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DISSEMINATED CANCER IN PREGNANCY : A RARE CASE OF KRUKENBERG TUMOR

Pathology

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ABSTRACT

Krukenberg tumor (KBT) in pregnancy is very rare and its diagnosis & management can present a dilemma for clinicians. We present a case of G3P1A1L1 who presented to us at 31 weeks of gestation and developed intestinal obstruction in immediate postpartum period. She had undergone bilateral oophorectomy with removal of part of omentum, histologically favouring bilateral KBT with omental deposits. Later further workup was done to know the exact location of primary malignancy. Multiple investigations of upper GI endoscopy, colonoscopy , mammography was done followed by biopsy of splenic flexure colon growth reported as infiltrative adenocarcinoma.Final diagnosis was KBT (secondary bilateral ovarian carcinoma) , metastasizing from colon cancer with omental metastasis. On Immunohistochemistry tumor cells were positive for CD 20, CDX2 & wild type of K-Ras mutations was observed on molecular analysis. She received 6 cycles of platinum based chemotherapy with initial response to the treatment.

KEYWORDS

krukenberg tumor(KBT),K-Ras mutations, Colon cancer

INTRODUCTION

Only 1:1000 pregnancies is complicated by cancers[1] . KBT is uncommon metastatic tumor of ovary & has an extremely poor prognosis. Gastric cancer has been reported as the most frequent primary source of KBT, however tumors of the colon, appendix, breast, lung & pancreas have also been reported to metastasize to the ovaries. The symptoms of pregnancy may mask its presentation by distention, constipation, vomiting leading to delay in diagnosis. KBT usually presents in the fifth decade of life, with an average age of 45 yrs and cases diagnosed during pregnancy is extremely rare.

Case Report

A 30 year old pregnant woman, gravida-3, para-1, was admitted with unbearable abdominal pain at 31 weeks of gestation. She complied well with her antenatal schedule and had complains of mild abdominal pain & slight difficulty in passing stools at 24th week . She had previous hospital admission for similar complaints just a week before and she was treated conservatively. Her obstetric history revealed full term normal vaginal delivery of male baby three years back with uneventful course in first pregnancy. No significant family & personal history was noted. She was thin built with BMI 19 kg/m2 and grade two haemorrhoids on per rectal examination. Her routine blood investigations were within normal limits. USG findings showed gravid uterus of approx. 30th week of gestation with sub serosal and broad ligaments fibroid with mild ascites. She gave birth to a female baby 1.6 kg at 31 weeks of gestation by normal delivery. On 4th post delivery day, patient developed pain abdomen which was dull aching in nature, over centre of abdomen radiating to right lower flank associated with 1-2episodes of nausea and vomiting, of watery content . Serum amylase & liver function tests were within normal limits, which ruled out acute pancreatitis. Pain was not settled with medications and she was posted for urgent exploratory laparotomy. Intraoperative findings were ascites , bilateral adnexal mass arising from ovaries, large hard mass involving sigmoid colon and obstructions it with dense adhesions, multiple & large omental metastatic nodules. Liver appeared to be free of metastasis. Sigmoid colon biopsy could not be taken due to obstruction & adhesions. She undergone went transverse colostomy & excision of bilateral ovarian masses along with partial omentectomy. Tumor marker results were CA $_{125}$ - 80.8U/ml (↑↑), CEA -17.42 U/ml (↑). Gross findings of both ovaries were well circumscribed ,enlarged solid masses with smooth outline. omentum cut section revealed creamish white tumor deposits (Fig 1- 3).

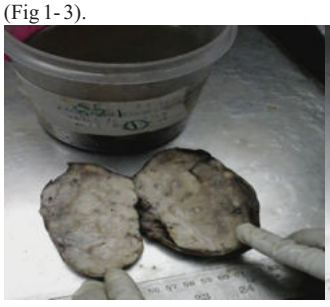

Fig1

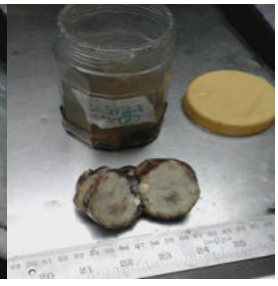

Fig2

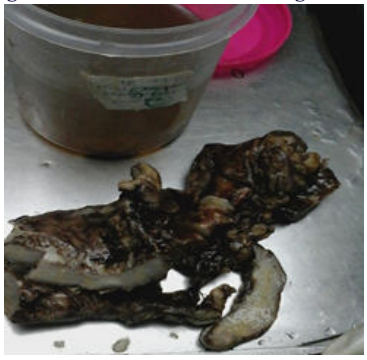

Fig3

Fig 1 – Left ovarian mass shows well circumscribed , smooth capsule. On cut section shows ovarian parenchyma replaced by creamish white growth ,lobulated and tiny cystic spaces.

Fig 2 – Right ovarian mass shows compressed normal ovary & well circumscribed tumor that findings similar to left ovarian mass.

