Case Report

Incidentally diagnosed Krukenberg tumor in pregnancy: A rare presentation with dismal outcome

Himani Bhankar, Surbhi Goyal, Neha Tyagi, Sufian Zaheer, Ashish Kumar Mandal

Department of Pathology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India

ABSTRACT

Krukenberg tumor is quite rare, accounting for 1–2% of all ovarian tumors. In pregnancy, its incidence is 0.4–0.5%. It is associated with very poor prognosis in pregnancy due to widespread metastasis at the time of diagnosis. We report a case of 25-year-old full term pregnant female presenting with fetal distress. Bilateral enlarged ovaries were found incidentally at the time of cesarean section. A diagnosis of Krukenberg tumor with a primary from stomach was rendered on histopathology. Our case is interesting in view of its unusual presentation, young patient age, and the diagnostic dilemma it poses. Our report highlights the fact that early diagnosis of Krukenberg tumor in pregnancy may be difficult at times owing to the masquerading effects, implying widespread metastasis and a poor maternal survival.

Key words: Gastric carcinoma, Krukenberg tumor, ovarian mass, pregnancy

INTRODUCTION

The most common malignant tumor in pregnancy is breast carcinoma followed by cervical cancer, Hodgkin's lymphoma, and ovarian carcinoma.[1,2] In pregnancy, only 3% of adnexal masses are malignant with a reported incidence of Krukenberg tumor being 0.4–0.5%. It is associated with very poor prognosis.[3] Usual presenting symptoms of Krukenberg tumor include epigastric pain, acid reflux, nausea, vomiting, and abdominal distension, which are obscured by physiological changes of pregnancy.[4] Possible primary sites include stomach, breast, gastrointestinal tract, urinary bladder, gall bladder, biliary tract, pancreas, and uterine cervix.[5] Because of rarity, nonspecific symptoms and lack of established treatment guidelines for these tumors in pregnancy, they often pose a challenge to the obstetricians and pathologists in terms of early diagnosis and management. Our case is interesting because of the fact that such a large Krukenberg tumor of 12 cm was missed during routine antenatal investigations in a young female owing to the masquerading effects of pregnancy.

CASE REPORT

A 25-year-old unbooked pregnant female with parity$_1$ and no live issue, presented to emergency of Obstetrics and Gynaecology Department at 40 weeks + 4 days gestation with reduced fetal movements. No previous ultrasound or antenatal records were available at the time of admission. On examination, abdominal tenderness was present and fetal heart rate was 80 beats/min. Nonstress test was performed which was nonreactive. In view of persistent fetal bradycardia and fetal distress, the patient was taken up for emergency caesarean section. A healthy baby boy

Address for correspondence: Dr. Surbhi Goyal,
Department of Pathology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi - 110 095, India.
E-mail: dr.surbhi4you@gmail.com

Access this article online

Quick Response Code:

Website: www.ccij-online.org

DOI: 10.4103/2278-0513.176242

Cite this article as: Bhankar H, Goyal S, Tyagi N, Zaheer S, Mandal AK. Incidentally diagnosed Krukenberg tumor in pregnancy: A rare presentation with dismal outcome. Clin Cancer Investig J 2016;5:196-9.

delivered. Per operatively, both ovaries were enlarged, and there were massive ascites along with mental caking. One liter of straw colored ascitic fluid was drained out which was sent for cytological examination. Right ovary measured 12 cm × 11 cm × 7 cm and left ovary measured 2 cm × 2 cm × 1 cm. Right sided oopherectomy with right salpingectomy was done. Biopsy was taken from the left ovary and omental nodule and sent for histopathological examination. A provisional diagnosis of malignant adnexal mass was made.

