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Case Report

A precarious outcome of incidentally diagnosed Krukenbergs tumor in antepartum eclampsia case: a rare case report and review of literature

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ABSTRACT

Krukenbergs tumors are the rare metastatic tumors of ovary with its incidence of 1-2%. It's occurrence along with pregnancy is very rare with reported incidence of 0.4-0.5%. The occurrence of Krukenbergs tumors along with gestational hypertension is also very rare and it has poor prognosis. The most common primary origin is from gastric site. We report a case of 28-year-old pregnant female presented with Antepartum Eclampsia with incidental findings of bilateral enlarged ovaries during caesarean section. The diagnosis of Krukenbergs tumor was made with histopathology and it's primary origin was rendered by postoperative gastroscopy guided biopsy. Our case is enthralling in view of its unusual presentation, young age, and the diagnostic dilemma it poses. Our case report highlights the fact that early diagnosis of Krukenbergs tumor in pregnancy may be difficult at times owing to the masquerading effects, implying widespread metastasis and a poor maternal survival. Tumor resection with concomitant Chemotherapy was given as treatment. The main aim of this paper is to evaluate whether earlier diagnosis can be made in such cases. A thorough literature review was also conducted, unfortunately no methods can be used for early detection. Furthermore, no consensus regarding diagnostics or treatment avail till date. Hence the need for more research regarding this rare condition to offer recommendations about early detection, diagnosis and therapeutic approaches can be prompted.

Keywords: Krukenbergs tumor, Ovarian tumor, Metastasis, Pregnancy, Gastric carcinoma

INTRODUCTION

The most common malignancy in pregnancy is breast carcinoma followed by cervical cancer, Hodgkin's lymphoma, and ovarian carcinoma. The incidence of adnexal mass malignancy in pregnancy is of 3% with Krukenbergs tumor incidence in pregnancy varies from 0.4-0.5%¹. Krukenbergs tumor in pregnancy is very rare and it has poor prognosis. A Krukenbergs tumor is a rare type of glandular carcinoma which metastasizes to the Ovaries. It accounts for approximately 1–2% of all ovarian tumors and up to 17.8% of all ovarian malignancies¹. The common symptoms of Krukenbergs tumor includes epigastric site pain, acid reflux, nausea, vomiting, abdominal distension, which are obscured by physiological changes of pregnancy. The primary sites of Krukenbergs tumor includes stomach, breast, small

intestine, appendix, colon, rectum, gall bladder, biliary tract, pancreas, urinary bladder and uterine cervix². Among the primary tumors, the most common site is gastric origin which includes two thirds of all cases. A few case reports describe Krukenbergs tumours in patients without any primary tumor. Occasionally it remains unclear if primary Krukenbergs tumor exist. Because of it's rare incidence, nonspecific symptoms and lack of treatment guidelines for these tumors in pregnancy, it remains challenge for the obstetricians and pathologists in view of early diagnosis and management. Our case becomes intriguing because of its presentation in pregnancy with antepartum eclampsia with history of persistent epigastric pain. The fact that such a large adnexal mass of size 8 cm was missed during previous pregnancy and present pregnancy antenatal investigations in a young female probably due to masquerading effects of

pregnancy. The primary tumor of gastric origin was also identified.

The objective of this paper is to present the adversity in the diagnosis and treatment of pregnant women diagnosed with Krukenbergs tumors and to look for any prospective on early detection of these cases based on the review of the literature.

CASE REPORT

A case of 28 years old pregnant female, Gravida 2, Para 1 and no live child (G2P1L0), with previous history of Hysterotomy done for AP Eclampsia, presented to the Emergency department of Obstetrics and Gynaecology, with history of two episodes of seizures at 32 weeks +2 days of gestation. At the time of admission, her previous antenatal or ultrasound records were not available.

On examination, patient was in post ictal confusion state, afebrile, with heart rate of 86/min, Blood pressure of 180/100 mmHg, and SPO2- 98% in Room Air. On physical examination, patient had bilateral pedal oedema, gravid uterus corresponding to 28 weeks of gestation with fetal heart rate of 100 bpm. The laboratory values revealed normal findings in serum creatinine, liver functions test, liver enzymes, coagulation profile and her haemoglobin was 10.3 g/ dl and Platelets were 181×10^3 u/ml. The Bedside Ultrasound Gynaecology singleton live intrauterine pregnancy which was small for her gestational age, a left adnexal mass of heterogeneous nature of size 8 cm in the diameter of its largest side which was distinct from uterine mass. After stabilization, Patient was taken up for emergency caesarean section in view of antepartum (AP) eclampsia/ previous history of hysterotomy.

