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Signet ring cell carcinoma of ovary secondary to adenocarcinoma of colon

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Abstract
Ovarian cancer is one of the most common gynaecological cancers. Tumor of the ovary are majority of the times primary with a small percentage of secondary malignancy. Metastasis to the ovaries can occur from many organs, including stomach, small intestine, colon, rectum, gall bladder, appendix, breast, uterus, fallopian tube and peritoneum. Stomach is the primary site in 70% of the cases. Carcinoma of colon, breast and appendix are the next common primary sites. These are referred to as Krukenberg tumor, accounting for 1-2% of all ovarian tumors. Here, we report a case of 34 year old female presenting with pelvic abdominal mass arising from right ovary, suspected as a primary ovarian malignancy that later turned out to be secondary due to adenocarcinoma of recto sigmoid colon. The case report highlights the importance of preoperative work up needed to search for primary malignant lesion as Krukenberg tumors known to have poor outcome.

Keywords: Signet ring, cell carcinoma, adenocarcinoma, colon

Introduction
Krukenberg Tumor (KT) is an infrequent metastatic tumor of the ovary, accounting for 1% to 2% of all ovarian tumors. It was first described in 1896, by Friedrich Krukenberg, who presumed it to be a primary ovarian neoplasm.
The criteria for diagnosis of Krukenberg tumor is
1. Cancer in the ovary
2. The presence of mucin producing neoplastic signet ring cells
3. Ovarian stromal sarcomatiod proliferation.

Recently, specific immunohistochemical methods have been tried in order to find the site of primary neoplasm. Immunohistochemistry is very useful in differentiating primary versus secondary which is very essential to known the outcome of the disease. Panel of IHC stains need to be carried out may inculde CK20, Ck7, CA-125, HAM56, and CEA. Positive for CEA and CK20 is typical for metastatic intestinal adenocarcinoma in the ovary, in contrast though not specific, positive staining for CA125,CK7, and HAM56 is much more typical for primary ovarian malignancies. Stomach is generally considered as the most common primary site of the disease (70%). Moreover, KT is mainly attributed to carcinomas of the GI tract (appendix, liver, pancreas, biliary tract and gallbladder) and rarely to that of the breast. The case here illustrates the difficulties encountered in the clinical and histopathological diagnosis of secondary over primary.

Case Report
34 year old female with history of two vaginal deliveries, with no past medical or surgical Illness came with complaint of pain in abdomen since one day and abdominal distension since 1month and an USG report revealed a pelviabdominal mass of 17.7*10.1*15.6cm arising from the right ovary, an ovarian cyst with mild internal vascularity. Without any evidence of torsion with CA-125 level (of 57.66unit/ml) within normal levels.
Before we could plan an FNAC/ USG Guided Biopsy for the patient she complained of immense pain and taken for emergency laparotomy surgery with an indication of suspected torsion. Intraoperatively a multilobulated right ovarian cystic mass of size 20*16*16 in size with slightly enlarged left ovary and normal uterus size was noted. And no malignant feature were seen intraoperatively.

Subsequent HpE report revealed signet ring cell carcinoma of ovary? primary?? Secondary. She was re evaluated to find the source of the tumour. She was further planned for CT scan and colonoscopy, endoscopy to ascertain the source. CT scan revealed complex left ovarian cyst of 4.3*3.2*5.2cm, short segment heterogeneously enhancing, asymmetrical circumferential bowel thickening in the recto sigmoid and proximal rectum of maximum thickness measuring 9mm and approx length 7cm. No luminal compromise with few subcentrimetric enlarged lymph nodes.

Findings of colonoscopy revealed an ulcerative growth seen from 17-20cm from the anal verge. Rest mucosa up to hepatic flexors was normal. Biopsy was taken and sent for HPE.

Immunohistochemistry was positive for CK 20 AND CDX2, while negative for CK 7 giving impression of poorly differentiated adenocarcinoma of signet ring morphology of recto sigmoid colon. The patient was posted immediately for laparoscopic low anterior resection with hysterectomy with left sided salpingoophrectomy. Post-operative histopathology of specimen confirmed diagnosis signet ring cell carcinoma of rectosigmoid colon and she was planned for chemotherapy sessions.

