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Case Report
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Krukenberg Tumour with Occult Gastric Primary in a 20 Year Old Presenting with Amenorrhea as Initial Symptom

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Abstract

Krukenberg tumor tends to occur in a younger age group and common presenting symptoms are abdominal pain and distension. We describe a case of Krukenberg tumor where amenorrhea was the only presenting symptom and the primary tumor was identified four months after resection of metastatic ovarian masses. A 20 year old female presented with amenorrhea of three months. On examination she had bilateral adnexal mass. Tumor markers were normal. Esophagogastroduodenoscopy and proctosigmoidoscopy revealed healthy mucosa. MRI showed bilateral 13 cm × 12 cm × 6 cm and 12 cm × 10 cm × 6 cm hypointense masses likely dysgerminoma. Intraoperative there was bilateral solid cystic ovarian mass and frozen section was s/o metastatic adenocarcinoma with signet ring cell differentiation. On final histopathology tumor cells were immunopositive for pan-cytokeratin (diffuse) and CK20 (focal). Postoperative PET CT done to identify primary was normal. After four months repeat PET CT was done which revealed uptake in stomach and mesenteric nodes. Repeat upper GI endoscopy detected an ulcer in posterior wall of stomach and biopsy showed signet ring cell adenocarcinoma. She received palliative chemotherapy with capecitabine and oxaliplatin for six cycles. Progressive disease was detected on follow up and she was started on second line chemotherapy with carboplatin and paclitaxel.

Introduction

Krukenberg Tumour (KT) accounts for 1% to 2% of all ovarian tumors and was first described by Fredrich Ernst Krukenberg in 1896 [1,2]. At first glance it may be confused with primary ovarian tumor. It is bilateral in 80% cases and the most frequent primary site of origin is stomach (76% of all cases) [3]. Identification of primary lesion is important since management and prognosis depends on the primary tumour [4-8].

In some cases, the primary tumour cannot be found until the diagnosis of a KT. In present case the diagnosis was not made until repeat PET CT, endoscopy and biopsy was done post surgical removal of metastatic deposit from ovaries. Patients mostly present with abdominal pain and distension. Menstrual irregularities may be seen less frequently [1]. In the current case amenorrhea was the sole presenting symptom.

Case Presentation

A 20 year old unmarried female presented with the chief complaint of amenorrhea for three months. Her menstrual cycles were regular with average flow prior to that and she had no symptoms of pain abdomen, abdominal distension, urinary problems, chest pain, cough, black stools, bleeding per rectum, jaundice or bone pain. She had no significant medical or surgical morbidities in past. Family history revealed colorectal cancer in a second degree relative. She had no history of cigarette smoking or alcohol use and she belonged to lower middle socioeconomic class. Her general physical examination was normal and systemic examination revealed bilateral 8 cm × 8 cm solid-cystic, mobile adnexal mass with smooth surface. Firm, mobile 2 cm × 1 cm lump was felt in upper outer quadrant of left breast.

Ultrasound abdomen and pelvis was s/o large mixed echogenic, solid-cystic masses arising from ovaries (Figure 1 and 2). Esophagogastroduodenoscopy and proctosigmoidoscopy was normal. USG breast revealed 2 cm × 2 cm benign mass and FNAC from mass revealed fibroadenoma. MRI abdomen was suggestive of bilateral 13 cm × 12 cm × 6 cm and 12 cm × 10 cm × 6 cm hypointense masses, possibly dysgerminoma (Figure 3). Tumor markers were within normal limits except CA 19.9 being on upper limit of normal. (CA 125-9.1 U/mL, CEA- 1.61 ng/ml, CA 19.9-29.9 U/mL, alpha fetoprotein-1.2 ng/ml, LDH-218 U/L, beta HCG-2.0 mIU/mL).

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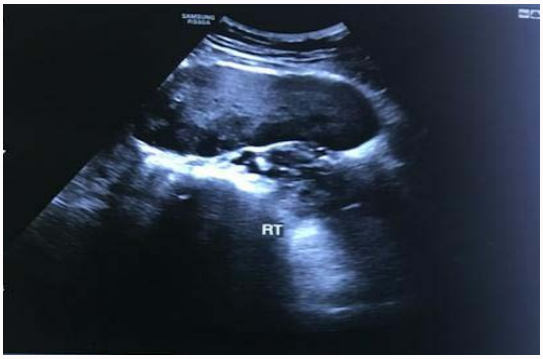

Figure 1: Ultrasound pelvis showing solid cystic mass in right ovary.

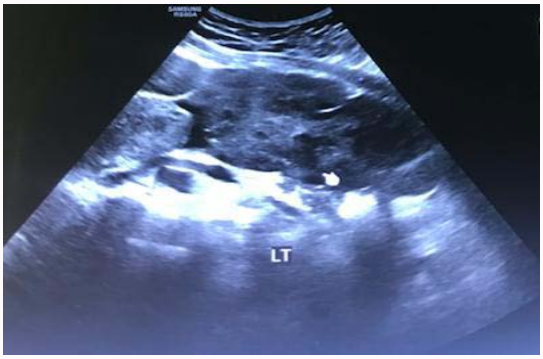

Figure 2: Ultrasound pelvis showing solid cystic mass in left ovary.