She delivered an alive girl baby of birth weight 963 grams with Apgar scores of 1/10, 6/10, no fetal anomalies were detected and baby was admitted in neonatal intensive care unit (NICU). Intra operatively, minimal ascites was noted and both ovaries were enlarged. Left ovary measured 8×6×4 cm and right ovary measured 2×2×1 cm. Ascitic fluid was sent for cytological examination. In our case, left salpingo oophorectomy was proceeded to remove left ovarian mass and left fallopian tube, whereas biopsy was taken from right ovary and omentum which was sent for histopathological examination.

A provisional diagnosis of malignant ovarian mass was made. Post operatively patient was observed in Obstetric ICU. Her past medical records showed H/o AP eclampsia at 31 weeks of gestation for which she had undergone emergency hysterotomy and delivered an alive baby of birth weight 820 grams which expired at 28 days of life and details of ovaries were not mentioned. She was advised to take antihypertensive drug till 6 weeks of postpartum but patient discontinued drug and lost follow up. In current pregnancy, patient had history of persistent epigastric pain since 20 weeks of gestation, for that she was treated with antacids. Postoperatively, she had

worsening abdominal pain. Physician opinion sought for persistent epigastric pain. Based on intra operative findings an esophagogastroduodenoscopy was performed in our centre, which revealed patchy areas of erythema on the non-peristaltic stomach wall, also superficial ulceration was noted along the lesser curvature and Multiple biopsies were taken from the same site.

On histopathological examination, left ovary was processed by frozen section. The whole left ovary was replaced by tumour cells which was separated by fibrous stroma with capsular breach with signet ring appearance microscopically. Biopsy report of contralateral ovary and omentum also showed infiltration of tumor cells. The overall morphological features were suggestive of Krukenbergs tumor with metastasis of omentum.

The immunohistochemistry test of alcain blue and mucicarmine was positive for intracytoplasmic mucin and also showed positivity for cytokeratin (CK) 7, 20, MUC 1, MUC-5AC, whereas it was negative for synaptophysin and vimentin. These features suggested a final diagnosis of Krukenbergs tumor with possible primary from gastrointestinal tract. The analysis of Ascitic fluid was negative for malignant cells. The diagnosis was also confirmed by gastric biopsies which showed diffuse type of adenocarcinoma. Serum levels of CEA, CA 19-9, LDH and PLAP were normal, the CA 125 levels were found to be elevated (768 U/ml). Patient was referred to Department of Medical oncology for chemotherapy but she refused for further treatment and lost follow up.



Figure 1: Intra operative findings of incidentally diagnosed Krukenbergs tumor in antepartum eclampsia case during caesarean section.

DISCUSSION

The occurrence of Krukenbergs tumor along with antepartum eclampsia in pregnancy is rare. These

occurrences impose poor prognosis. Most of the cases of Krukenbergs tumors noted from Japan due to higher incidence of gastric carcinoma. The median age of presentation is at 35-45 years. The down regulation of epithelial cadherin in primary tumors might be responsible for ovarian specific metastasis. This signet ring cell tumors usually arise from glandular origin like from gastrointestinal tract (stomach, small intestine, colon, rectum, pancreas, biliary tract), breast, lung.^{1,2} Metastasis route includes haematogenous, lymphatic, trans coelomic spread. The clinical features vary from abdominal pain, abdominal distension, weight loss, dyspareunia, and sometimes heavy menstrual bleeding. Often symptoms of Krukenbergs tumor manifest earlier than primary tumor³.

Kiyokawa et al performed a clinicopathologic analysis of 120 Krukenbergs tumor cases where clinical presentation varies from abdominal pain, abdominal distension, abnormal vaginal bleeding, virilization and hirsutism features.⁴ 63% of cases had bilateral involvement, two third of cases had gastric origin. Papantoniou et al also reported hirsutism with Krukenbergs tumor.