Fig 3 – Omentum shows tan brown coloured thick fibrofatty tissue.C/S - creamish

Histopathology findings was suggestive of bilateral diffuse signet ring cell carcinoma of ovaries (Fig 4-6) with omental metastatic deposits (Fig 7) with suggested possibility of primary malignancy in gastrointestinal system.

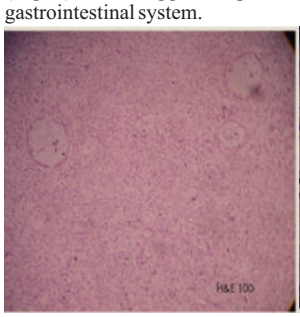

Fig 4

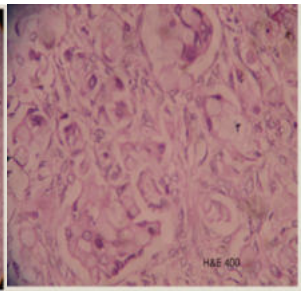

Fig 5

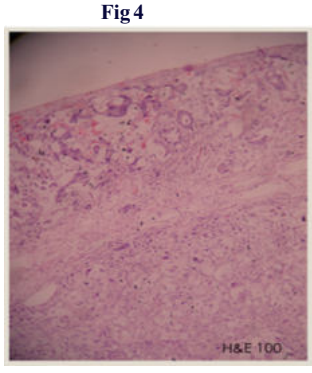

Fig 6

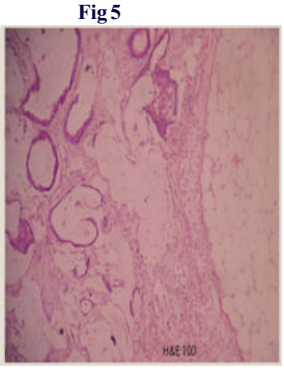

Fig 7

Fig 4 – Left ovarian mass M/E- sheets of signet ring cells & few cystic spaces filled with mucin pools.
Fig 5 – Left ovarian mass M/E - High power image shows fair no. of signet ring cells with intra & extracellular lakes of mucin.
Fig 6 – Right ovarian mass M/E- Tumor cells reached up to the capsular surface.
Fig 7- omentum invaded by part of tumor component.

PET Scan done showed extensive FDG avid peritoneal & serosal deposits in abdomen & pelvis with a 6 cmx 5 cm sized mass in left lumbar region showing areas of calcification & mild Ascites. Non FDG avid calcified iso dense lesion was noted in the left breast likely to be benign. Few non FDG avid hypo dense lesions were noted in the bilateral breasts- ? Due to lactating breast. Few infective/ inflammatory changes were noted in the left lung. Rest of the study showed physiological tracer uptake. Mammography of left breast showed irregular well defined mass measuring 2.1x2.1 cm in UO upper outer quadrant , suggested ACR-BIRADS category 4A in which biopsy was advised. And also complex cyst identified in upper central region reported as ACR-BIRADS category II (Benign).Right Breast appeared normal. Upper lumbar mass USG biopsy was taken which suggested adenocarcinoma with mucinous differentiation & signet ring cell morphology, favouring gastrointestinal type. Upper GI endoscopy findings were normal except hiatus hernia. Lower GI endoscopy was done per stoma which showed mucosa visualised as normal proximally till caecum & distally revealed a proliferative lesion near splenic flexure. Scope could not be negotiated beyond. Biopsy was taken from the splenic flexure growth which showed features consistent with moderate to poorly differentiated adenocarcinoma with glandular as well as signet ring cell morphology**.** Tumor cells positive for CD20, CD X2 and wild type of K-Ras mutations were detected. Our Final impression was secondary krukenberg tumor with signet ring cell carcinoma of sigmoid colon & omental metastasis. She received 6 cycles of platinum based chemotherapy and had initial response to the treatment. On follow up she developed chemotherapy induce gastropathy and uncontrolled bleeding, loose motions passed through colostomy site ,later succumbed to death after 11 months of diagnosis.

DISCUSSION

Malignancy during pregnancy is a rare occurrence, commonest presentations are of breast cancer (1:3000)[1], followed by cervix, Hodgkin's lymphoma and ovarian cancer. Krukenberg tumor is a rare metastatic ovarian malignancy that accounting for 1-2% of all ovarian tumors[2]. First named by **Friedrich Ernst Krukenberg** in 1896 [3]. It affects all age groups, with an average age of 45 years. The primary sites are stomach (70%),followed by colon, appendix and breast. More recently, in the past five years only ten cases of KBT during pregnancy have been reported[2,4]. The persistent gastrointestinal symptoms like constipation, distension, pain mimicking the features of late pregnancy masks the presentation of the tumor in the abdomen. Early diagnosis of the tumor may be delayed[5]. There might be an increased risk of acute abdomen secondary to tumor torsion or rupture & it may induce preterm labour [6]. Cases diagnosed during pregnancy are extremely rare. Our patient 30 yr female with 31 wks pregnancy presented with bilateral ovarian mass and growth in left colon; histological findings of signet ring cell differentiation favouring krukenberg tumor, primarily originating from colon cancer.

