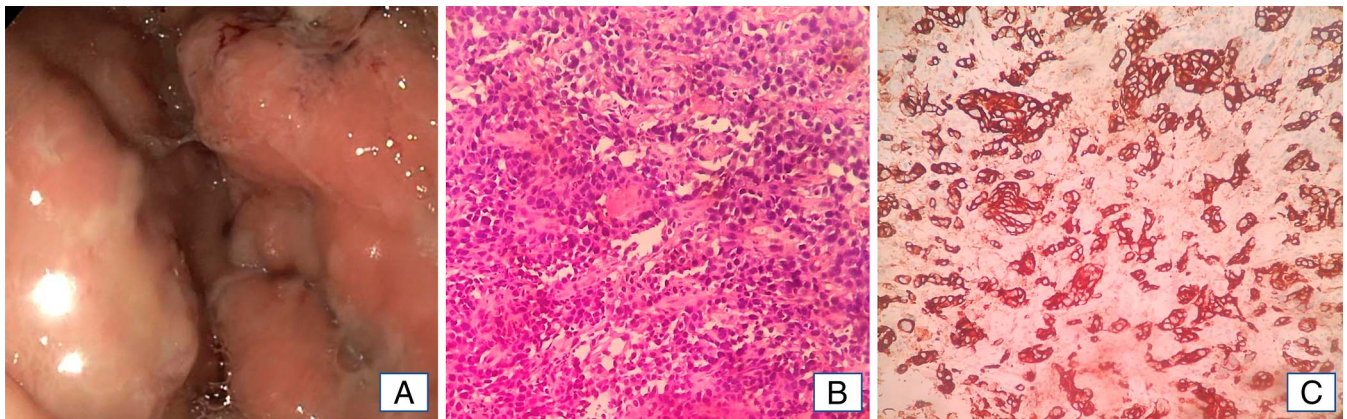


Figure 2. (A) Gastroscopy image showing ulceroproliferative growth with luminal narrowing in the antrum/pyloric region. (B) Photomicrograph of biopsy from antrum/pyloric growth showing features of poorly differentiated adenocarcinoma (hematoxylin and eosin stain, 20× magnification). (C) Photomicrograph of immunohistochemistry showing cytokeratin-positive tumor cells (cytokeratin stain, 20× magnification).