We received a specimen of the enlarged ovary with a boss elated surface measuring 12 cm × 11 cm × 7 cm [Figure 1]. Attached fallopian tube measured 4 cm in length. On cut tumor was gray, white, solid, homogenous, and firm with few myxoid areas [Figure 1]. On histopathological examination, almost whole of the ovary was replaced by sheets and lobules of tumor cells separated by fibrous stroma [Figure 2]. The capsular breach was noted. Tumor cells were predominantly round, had abundant clear to the vacuolated cytoplasm with elongated eccentrically pushed hyperchromatic nuclei giving a "signet ring appearance" [Figure 2]. Intracytoplasmic mucin was confirmed by positivity for Alcian blue and mucicarmine. Few mitosis including atypical forms was seen. Fallopian tube was histologically unremarkable. Biopsy from the contralateral ovary and omentum showed infiltration by sheets of similar tumor cells. Morphological features were suggestive of Krukenberg tumor with omental metastasis. On immunohistochemistry, tumor cells showed cytoplasmic positivity for cytokeratin (CK) 7, CK 20, MUC-1, MUC-5AC and were negative for vimentin and synaptophysin [Figure 3]. A final diagnosis of Krukenberg tumor with possible primary from gastrointestinal tract was suggested. Serum carcino embryonic antigen, lactate dehydrogenase, and placental alkaline phosphatase were within normal limits. X-ray chest, contrast-enhanced computed tomography abdomen, and mammography were unremarkable. Gastric biopsy confirmed the diagnosis of diffuse type adenocarcinoma. Ascitic fluid was negative for malignant cells. Postoperative period was uneventful. The patient was referred to medical oncology department for chemotherapy, but she refused any further treatment and was lost to follow-up.

DISCUSSION

Incidence of Krukenberg tumor in pregnancy is rare (0.4–0.5%). On literature search in PubMed, around 50 cases have been documented in pregnancy [Table 1]. Many of these are from Japan due to the high incidence of gastric carcinoma. Only two cases have been reported from Indian subcontinent until date.

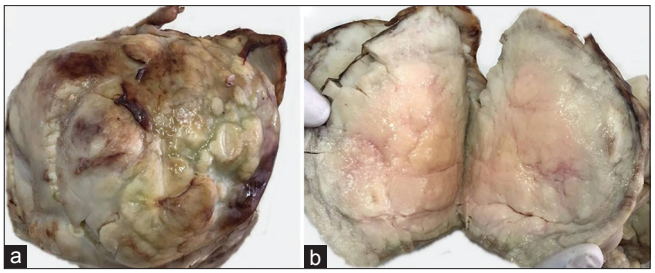

Figure 1: Gross photograph of right ovary with attached fallopian tube (a) external surface is bosselated with multiple nodules outside the capsule. Focal areas of congestion seen (b) cut surface shows a gray white homogenous tumor with focal myxoid areas

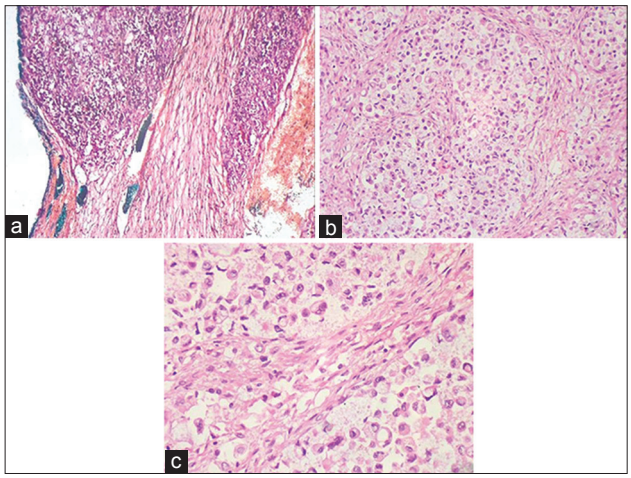

Figure 2: Microscopic examination shows (a) capsular breech by tumor nodule (H and E, ×40) (b) tumor cells arranged in lobules and nests separated by fibrous septa (H and E, × 100) (c) Higher magnification shows round to oval tumor cells having abundant clear cytoplasm (mucin) and peripherally pushed nuclei, giving a "signet ring" appearance (H and E, ×400)

