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Case Report

Ovarian Teratoma with Squamous Cell Carcinoma: A Rare Entity

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Abstract

Malignant transformation in a mature cystic teratoma of the ovary is rare, occurring in only 1-2% of cases, with squamous cell carcinoma consisting of about 75% of malignant transformations. Various genomic alterations take part in this pathogenesis but due to its rare incidence, not many cases have been reported in respect to this transformation. Hence, we describe a rare case of 45-year-old female with a 7.5 cm ovarian mature teratoma with an incidental finding of squamous cell carcinoma. With this case report, we also wish to create an awareness of this entity among pathologists and physicians while dealing with dermoid cysts of large sizes in older patients.

Keywords: Malignant transformation, Mature cystic teratoma, Squamous cell carcinoma.

INTRODUCTION

Ovarian tumors represent around 30% of all female genital tract (FGT) lesions with mature cystic teratoma of the ovary (MCTO) ranging from 10 to 20% of all ovarian tumors and 95% of all ovarian germ cell tumors [1]. Although the biological behavior of MCTO is benign and comprises of all the three germ layers namely, ectoderm, mesoderm and endoderm, 0.17–2% may undergo malignant transformation [2]. This transformation includes squamous cell carcinoma (SCC), adenocarcinoma, small cell carcinoma, sarcoma, malignant melanoma and mixed histology. Among them, SCC transformation in MCTO is most common and is seen arising from ectoderm, accounting for 75% of all malignant transformations [3]. Most MCTO are detected 15-20 years before they undergo malignant transformation. This entity is more commonly witnessed in postmenopausal patients whereas, among women in childbearing age group, pelvic ultrasonography helps in early detection.

Various theories describe this entity to be a continuous process of squamous metaplasia, atypical hyperplasia, carcinoma in situ, interstitial infiltration and invasive carcinoma [4]. As malignant transformation is rare, no standard treatment plan has been devised, although literature search advocates early treatment of MCTO in view of tumor staging and optimal debulking being critical for survival. Prognosis depends on various factors with FIGO stage being the most important among all. Unlike SCCs of the uterine cervix, postoperative adjuvant chemotherapy may produce a better result than adjuvant radiotherapy for advanced-stage cases [5].

Purpose of this case presentation is to create awareness among pathologists and physicians while dealing with dermoid cysts of large sizes in older patients, and also to emphasize on the importance of histopathology in making this diagnosis.

CASE REPORT

A 45-year-old post-menopausal female presented to us with complaints of weight loss and reduced appetite along with generalized weakness and body ache for the last 15 days. On examination, her vitals were stable. Her cardiovascular and respiratory examination was also unremarkable. Blood investigations showed an increase in total leucocyte

count of 10,000 /cumm with remaining parameters being within normal limits (hemoglobin 12.2 gm%, platelets 3,35,000/cumm, hematocrit 37%, mean corpuscular hemoglobin 26.2 pg, mean corpuscular volume 79 fL, mean corpuscular hemoglobin concentration 33 g/dl, red cell distribution width 16.2 %). Her random blood sugar levels (76 mg/dl) and liver profile (serum bilirubin 0.2 mg/dL, serum glutamic-oxaloacetic transaminase 13 U/L, serum glutamic pyruvic transaminase 16 U/l) were also normal. Although, her coagulation profile was deranged with prothrombin time of 18.21 seconds and raised C-reactive proteins 35.2 mg/dL. Serum markers including beta Human Chorionic Gonadotropin (1.66 mIU/ml) and alpha fetoprotein (0.80 ng/ml) were done. Her viral markers were non-reactive. She had a personal history of surgical menopause post hysterectomy 6 years back. On abdominal examination, a lump was palpable just below the umbilicus. Radiography was done in which ultrasound showed large complex cystic pelvic mass and contrast enhanced computerized tomography abdomen revealed large 11.6 x 9.7 x 8.8 cm complex cystic lesion with fat and calcification in the pelvis, pointing towards a possibility of mature teratoma. The patient was undertaken for laparotomy exhibiting large left solid cystic mass with dense adhesions to both bowel and bladder. Bilateral salpingo-oophorectomy was performed with cystic mass removal and specimen was sent for histopathological examination.

On gross examination, a single globular grey white soft tissue piece measuring 13 cm in maximum dimension was received. On sectioning, a cyst, measuring 8 x 7.3 x 5 cm, filled with whitish cheesy material and hair and a greyish white solid area, measuring 7.5 x 5 x 3 cm, was identified (Fig 1). The contralateral ovary with fallopian tube was unremarkable. Histopathological examination of cyst showed stratified squamous lining epithelium along with a focus of invasive tumor arranged in sheets, nests and few lying singly (Fig 2). These individual cells showed moderate amount of cellular pleomorphism with abundant eosinophilic cytoplasm, hyperchromatic nuclei and inconspicuous nucleoli. Sparse mitotic figures and abundant necrosis was also seen. Few areas also showed numerous sebaceous glands, stratified squamous epithelium, respiratory epithelium, bony cartilage & muscle tissue along with focal areas of hemorrhage, keratin pearls and calcification (Fig 3). One of the sections examined show normal ovarian parenchyma with numerous corpus albicans. Hence the diagnosis of ovarian teratoma with a focus of moderately differentiated squamous cell carcinoma was made.