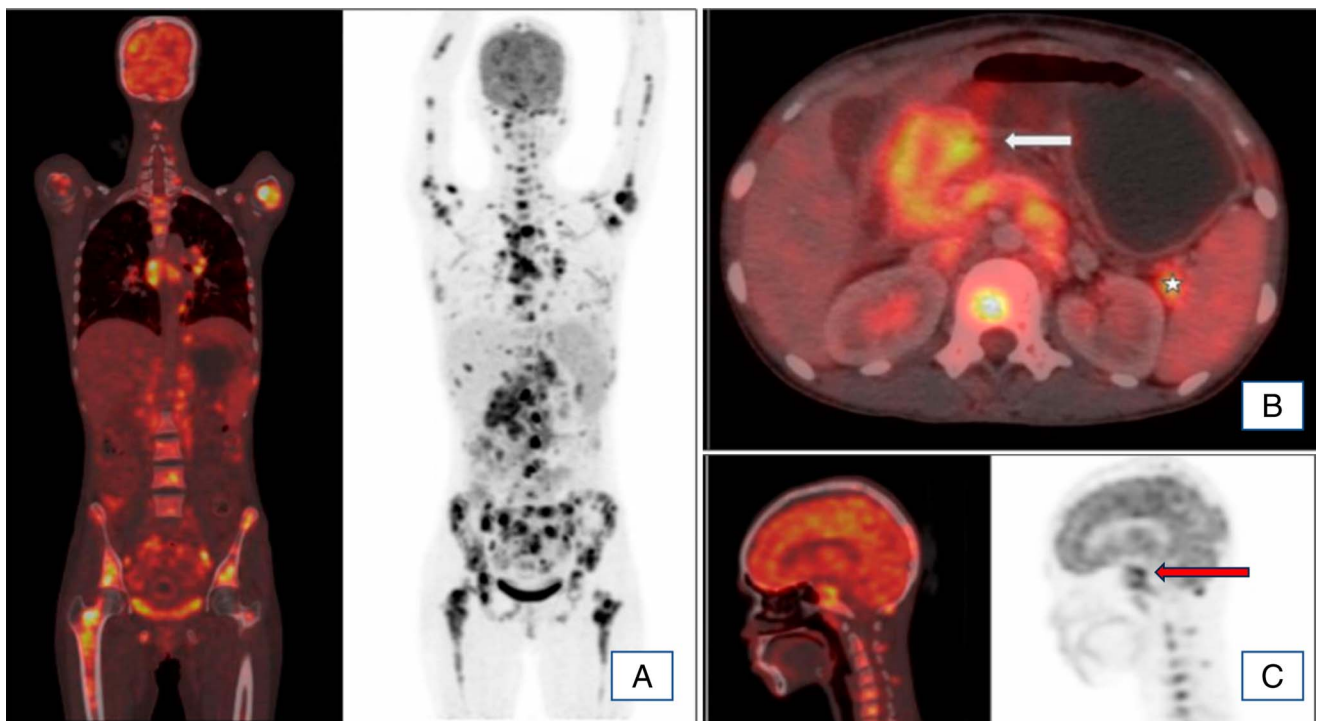


Figure 3. PET-CT images (fused PET/CT and maximum intensity projection). (A) Images in coronal views showing increased FDG uptake in lytic lesions, extensively involving the axial and proximal appendicular skeleton. (B) Images showing metabolically active diffuse circumferential wall thickening involving the antrum/pyloric region of the stomach (white arrow), perigastric lymph nodes, and a splenic hilar lymph node (white star). (C) Images in sagittal view showing increased FDG uptake in the skull base and sella turcica region (red arrow). PET-CT, positron emission tomography-computed tomography.

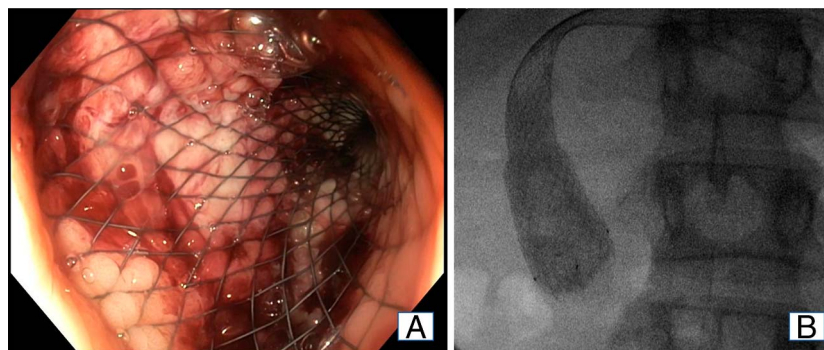


Figure 4. (A) Gastroscopy image showing the self-expanding metallic stent in the antropyloric region. (B) Fluoroscopy image of the self-expanding metallic stent.

Table 1. Summary of previous reported cases of gastric cancer with skull base metastases

Case report	Age (yr)/sex	Presenting feature	History	Course
Hirai et al, 1992 ⁴	48/male	Double vision	No gastrointestinal symptom on diagnosis	Underwent transsphenoidal hypophysectomy followed by chemotherapy
Fukushima et al, 2012 ⁵	64/male	Headache, double vision	Presented 10 yr after surgery for gastric cancer	Underwent endoscopic transsphenoidal resection of solitary clival metastasis
Yoshikawa-Kimura et al, 2020 ⁶	73/male	Headache, tongue deviation, difficulty in speaking	Presented after 1 yr of chemotherapy for gastric cancer	Underwent palliative radiotherapy, and symptoms improved

