Case Report

A rare case of giant mucinous cystadenocarcinoma of the right ovary with metastatic deposits and Brenner tumor in the left ovary

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ABSTRACT

Ovarian cancer is the second most common gynecological malignancy. Mucinous tumor accounts for 3% of ovarian tumors and is a challenging task for a surgical pathologist. Association of Brenner tumor, a subtype of epithelial malignancy is a rare entity reported in the literature. Herein, we report a unique case of a 57-years old post-menopausal woman who presented with progressive abdominal distention for 3 years and constipation for 1 year. Clinically, it was suspected as a case of complex ovarian cyst and the patient underwent staging laparotomy. Intraoperatively, a giant mucinous cystadenocarcinoma of the right ovary with deposits in the pouch of Douglas, omentum, umbilical, and the sub-umbilical region was found along with a benign Brenner tumor of the left ovary.

Key words: Brenner tumor, Mucinous carcinoma metastasis, Mucinous ovarian neoplasm

Ovarian malignancy is the second most common gynecological cancer [1]. This lethal ovarian malignancy is divided into surface epithelial tumors, sex-cord stromal tumors, germ cell tumors, and metastatic tumors. Epithelial ovarian carcinoma is the most common histological type of ovarian malignancy which is further classified based on molecular and clinicopathological differences into two types [2]. Type 1 tumor includes low-grade serous carcinoma, endometroid carcinoma, clear cell carcinoma, and mucinous carcinoma, whereas, Type 2 includes high-grade serous carcinoma [3]. Among the high-grade carcinoma, the most frequent histological type is sporadic mucinous carcinoma. Although mucinous carcinoma is most frequent in women <40 years, its incidence is reduced from 12% to 3% with evolved criteria in differentiating benign from malignant and primary from metastatic with the help of clinicopathologic-molecular diagnostic features. The only known risk factor for mucinous carcinoma is tobacco smoking [4]. About 80% of the cases presents at an early stage with better prognosis [5]. Mucinous carcinoma has been associated with early KRAS, TP53, and HER-2 mutations [6]. It has a strong association with endometriosis and is frequently associated with Brenner tumors [7].

CASE REPORT

A 57-years-old post-menopausal woman from the outskirts of Odisha, India, presented with complaints of progressively increasing abdominal distention for the past 3 years and constipation on and off for the past 1 year. Her obstetric score was P11 L4 D7 and attained menopause 10 years ago. She had a history of use of tobacco leaves, cigars, and reverse smoking for the past 30 years.

On general examination, the patient appeared malnourished and afebrile with a pulse rate of 86/min, blood pressure of 150/80 mmHg, and respiratory rate of 18/min. Abdominal examination showed gross abdominal distention with engorged veins, umbilical hernia of size 5×6 cm, and abdominal girth of 109 cm. Ascites was confirmed with flank fullness and positive fluid thrill. Respiratory examination showed the presence of the left basal crepitation. External genitalia was atrophic and per speculum examination showed mild cystocele and rectocele.

Ascitic fluid analysis showed inflammatory cell infiltration with predominate lymphocytes, few neutrophils, and cyst macrophages. Tumor markers were done and showed AFP-3.73 ng/ml, beta HCG-14.88 µg/mL (elevated), CA125-103.8 u/ml (elevated), and CA 19.9–61.17 ngm/mL (elevated). Ultrasound abdomen showed gross ascites and right abdominal pelvic mass suggesting the features of a complex cystic mass arising from the right ovary along with the lobulations of the left ovary with an internal solid component. Chest X-ray showed left pleural effusion. Based on the history, examination, and investigation, a provisional diagnosis of the right complex ovarian cyst (possibly malignant) with gross ascites and the umbilical hernia was made. The patient was planned for staging laparotomy.

Access this article online	
Received - 28 December 2022 Initial Review - 12 January 2022 Accepted - 11 February 2022	Quick Response code
DOI: 10.32677/ijcr.v9i2.3810	

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In the operation theater, the umbilical hernia was excised and 6 L of ascites fluid was drained. A right complex ovarian cyst of weight 4 kg, measuring 20×14 cm was excised and peritoneal metastasis of size 3×3 cm was identified and excised. Omentectomy was done and intraoperatively, a 2×2 cm node was excised. A sub-umbilical node of 2×2 cm was excised along with total abdominal hysterectomy and bilateral salpingo-oophorectomy. The specimens were sent for histopathological examination (HPE).