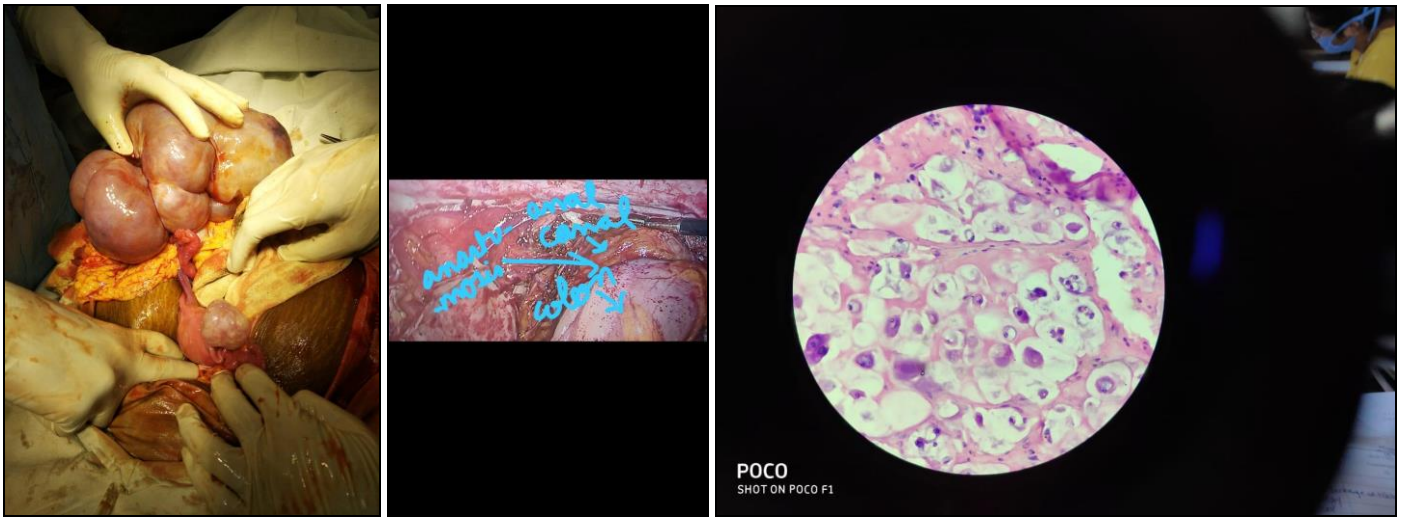

Fig 1: Following diagram shows intraoperative pictures of rectosigmoid colon and also the microscopic evidence of signet ring pathology.

Discussion

Ovarian cancers could be primary or secondary due to metastasis from other organs. Ovarian cancer being the third leading cause of cancer in women in India with metastatic occurrence accounting for 1-2%.

Stomach is primary site in 70% cases, presenting at an average age of 45 years. tumour metastasis occur via 3 major pathway lymphatic, hematogenous, transcoelomic.

Lymphatic spread is most common route of metastasis because of

a. Microscopically Hilum and cortex have demonstrated lymphatic permeation
b. Primary tumor is confined to mucosa and submucosa having rich vascular supply
c. Lack of involvement of peritoneum without any evidence of seedlings or adhesions
d. Risk of metastasis is high if lymph node are involved

The rate of lymphatic metastasis was common from stomach to ovary while hematogenous metastasis was more common In spread from colon to ovary.

The reason being: urogenital lymph vessel tract gives rise to receptaculum chili which joins the intestinal trunk that further join the gastric node.

Since the distance from the receptaculum chili to gastric node is shorter then to mesenteric nodes, gastric cancer metastasise via the receptaculum chili to ovaries. Vascular network in colon is larger and also the laterality of metastasis to the ovary in colon cancer did not correspond to the side of primary lesion, thus concluding rate of vascular metastasis to be more common in colonic cancer.

On histolpathology krukenbergs tumor can be diagnosed as

1. Ovaries are asymmetrically enlarged with bosselated tumor
2. Tumor are usually solid
3. Capsular surfaces are free of tumor infiltrates, adhesions and deposits
4. Signet ring cell that lack tubular formation. The tumour stains positive for cytokeratin and epithelial membrane antigen while negative for inhibin and vimentin.

Presence of signet ring cells in an ovarian mucinous carcinoma is highly suspicious of metastatic neoplasm with primary site being the GIT tract.

The distinction between primary and secondary signet ring cell carcinoma can be difficult. Primary ovarian cancer

Metachronous with colorectal is well known and it is presentation of HNPCC mostly lynch 2 syndrome. Ovarian cancer is the 2nd most common site of extracolonic cancer in these women. Our case presented with features that directed our suspicion towards benign pathology and most probably a primary ovarian tumor. However, considering the unilaterality, large size, lack of surface implants, lack of lymphovascular invasion, lack of extra ovarian spread and most importantly lack of any symptoms of GI tract abnormality favoured more towards primary ovarian neoplasm.

Immunohistochemistry is less reliable to distinguish primary from secondary as few ovarian neoplasm also express enteric markers CK 20 AND CK7 as seen in our case.

No mention about markers like synaptophysin, chromogranin and CD 56 (that rule out other primary tumours. With signet ring morphology like goblet cell carcinoid tumours) left us further in dilemma about the origin.

While dealing with a case of ovarian tumour, all aspects of pathological and clinical correlations are crucial for accurate diagnosis.
This case of an asymptomatic rectosigmoid malignancy makes it crucial step to rule out primary GI MALIGNANCY before landing at a diagnosis of ovarian primary.

Conclusion
Krukenberg tumor is a rare bilateral ovarian metastatic tumor with primary usually from stomach, usually they are solid tumor with signet ring cell adenocarcinoma features on. The case reports highlights the importance of preoperative workup needed to search for primary tumor, a primary ovarian diagnosed at later stage has a better prognosis than a secondary malignancy as in latter the primary malignancy has already reached an advanced stage.

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