Primary Carcinoid Tumour of Ovary Presenting with Severe Constipation - A Case Report

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INTRODUCTION

Carcinoid is an uncommon tumour in ovary comprising 0.1 % of primary ovarian neoplasms and 1 % of all carcinoid tumours. It was first described by Stewart et al. in 1939 following which many case reports have come out.[1]They usually occur in the peri-menopausal age. Primary ovarian carcinoids are usually unilateral, but can show a cystic teratoma or mucinous neoplasm in the same or opposite ovary. Histological variants include insular, stromal, trabecular, and mucinous among which insular is the most common type, and around 30 % of them are associated with a carcinoid syndrome. Insular type is reported to be more common in western countries, whereas trabecular / stromal cases are more reported in Asian countries. Most carcinoids in ovary are diagnosed as an incidental radiological finding as an abdominal or pelvic mass or they may present with typical carcinoid syndrome - diarrhoea, flushing, bronchospasm, oedema, increase skin pigmentation, carcinoid heart disease. Another uncommon presentation is severe constipation associated with peptide YY production in the tumour. The clinical behaviour of carcinoid ranges from indolent unrecognisable to highly active metastatic secretory tumours. Carcinoid ovary being an uncommon tumour presenting in an uncommon site with varied presenting features, clinical confusion may lead to delayed diagnosis and management for patient. This case report aims to describe the clinicopathologic features of primary carcinoid ovary presenting in a female with severe constipation.

PRESENTATION OF CASE

48-year-old female presented with complaints of constipation for 8 months in the surgery clinic. She has previous history of haemorrhoidectomy before one year. On evaluation, she was found to have abdomen swelling and ultrasound revealed a left ovarian complex cystic mass suggestive of dermoid cyst. Thyroid stimulating hormone (TSH) was normal and other tumour markers were within normal limits. Patient underwent total abdominal hysterectomy with bilateral salpingooopherectomy and was discharged on postoperative day 7. No adjuvant therapy was given; she underwent laparoscopic appendicectomy after 2 months. Patient is alive, cxv healthy and free of disease 21 months later.

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Pathological Findings

On gross examination, left ovary appeared as an enlarged tense cystic mass measuring 6 x 5.5 x 4.5 cm filled with yellowish pultaceous material admixed with hair. No solid areas were identified. Uterus showed multiple fibroids, both tubes were normal. Right ovary appeared mildly enlarged and cystically tense, cutting open clear straw colour fluid was let out. A yellowish homogenous lobulated solid area measuring 2.5 x 2.5 x 3 cm was identified.

Microscopically, left ovarian cystic mass showed cyst wall with lining by stratified squamous epithelium with adipose tissue, hair follicles and sebaceous glands. Right ovary showed a neoplasm composed of cells arranged predominantly in ribbons, cords, trabeculae separated by fibrous septa. Individual cells had moderate to abundant eosinophilic cytoplasm, round vesicular nucleus, stippled chromatin. There was no evidence of a carcinomatous or teratomatous element in the right ovary. Immunohistochemically tumour cells were strongly positive for synaptophysin and neuron specific enolase. Chromogranin was found to be negative. A diagnosis of carcinoid tumour in right ovary and mature cystic teratoma in left ovary was given. After clinical discussion, an appendicectomy was done for the patient after 2 months to rule out the possibility of a metastatic carcinoid from appendix, but the appendix showed normal histology.

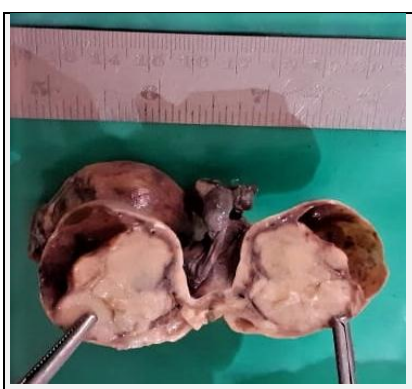

Figure 1. Right Ovary-Cut Section Showing Solid and Cystic Areas with Solid Area Measuring 2.5 x 2.5 x 3 cm, Yellowish Appearance

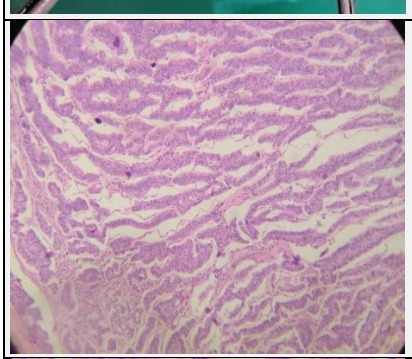

Figure 2. Microscopy H&E-Neoplasm Arranged in Trabeculae Separated by Fibrous Septa, Low Power 10 x

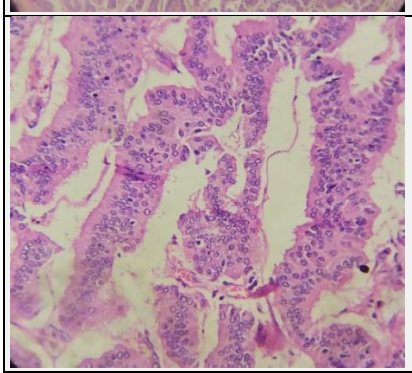

Figure 3. Microscopy H&E100x-Individual Cells Have Moderate Amount of Eosinophilic Cytoplasm, Round Vesicular Nucleus with Stippled Chromatin