Gastroscopy revealed ulceroproliferative growth in the antropyloric region, causing luminal narrowing (Figure 2). Histopathological examination showed poorly differentiated carcinoma, with immunohistochemistry suggesting cytokeratin 7-positive and CD 20 and CDX2-negative (Figure 2). A positron emission tomography-computed tomography scan revealed increased FDG uptake in the antropyloric region of the stomach, sella turcica, clivus occipital bone, humerus, clavicle, sternum, ribs, multiple vertebrae, cervical, mediastinal, abdominal and pelvic nodes, peritoneum, omentum, and bilateral ovaries (Figure 3). Based on the above investigations, we diagnosed gastric cancer with metastases to the skull base and multiple sites of the axial and appendicular skeleton and KT. The abducent nerve palsy was attributable to parasellar metastasis because no other neurological disease was evident in this patient. She underwent an antropyloric self-expanding metallic stent placement for gastric outlet obstruction and received best supportive care (Figure 4). However, she died of her illness 2 months later.

DISCUSSION

The most common cancers diagnosed during pregnancy arise from the breast and cervix and even may be hematological.⁷ Gastric cancer is very rarely encountered during pregnancy.¹ The symptoms, namely nausea, vomiting, and fatigue, may be misinterpreted as early gestational symptoms. Hence, gastric

cancer is diagnosed in an advanced stage. Hence, it is associated with very poor maternal and fetal outcomes. The pathomechanisms of accelerated tumorigenesis include excess estrogen hormone and placenta-derived growth factor during pregnancy.^{8,9} KT is ovarian metastasis originating from glandular carcinomas. It constitutes 1% to 2% of all ovarian malignancies.¹⁰ The most common primary site is the stomach (76%), followed by the colon, appendix, and breast.¹¹ Patients with KT usually present with abdominal pain and ascites rather than the symptoms of the primary organ. The occurrence of KT during pregnancy is infrequent, and so far, only 44 cases have been reported in the literature.¹²⁻¹⁵

SBM has been reported in 4% of patients with cancer. The common primary site includes the prostate, breast, and lung. However, it can occur in the colon, kidney, thyroid, lymphoma, melanoma, and thyroid.¹⁶ Direct hematogenous spread and retrograde seeding from the Batson venous plexus from the pelvis are the 2 mechanisms of SBM.¹⁷ Patients with SBM are usually asymptomatic in the initial stages; they seek medical attention if they develop craniofacial pain or cranial nerve palsy.¹⁸ The manifestations usually depend on the site at which metastasis occurs. Previous reports by Greenberg et al¹⁶ showed 5 syndromes in SBM, namely orbital (7%), parasellar (16%), middle-fossa (35%), jugular foramen (16%), and occipital condyle (21%) syndromes. The sellar and parasellar metastases are observed in 29% of patients with SBM. Oculomotor cranial

neuropathy (III, IV, VI) and facial pain hypesthesia (V1, V2) occur because of cavernous sinus involvement.¹⁹

Metastasis of gastric malignancy to the skull base is extremely rare, and only 3 cases were reported to date (Table 1).⁴⁻⁶ In our case, both KT and skull base metastasis were present at initial diagnosis in a pregnant woman. Such patient management must involve a team comprising an obstetrician, gastroenterologist, surgeon, and oncologist. The critical decision to be made is regarding the continuation of pregnancy and early initiation of cancer treatment. The treating doctors should discuss management options clearly with the patient and her family before making a final decision.

In conclusion, although very rare in pregnancy, gastric cancer should be considered when features like profound weight loss and mass per abdomen are present. The associated gestational symptoms might delay the diagnosis. When in doubt, performing an endoscopy is prudent, especially in the second trimester.

DISCLOSURES

Author contributions: All authors contributed equally to this manuscript. K. Senthamizhselvan is the article guarantor.