The exact mechanism of tumor spread is still unknown .The tumor is thought to spread via one of the following mechanisms: (1) the lymphatic system, (2) the hematogenous system, or (3) the transcoelomic pathway. The gastric neoplasms selectively metastasize to the ovaries without involvement of other tissues[7], retrograde lymphatic spread is the most likely route of metastasis. A hematogenous spread seems to be the most frequent pathway in colon cancer[8].

The average age of diagnosis co-relates to increased vascularity of the ovaries which supports the lymphatic and hematogenous spread hypothesis[9].

C.Y .Cheng,et al reported a case report krukenberg tumor in pregnancy with deliver of a normal baby[6]. Oztas E et al reported a case of KBT metastasized from colon cancer in pregnancy. Review of literature has identified a number of diagnostic & management issues that appear to have an impact on the survival. These include timing of definitive diagnosis of KBT i.e . before , after or at the same time as diagnosis of the gastrointestinal primary tumor, menopausal status ,concurrent pregnancy, role of debulking &prophylactic oophorectomy, the platinum based chemotherapy can be reasonable and relatively safe to be administered during pregnancy[10]. The prognosis worsens when the primary tumor is identified after the metastasis to the ovary is discovered[11] . A retrospective study including 38 cases of ovarian metastases from colorectal cancers used next-generation somatic mutation profiling to assess 341 cancer-associated genes [12], finding an increased number of mutations in the *KRAS, SMAD4*, and *NTRK1* genes in ovarian metastases, compared to a cohort of 543 cases without ovarian metastases.

CONCLUSION -

Due to the rarity of the condition, pregnancy associated with advanced stage of malignant disease. Index of suspicion should be high ,when persistent unusual gastrointestinal symptoms. It must be carefully evaluated by pan endoscopic examination, so delays in diagnosis could be avoided[13].

REFERENCES

[1] P. Morice, C. Uzan, S. Gouy, C. Verschraegen, and C. Haie-Meder, "Gynaecological cancers in pregnancy," The Lancet, vol.379, no. 9815, pp. 558–569, 2012.
[2] S. R. Singhal, S. Nanda, P. Chaudhry, J. Sen, and S. K. Singhal,"Metastatic bilateral malignant ovarian tumors associated with pregnancy," *Taiwanese Journal of Obstetrics and Gynecology*, vol.48, no. 2, pp. 167–168, 2009.
[3] F. Krukenberg, "Uber das fibrosarcoma ovarii mucocellulase (carcinomatoses)," *Archives of Gynecology and Obstetrics,* vol.50, pp. 287–321, 1896.
[4] F. Tulek, A. Kahraman, S. Taskin, A. Sertcelik, and F. Ortac,"Pregnancy complicated by a Krukenberg tumor with an undetermined origin and its management," The Journal of Obstetrics and Gynaecology Research, vol. 40, no. 9, pp. 2076–2080, 2014.
[5] Chou MM, Ho ES, Lin NF, Lee YH: Color Doppler sonographic appearance of a Krukenberg tumor in pregnancy. Ultrasound Obstet Gynecol 11: 459-460, 1998
[6] C. Y. Cheng, T. Y. Chen, C. K. Lin, S. M. Tsao, I. F. Shih, and S. W. Shy, "Krukenberg tumor in pregnancy with delivery of a normal baby: a case report," *Chinese Medical Journal*, vol. 54,no. 6, pp. 424–427, 1994.
[7] Fujimoto D, Hirono Y, Goi T, Yamaguchi A. Sigmoid colonic metastasis by lymphatic spread occurring with unilateral Krukenberg tumor considered to be caused by stage IA early gastric cancer: A case report. Oncol Lett. 2016 Jan;11(1):668-672. [PMC free article] [PubMed]
[8] Moore RG, Chung M, Granai CO, Gajewski W, Steinhoff MM (2004) Incidence of metastasis to the ovaries from nongenital tract primary tumors. Gynecol Oncol 93(1):87–91. doi:10.1016/j.ygyno.2003.12.039
[9] Shah B, Tang WH, Karn S. Transcoelomic spread and ovarian seeding during ovulation:

A possible pathogenesis of Krukenberg tumor. J Cancer Res Ther. 2017 Jan-Mar;13(1):152-153. [PubMed]

[10] A. Cosme, E. Ojeda, L. Bujanda, J. Torrado, and J. Barrio,"Krukenberg tumor secondary to gastric carcinoma in a woman in her eighth month of pregnancy," *Gastroenterologiay Hepatologia*, vol. 24, no. 2, pp. 63–65, 2001

[11] Tamussino K, Scholl W, Reich O, Winter R: Gastric carcinoma presenting as a Krukenberg tumor in the 24th week of gestation. Eur J Obstet Gynecol Reprod Biol 62: 251-252, 1995

[12] Ganesh K, Shah RH (2017) Clinical and genetic determinants of ovarian metastases from colorectal cancer. Cancer 123(7):1134–1143. doi:10.1002/cncr.30424

[13] Sandmaier D, Lobrinus JA, Vial Y, et al: Bilateral Krukenberg tumor of the ovary during pregnancy. Eur J Gynecol Oncol 21:58-60, 2000