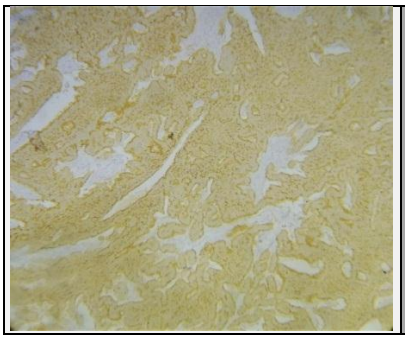

Figure 4. Cytoplasmic Positivity for Neuron Specific Enolase, 40x

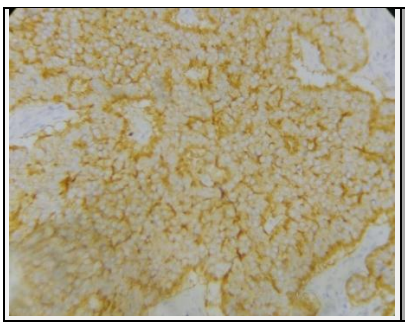

Figure 5. Synaptophysin Strong Diffuse Membrane Positivity, 100x

DISCUSSION

Classical features of carcinoid syndrome occurs due to prolonged and persistent exposure of body to neurohormonal substances produced by carcinoid (serotonin, histamine, tachykinin, bradykinin, kallikrein, corticotrophs, substance P, motilin, prostaglandin).[2] Typical carcinoid syndrome presents in around 1 / 3rd of insular carcinoids. Strumal or trabecular types are not usually associated with carcinoid syndrome. Metabolic syndrome associated with thyroid hormone production may occur in strumal carcinoids. When carcinoid ovary presents with carcinoid heart disease, the direct venous drainage of ovary bypassing the portal venous system plays a role in amplifying the cardiac associated effects.

Severe intractable constipation as in our case is another rare and peculiar presentation in primary ovarian carcinoid especially with trabecular histology. 14 cases of trabecular carcinoids have been reported in the world of literature, peptide YY has been demonstrated via immunohistochemistry or m RNAa analysis in most of these cases.[3-6] Peptide YY is a 36 amino acid gastrointestinal hormone of pancreatic polypeptide family. Normal physiological functions of this hormone include vasoconstriction, inhibition of gastric acid secretion and GI mobility, reduction of pancreatic and intestinal secretion. Also, it has been shown to be increased in postprandial states and suppress appetite. Production of peptide YY explains the severe constipation and associated weight loss in these patients with trabecular carcinoid. World literature points out that most of the patients who experienced carcinoid syndrome with the tumour were relieved of symptoms after resection of the neoplasm.

Ovarian carcinoid tumours show variable positivity for neuroendocrine markers. CD56, synaptophysin and chromogran in are the classical markers. Serotonin may show cytoplasmic positivity in functioning tumours. Immunostaining for thyroglobulin or peptide YY may help in further classifying and understanding of the tumour. They are

usually CK7 + / CK20 - ve. They are negative for ER, PR markers (differentiating between an adenocarcinoma).

Primary ovarian carcinoids (POC) are usually unilateral but may be associated with a teratomatous component in the same or opposite ovary. They are rare compared to metastatic carcinoid in ovary. Distinction between the two entities is not possible entirely on morphology or immunohistochemistry. Metastatic carcinoid in ovary has a bilateral presentation and they are mostly associated with carcinoid syndrome. Mostly in these cases, the primary carcinoid is in the gastrointestinal tract (small intestine or appendix). Primary ovarian insular carcinoids are positive for CDX2 and hence unable to differentiate between primary and metastatic GI origin. Gross presentation as multiple nodules in ovary, metastases to other sites (mesenteric lymph nodes, liver), microscopic presence of lymphovascular invasion and post-operative clinical or laboratory evidence of the carcinoid syndrome are useful clues for identifying metastatic carcinoid ovary. Insular carcinoid is the most common histologic type in both primary and metastatic ovarian carcinoid. Zhang et al. reports metastatic ovarian carcinoids to have higher ki67 proliferation index when compared to the primary carcinoid.[7] A high ki67 index signifies a more worse prognosis for patient survival in both primary and metastatic carcinoid ovary.

Primary carcinoid ovary is a tumour with an indolent course and excellent outcome. Metastatic tumours and poorly differentiated mucinous carcinoids show comparatively worse prognosis. Advanced stage of disease, though rare, causes bad outcome. There is no established guideline for management of ovarian carcinoids, due to the rarity of the tumour. Neither chemotherapy nor radiation is effective in treating carcinoid. Total abdominal hysterectomy with bilateral salpingooophorectomy is usually curative for a primary ovarian carcinoid: in case of extra ovarian spread or metastasis, surgical debulking is done. For functioning tumours, post-operative monitoring for serum serotonin and urinary 5 HIAA levels may be done to assess response to therapy.

For functioning ovarian carcinoids with serum chromogranin and urinary 5 HIAA, vergani et al. claims adjuvant octreotide therapy, a somatostatin analogue to be useful. A peri-operative cover with octreotide infusion is also recommended in these cases to prevent anaesthesia related complications.[8,9] Few cases of recurrent ovarian carcinoids are reported.[10]Hence, careful follow up for extended period of time is recommended for patients who present with carcinoid syndrome.

CONCLUSIONS

Primary ovarian carcinoid is a rare tumour with varying clinical presentation. Severe intractable constipation presenting in female patient should warrant clinician a suspicion for this rare type of presentation associated with carcinoid ovary. The final diagnosis by pathologist must be aided by immunohistochemistry confirmation. A thorough sampling of cystic teratomas for a carcinoid tumour component should be done in all clinically suspicious cases. Adequate guidelines for treatment are not well defined, but for primary carcinoid confined to ovary, surgical treatment seems to be curative.

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Disclosure forms provided by the authors are available with the full text of this article at jemds.com.

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