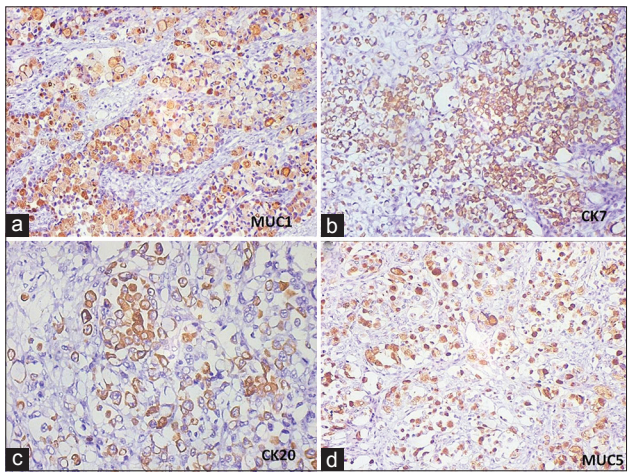

Figure 3: Immunohistochemistry tumor cells show cytoplasmic positivity for (a) MUC-1, (b) cytokeratin 7, (c) cytokeratin 20, (d) MUC-5

There are no current standardized guidelines for diagnosis and treatment of this tumor in pregnancy due to its rarity.[1] Abdominal distension due to the growing fetus often masks the presence of metastatic ovarian tumor in the pelvic cavity. Thus, it is difficult to establish an early diagnosis

Table 1: Review of reported cases of Krukenberg tumor in pregnancy with a primary gastric carcinoma

Symptoms	Total number of reported cases (*n*=50)
Epigastric pain, nausea and vomiting, bloating	42
Maternal virilization (rapid onset)	05
Rapid increase in abdominal girth	03
Diagnostic criteria	
Signet ring morphology	50
Supportive findings	
Mucin positivity	09
Raised CEA	03
Raised CA-125	05
CK7/CK20 positivity	03
Radiology-ultrasound/CT scan	38
Outcome	
Healthy fetus	49
Fetal demise	01
Maternal outcome (average survival) (months)	6-12
Decision	Delivery of baby Platinum-based chemotherapy Salpingooopherectomy and gastrectomy in resectable tumor

CEA: Carcinoembryonic antigen, CA: Cancer antigen, CT: Computed tomography, CK7: Cytokeratin 7, CK20: Cytokeratin 20

during the antenatal period.[6] The role of endoscopy and gastric biopsy has been proposed in females complaining of persistent epigastric symptoms in the second trimester of pregnancy, especially if it is accompanied with weight loss and hemoptysis.[7]

Differential diagnosis of a solid ovarian mass includes sex cord stromal tumor, primary signet-ring stromal tumor, Krukenberg tumor, yolk sac tumor, and malignant epithelial ovarian tumor. Lack of necrosis, hemorrhage, and variegated appearance, and presence of a bilateral ovarian mass in a 25-year-old female excluded the possibility of yolk sac tumor and malignant epithelial tumor. Bilateral enlarged ovaries with a homogenous solid gross appearance as was seen in our case favors the differential diagnoses of Krukenberg tumor and sex cord stromal tumor. Characteristic signet ring cell morphology with intracytoplasmic mucin narrowed to two possibilities Krukenberg and primary signet-ring stromal tumor. Primary signet-ring stromal tumors are mostly unilateral and are nonreactive to mucins and CK.

On literature review, very few authors had resorted to immunohistochemistry as most of the authors had relied on radiological investigations to search the primary [Table 1]. A panel of immunohistochemical markers is helpful in identification of the possible primary. Common sites of primary in Krukenberg in the descending order of frequency include stomach (76%), appendix/colorectum (11%), breast (4%) and gallbladder/biliary tract (3%).[8] CK7 positivity excluded the possibility of appendiceal/colorectal carcinoma in our case. We excluded the possibility of primary breast carcinoma on the basis of CK7 and CK20 positivity. CK7/CK20 positive immunophenotype along with MUC-5AC positivity suggests a primary from the stomach or hepatobiliary tract. Since the reported incidence of primary in gallbladder and biliary tract in Krukenberg is very less (3%), the possibility of the stomach was suggested.