Uterus with cervix was received which was attached with the left ovary and tube measuring 8×2×1 cm and 3×2×1 cm, respectively. The cut section showed yellowish and grey-white areas. The right ovary appeared as a cystic mass measuring 21×12×10 cm. The external surface was nodular (Fig. 1). The cut section showed multiloculated, multiple grey solid cystic areas, grey-white, grey-brown, yellowish, and hemorrhagic areas were seen along with mucoid material. Along with the uterus and ovary, masses from the omentum, Pouch of Douglas, and sub-umbilicus were received (Fig. 2). HPE showed complex papillae with pleomorphic and hyperchromatic nuclei along with infiltration of malignant cells into the stroma (Fig. 3).

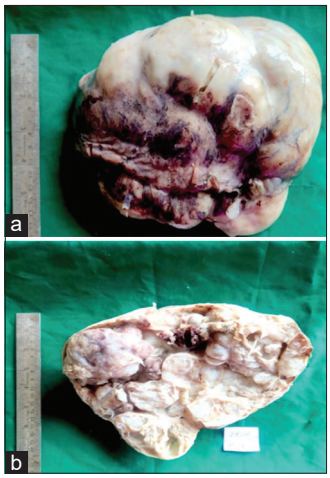

Figure 1: Gross examination of right ovary. (a) Bosselated smooth glistening surface; (b) Cut section – variegated appearance – solid, cystic, and hemorrhagic areas

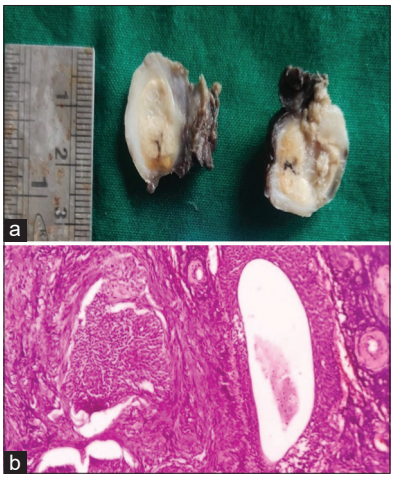

Figure 2: (a) Left ovary gross image – cut section grey white and yellow areas; (b) H and E stained left ovary microscopy image – nests of transitional cells showing coffee bean nuclei, surrounded with dense stroma and cystic spaces contain eosinophilic secretions

DISCUSSION

Ovarian tumors are diagnosed at early stages at around 40 years of age due to the recent advancement, awareness, and reach of medical facilities. On rare occasions and in underprivileged areas, these tumors grow to massive-sized tumors which was so with this present case.

Ovarian carcinoma is considered large if they have a diameter between 5 and 15 cm and when bigger than 20 cm, it is considered giant [8]. In the present case, the right ovary was 21 cm in diameter and thus fall into the giant category. These tumors are clinically asymptomatic at early stages and later present as abdominal fullness, dyspepsia, early satiety, bloating, constipation, ascites, or abdominopelvic mass [8] and need consideration in premenopausal women with any of these symptoms.

An interesting fact is that recent advancement in pathology and molecular data has proved mucinous carcinoma as a separate entity from epithelial ovarian carcinomas and as a genetically unique entity [9]. Large solid-cystic mass needs judicious sampling and cautious microscopic examination due to their histological similarity to other mucinous carcinomas especially that of colorectal carcinoma as they are frequently metastatic solid cystic. Seidman *et al*. proposed an algorithm based on tumor size to distinguish primary from metastatic [5]. This patient's right ovary had a variegated appearance with the mucinous area and areas of pultaceous material. Definitive diagnosis is made on immunohistochemistry (IHC) and molecular genetics. Tumor markers such as CA-125, CEA, and CA19-9 do help to narrow down to mucinous origin of ovarian carcinomas, definitive investigation would be the IHC pattern with CK20+, CEA+, C19+, CK7+|, PAX- ve, ER - ve, PR - ve, SATB2 - ve. CEA, CA19.9, and CA-125 were elevated in the present case and associated genetic alterations in mucinous ovarian carcinoma were the mutation in KRAS, TP53, and HER- 2.