Ozdegirmenci et al also reported Krukenbergs tumor with hirsutism and ascites.^{5,6} In our case she presented with two episodes of GTCS along with history of persistent epigastric pain from 20 weeks managed by antacids. Abdominal distension due to the growing fetus of women often conceals the metastatic ovarian tumor in the pelvic Cavity. Hence, it is difficult to establish an early diagnosis during the antenatal period.

Upper GI endoscopy and gastric biopsy can be considered in women with complaints of persistent epigastric symptoms, weight loss, haemoptysis in the second trimester of pregnancy.⁷ Servo and Scully established diagnostic criteria for Krukenbergs tumor which later adopted by WHO 1) poorly differentiated adenocarcinoma of ovarian stroma 2) presence of mucin laden signet ring cells 3) presence of ovarian stroma sarcomatoid proliferation.^{8,9} The gross appearance in Krukenbergs tumor is symmetrically enlarged ovaries with bosselated appearance usually in solid consistency and occasionally cystic appearance.

The characteristic histopathological appearance is mucin laden signet ring cell. Differential diagnosis of a Krukenbergs ovarian mass includes sex cord stromal tumor, primary signet-ring stromal tumor, yolk sac tumor and malignant epithelial Ovarian tumor. Primary signet-ring stromal tumors are mostly unilateral and remain nonreactive to mucins and CK.¹⁰ Mostly diagnosis of primary tumor is made by radiological investigation while some authors prefer immunohistochemistry to look for primary tumor. The CK7+/CK20+ noted in primary gastric carcinoma. MUC5AC positivity noted in gastric carcinoma. CK7/CK20+ indicates colorectal carcinoma as primary tumor. CK7+/CK20+ favours primary ovarian carcinoma.⁹ MUC5AC+ also seen in mucinous ovarian carcinoma, pancreatic adenocarcinoma, biliary tract, lower

gastrointestinal tract.^{9,14} The diagnosis of gastric cancer with Krukenbergs tumor in pregnancy is difficult due to vague symptoms and its rare occurrence. Smith et al¹¹. revealed that the most common tumor types per 10,000 live singleton births were breast (1.3), thyroid (1.2), cervical (0.8), Hodgkin's disease and ovarian (each 0.5), acute and chronic leukaemia (0.37), and lymphoma (0.28). Symptoms like nausea, vomiting, epigastric pain, abdominal distension can be masquerading as pregnancy symptoms. Even if gastric carcinoma is considered in pregnancy the confirmation via endoscopy and biopsy is risk for fetus due to maternal hypoxia and hypotension.

The American society for gastrointestinal endoscopy recommends the procedure of endoscopy in second trimester⁷. There are no current standardized guidelines for the management of Krukenbergs tumor in pregnancy. Ultrasound and MRI are the choice of diagnosis for adnexal masses in pregnancy.¹² Shimizu and colleagues described the ultrasound features of Krukenbergs tumor in non-pregnant women as the tumors with distinct margins and irregular hyperechoic solid pattern and moth-eaten cyst appearance.¹³ The management of Krukenbergs tumor in pregnancy is based on gestational age, primary tumor site and stage.

In case of gastric carcinoma as primary, partial or total gastrectomy, lymph node dissection bilateral oophorectomy with platinum-based chemotherapy are relatively safe in early pregnancy. If diagnosed during third trimester delivery with surgical resection with chemotherapy is preferred. Fetal survival rate has been good. Most of the cases diagnosed after metastasis from primary tumors. Presence of gastric carcinoma in pregnancy leads to aggressive nature due to presence of oestrogen receptors.

Most of Krukenbergs tumor patients with bilateral and metastatic features die in 2 years with median survival of 14 months¹⁵. The role of tumor markers remains controversial. CA 125 along with human chorionic gonadotropin, alpha-fetoprotein, CEA are difficult to interpret in pregnancy due to its role in fetal development, maturation, differentiation.¹⁴ The treatment decides by multidisciplinary team with neonatologist, obstetrics specialists, oncologists.

CONCLUSION

Due to the rare occurrence of gastric carcinoma in pregnancy, there is no feasible and reliable methods available for early screening and diagnosis in pregnancy. Although the diagnosis of Krukenbergs tumor during pregnancy was delayed, the symptoms of nausea and vomiting after the first trimester of pregnancy should be considered as alarming feature of gastric ulcers which needs further evaluation. The median survival rate in advanced stage of gastric cancer was six months. So, further research needs to be conducted in this field to

standardize procedures for screening, diagnosis and treatment.

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