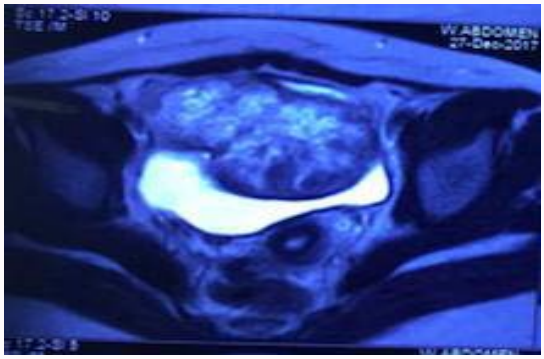

Figure 3: MRI pelvis- hyperintense mass on T2 likely dysgerminoma.

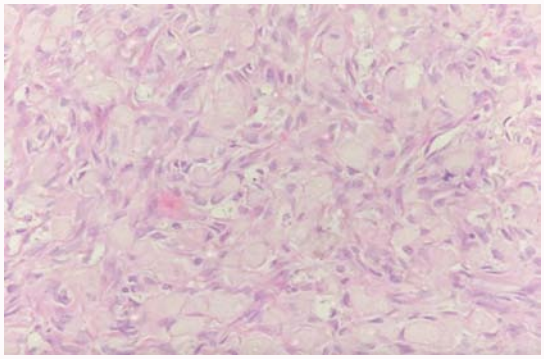

Figure 4: Histopathology- metastatic adenocarcinoma with signet cell differentiation.

She underwent laparotomy, ascitic fluid cytology, bilateral ovarian mass excision, reconstruction of remaining ovarian parenchyma and omentectomy. Postoperative histopathology was suggestive of metastatic adenocarcinoma in bilateral ovaries with capsular breach and signet cell differentiation (Figure 4). Tumor cells were pan CK, CK 20 and GATA3 positive, and CK 7, ER, PR negative. Omentum was involved with similar cells. PET CT was done in immediate postoperative period and it revealed no uptake. Repeat PET CT after four months of surgery showed uptake in stomach and mesenteric lymph nodes. Upper GI endoscopy was repeated and an ulcer in the post wall of stomach was found and biopsy was s/o signet ring cell adenocarcinoma.

She was planned for palliative chemotherapy with capecitabine and oxaliplatin three weekly. After six cycles of chemotherapy there was residual uptake in stomach which progressed subsequently with raised CA 19.9 (48 U/mL) and currently she is receiving second line chemotherapy with carboplatin and paclitaxel. She has remained asymptomatic post surgery.

Discussion

Krukenberg tumor tends to occur in a younger age group with median of 45 years and common presenting symptoms are abdominal pain and distension [9]. In most cases, primary tumor and its metastasis to ovary are diagnosed at the same time but in 20% to 30% cases, ovarian metastasis is detected after primary tumor resection [10]. In our case, the primary tumor was diagnosed four months after ovarian mass excision. Although abdominal pain and distension are seen frequently at initial presentation, in our case the only initial symptom was amenorrhea. Abdominal pain, abdominal mass, ascites, nonspecific gastrointestinal symptoms and fatigue were absent at initial presentation. In prior reports by Hatwal et al. [11] and Hiremath et al. [12] patient presented with abdominal pain, lump, distension and amenorrhea. In a case report by Sahin et al. [13] the sole presentation was amenorrhea.

Hematogenous, peritoneal seeding and lymphatic route are the three pathways of metastasis with later being the most common [10]. Differential diagnosis must be made from the primary ovarian tumors. The major signs of metastasis are: Bilaterality (74% has bilateral ovarian involvement and 26% has unilateral tumour), size of the tumor (less than 10 cm), surface involvement, extensive intra-abdominal spread and a widespread infiltrative pattern.

On ultrasonography, a characteristic feature is an irregular hyperechoic solid pattern and a moth eaten like cyst formation. Another suggestive sign is the presence of a large lead vessel penetrating the mass from the periphery and nourishing the tumour by branching in tree pattern, known as lead vessel sign, with high speed and low resistance on spectral Doppler. This color Doppler sign is more frequently detected in ovarian metastases compared with primary invasive ovarian carcinomas. Sonography and color Doppler imaging are decisive in raising the suspicion of a metastatic tumour [14].

Diagnosis is based on the light microscopic feature of dense fibroblastic stroma, diffusely infiltrated by malignant signet-ring cells. Immunohistochemistry helps to differentiate KT from primary ovarian cancers. CK7 and CK20 are commonly used to distinguish metastatic ovarian neoplasia from primary ovarian tumors [1]. Primary ovarian tumors usually tend to be positive for CK7 and negative for CK20 in contrast to metastatic gastric cancers. Metastatic gastric carcinomas tend to be positive for CK20 in the 70% of cases and much less frequently positive for CK7. In

our case, tumor was negative for CK7 and focally positive for CK20. Till date, the optimal treatment modality has not been clearly established. Surgery is the main treatment for the medically fit patients who have a resectable lesion. Chemotherapy and radiotherapy are found to have no significant effects on prognosis [1]. But in one study, Weiqi Lu et al. [15] showed that use of postoperative aggressive chemotherapy is a favorable prognostic factor on survival of patients with Krukenberg. In another study Wei Peng et al. [7], showed that if the primary tumor is resected and patient has no ascites then ovarian metastasectomy may prolong the survival time of the patients. Wei Peng et al. [7], also recommend that patients should not undergo ovarian metastasectomy if the primary tumor is unresected and the patient has ascites. It has been reported that serum levels of CA-125 may be helpful for the early diagnosis of KT [16]. In our patient, level of CA-125 was normal. KT has a poor prognosis with a median survival time of 14 months and most patients die within 2 years [17]. In conclusion a resectable primary tumor and absence of residual metastatic lesion seem to be the most important prognostic factors for long term survival.

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