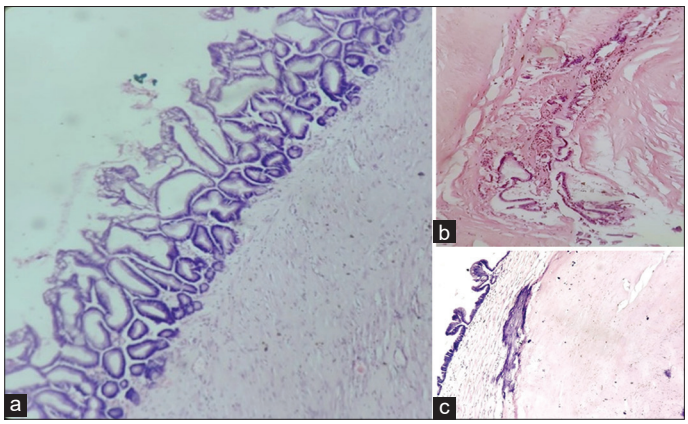

Figure 3: H and E stained Right ovary microscopy images (a) complex papillae with pleomorphic and hyperchromatic nuclei. (b) malignant cells infiltrating into the stroma; (c) H and E stained Right ovary microscopy images – focal cartilaginous component

Microscopically, mucinous tumors are lined by tall columnar epithelium with apical mucin which can be intestinal or endocervical. These mucosal linings may be complex, pleomorphic having expansile, or infiltrative patterns. Mucinous carcinoma is a heterogeneous tumor that follows the adenocarcinoma sequence, that is, "stepwise fashion." All three stages of the tumor can be seen in the same tumor, benign, borderline, and malignant, the present case also had a focal area of the single epithelial layer without atypia and focal areas showing stratification with pleomorphic cells. Focal areas showed tumor cells invading the stroma with desmoplastic reaction and tumor immunity. Invasion is termed as microscopic if it is <5 mm and true invasive if >10 mm. In 2014, the World Health Organization adopted the Lee and Schully classification of mucinous carcinoma into expansile and infiltrative classification helps in treatment and prognostication. The infiltrative subtype had a high risk of recurrence and mortality spread to the peritoneum and lymph nodes [10]. This patient had a stromal invasion and was started on chemotherapy after the surgical removal of the tumor.

A focal area of a cartilaginous component which could be focal metaplastic change or a collision tumor could be considered. A collision tumor is the coexistence of the two adjacent but histologically distinct tumors without histological admixture in the same tissue or organ that have been reported in various organs but the location in the ovary is rare [11]. Mucin seen metastasized to the pouch of Douglas, omentum, umbilical region, and sub-umbilical region.

The left ovary showed nests of transitional cells, some of which have coffee-bean appearing nuclei with a central lumen containing eosinophilic material (microcyst), these nests are surrounded by hyalinized fibrous stoma with areas of calcification which are classical of Brenner tumor.

Mucinous ovarian carcinoma coexistence with Brenner tumor is well known yet the coexistence of two types of ovarian tumors in the same patient is rarely been reported [12]. Despite many controversies with these two tumors, they have common histogenesis which had been always interesting. Approximately 10% of Brenner tumor is associated with mucinous carcinoma of the ovary. Brenner tumor may have evolved from transitional cells/metaplasia at the fallopian tube-peritoneal junction [7]. Brenner tumor's origin could be a Walthard nest, Graafian follicle, follicular epithelium, mesonephric remnants, coelomic epithelium, or rete ovarii [13]. Brenner tumors are asymptomatic and most of them are benign and occasionally, they secrete steroid hormones.

The left ovary of this patient is characteristically made up of abundant dense fibroblastic stroma with a solid cystic epithelial nest of transitional cells resembling those of the urinary bladder [6]. Cells show oval nuclei with distinct nucleoli and frequent nuclear grooves giving a coffee bean appearance. These microcysts are lined by metaplastic columnar epithelium with eosinophilic secretion in the lumen. Stroma shows focal hyalinization and calcific deposits confirm the coexistence of Brenner tumor in this patient.

CONCLUSION

The coexistence of Brenner with a mucinous ovarian tumor is a very rare entity. There are very few cases reported. Our case was belonging to the same age and had similar clinical symptoms to previously reported cases. Even though there is awareness in this modern era and has helped in the early detection and intervention of such malignancies; yet, there are neglected cases presenting in the advanced stage, especially in rural areas, thus meticulous approach in suspicious cases would help in earlier diagnosis.

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Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Kandhalu SK, Sameeraa PR, Mohan KV, Jayalakshmi M. A rare case of Giant mucinous cystadenocarcinoma of the right ovary with metastatic deposits and Brenner tumor in the left ovary. Indian J Case Reports. 2023; 9(2):41-43.