MUC-5AC is a gastric mucin gene found in surface foveolar cells. In gastric carcinomas, MUC-5AC positivity is related to good prognosis and low tumor stage.[9] Apart from gastric carcinoma, MUC-5AC expression is seen in primary ovarian mucinous carcinoma (97.2%), pancreatic adenocarcinoma (94.4%), lower gastrointestinal tract (42.9%) and biliary tract (16.7%).[10]

The management of tumor depends on gestational age, the desire of patient, site of primary and tumor stage. Debulking surgery including partial or total gastrectomy, lymph node dissection and bilateral oophorectomy with platinum-based chemotherapy are relatively safe and can be implemented during early weeks of pregnancy.[1] However if the diagnosis is made during the third trimester of pregnancy, the caesarean section must be done to deliver the fetus followed by chemotherapy and surgical resection.[3,6] There is no significant impact on fetal survival as most (97%) of the reported cases have led to the delivery of healthy baby [Table 1]. In the majority of the cases, the primary tumor remains undiagnosed until it metastasizes. Therefore, most of the patients die within 1 year with 3 years maternal survival rate of only 8%.[1,3,6] Krukenberg tumors with a primary in the stomach carry a more daunting prognosis in pregnancy due to presence of estrogen receptors in a high proportion of gastric carcinoma leading to an aggressive behavior.[11]

To conclude, we report an unusual presentation of Krukenberg tumor in a young female, which despite being of considerable size, went unnoticed during antenatal period. Our case highlights the fact that signs and symptoms of primary gastric carcinoma can be concealed due to physiological symptoms of pregnancy, leading to widespread metastasis at the time of diagnosis, implying a very poor maternal survival.

Financial support and sponsorship
Nil.

Conflicts of interests
There are no conflicts of interest.

REFERENCES

1. Dueñas-García OF, Diaz-Sotomayor M, Chanana C. Bilateral ovarian krukenberg tumor in a full-term pregnancy. ISRN Obstet Gynecol 2011;2011:620380.

2. Morice P, Uzan C, Gouy S, Verschraegen C, Haie-Meder C. Gynaecological cancers in pregnancy. Lancet 2012;379:558-69.
3. Mahfoud T, Elhassani ME, Hafidi MR, Babahabib MA, Tanz R, Khmamouche MR, *et al*. Krukenberg tumor secondary to gastric carcinoma in a pregnant woman: A case report and literature review. Biol Biomed Rep 2012;2:32-6.
4. Kim SH, Abd Halim SR, Siddiqui N, Park WH. Disseminated cancer in pregnancy: Krukenberg tumour. Case Rep Obstet Gynecol 2014;2014:216969.
5. Hatwal D, Joshi C, Chaudhari S, Bhatt P. Krukenberg tumor in a young woman: A rare presentation. Indian J Pathol Microbiol 2014;57:124-6.
6. Glisic A, Atanackovic J. Krukenberg tumor in pregnancy. The lethal outcome. Pathol Oncol Res 2006;12:108-10.
7. Jaspers VK, Gillessen A, Quakernack K. Gastric cancer in pregnancy: Do pregnancy, age or female sex alter the prognosis? Case reports and review. Eur J Obstet Gynecol Reprod Biol 1999;87:13-22.
8. Kiyokawa T, Young RH, Scully RE. Krukenberg tumors of the ovary: A clinicopathologic analysis of 120 cases with emphasis on their variable pathologic manifestations. Am J Surg Pathol 2006;30:277-99.
9. Boltin D, Niv Y. Mucins in gastric cancer – An update. J Gastrointest Dig Syst 2013;3:15519.
10. Wang J, El-Bahrawy MA. Expression profile of mucins in ovarian mucinous tumors: Distinguishing primary ovarian from metastatic tumors. Int J Gynecol Pathol 2014;33:166-75.
11. Furukawa H, Iwanaga T, Hiratsuka M, Imaoka S, Ishikawa O, Kabuto T, *et al.* Gastric cancer in young adults: Growth accelerating effect of pregnancy and delivery. J Surg Oncol 1994;55:3-6.