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REFERENCES

- Sakamoto K, Kanda T, Ohashi M, et al. Management of patients with pregnancy-associated gastric cancer in Japan: A mini-review. *Int J Clin Oncol*. 2009;14(5):392-6.
- Lee HJ, Lee IK, Kim JW, Lee KU, Choe KJ, Yang HK. Clinical characteristics of gastric cancer associated with pregnancy. *Dig Surg*. 2009;26(1):31-6.
- Clinical characteristics of gastric cancer associated with pregnancy. *Dig Surg*. 2009;26(1):31-6.
- Wang J, Shi YK, Wu LY, et al. Prognostic factors for ovarian metastases from primary gastric cancer. *Int J Gynecol Cancer*. 2008;18:825-32.
- Hirai O, Kikuchi H, Hashimoto N. Skull base metastasis from gastric cancer: Case report. *Neurol Med Chir (Tokyo)*. 1992;32(12):908-10.
- Yoshikawa-Kimura A, Taira K, Katanosaka Y, et al. A rare case of clival metastasis in a patient with gastric cancer. *Intern Med*. 2020;59(24):3161-4.
- Fukushima M, Katayama Y, Shigemori Y, Miyake H, Hirayama T, Kotani A. Clivus metastasis from gastric signet ring cell carcinoma after a 10-year disease-free interval: Case report. *Neurol Med Chir (Tokyo)*. 2012;52(10):751-3.
- Pavlidis NA. Coexistence of pregnancy and malignancy [published correction appears in *Oncologist* 2002;7(6):585]. *Oncologist*. 2002;7(4):279-87.
- Harrison JD, Morris DL, Eliis IO, Jones JA, Jackson I. The effect of tamoxifen and estrogen receptor status on survival in gastric carcinoma. *Cancer*. 1989; 64(5):1007-10.
- Chen CN, Hsieh FJ, Cheng YM, et al. The significance of placenta growth factor in angiogenesis and clinical outcome of human gastric cancer. *Cancer Lett*. 2004;213(1):73-82.
- Al-Agha OM, Nicastrì AD. An in-depth look at Krukenberg tumor: An overview. *Arch Pathol Lab Med*. 2006;130(11):1725-30.
- Young R. From Krukenberg to today: The ever present problems posed by metastatic tumors in the ovary: Part I. Historical perspective, general principles, mucinous tumors including the Krukenberg tumor. *Adv Anat Pathol*. 2006;13:205-27.
- Kodama M, Moeini A, Machida H, Blake EA, Grubbs BH, Matsuo K. Feto-maternal outcomes of pregnancy complicated by Krukenberg tumor: A systematic review of literature. *Arch Gynecol Obstet*. 2016;294(3):589-98.
- Goidescu IG, Nemeti G, Preda A, et al. Krukenberg tumor in pregnancy: A rare case and review of the literature. *J Matern Fetal Neonatal Med*. 2022; 35(25):7290-5.
- Jha S, Mitra S, Patra S, Sethi P, Jena SK. Krukenberg tumor of ovary during pregnancy: Learning from a mistake. *Int J Gynecol Pathol*. 2021;40(6): 617-20.
- Greenberg HS, Deck MD, Vikram B, Chu FC, Posner JB. Metastasis to the base of the skull: Clinical findings in 43 patients. *Neurology*. 1981;31:530-7.
- Svare A, Fossa SD, Heier MS: Cranial nerve dysfunction in metastatic cancer of the prostate. *Br J Urol*. 1988;61:441-4.
- Stark AM, Eichmann T, Mehdorn HM. Skull metastases: Clinical features, differential diagnosis, and review of the literature. *Surg Neurol*. 2003;60: 219-25.
- Laigle-Donadey F, Taillibert S, Martin-Duverneuil N, Hildebrand J, Delattre JY. Skull-base metastases. *J Neurooncol*. 2005;75(1):63-9.

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