As the English literature falls short of such cases and no standard treatment plan has been devised, this SCC component mandated further treatment. Adjuvant chemotherapy based on paclitaxel, ifosfamide and cisplatin (TIP) for 4 cycles was planned to be offered to the patient. The patient responded well to the treatment and is currently on follow up.

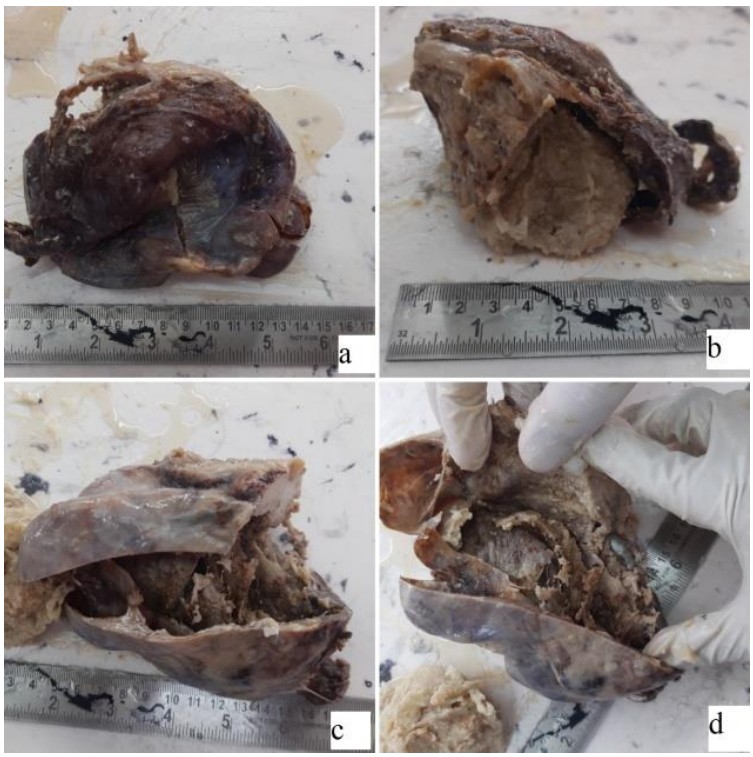

Figure 1: Gross examination of Left Ovary (a. Outer surface of ovary; b. Cheesy material after cutting open the specimen; c. & d. Cut surface of ovary with elements of mature teratoma)

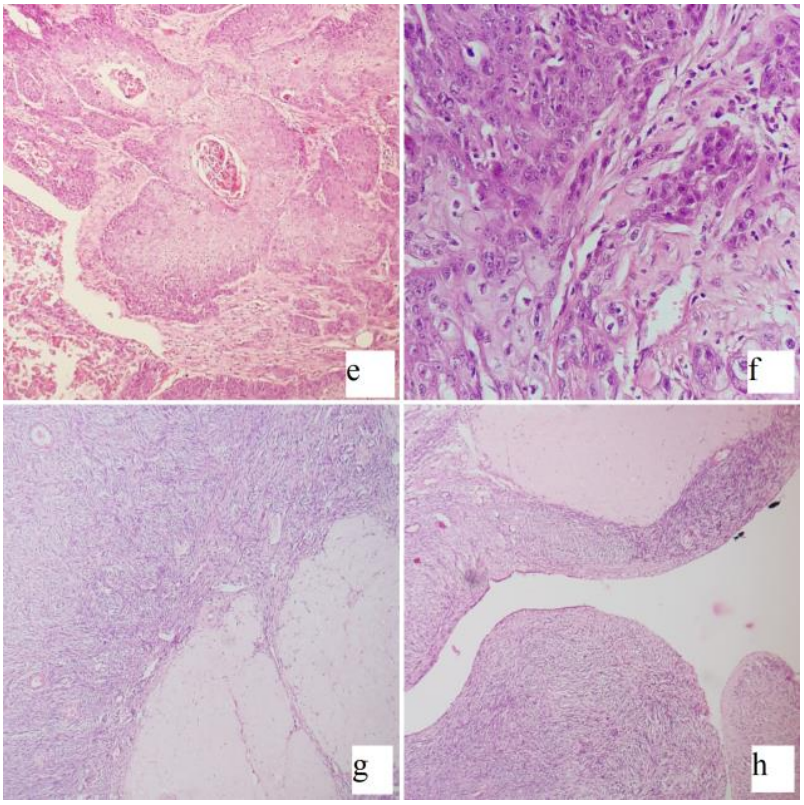

Figure 2: Microscopy of Teratoma with Squamous cell carcinoma (e. Sheets and nests of SCC, H&E,100x; f. SCC tumor cells invading into the underlying stroma, H&E,400x; g. & h. ovarian parenchyma with corpus albicans, H&E,100x)

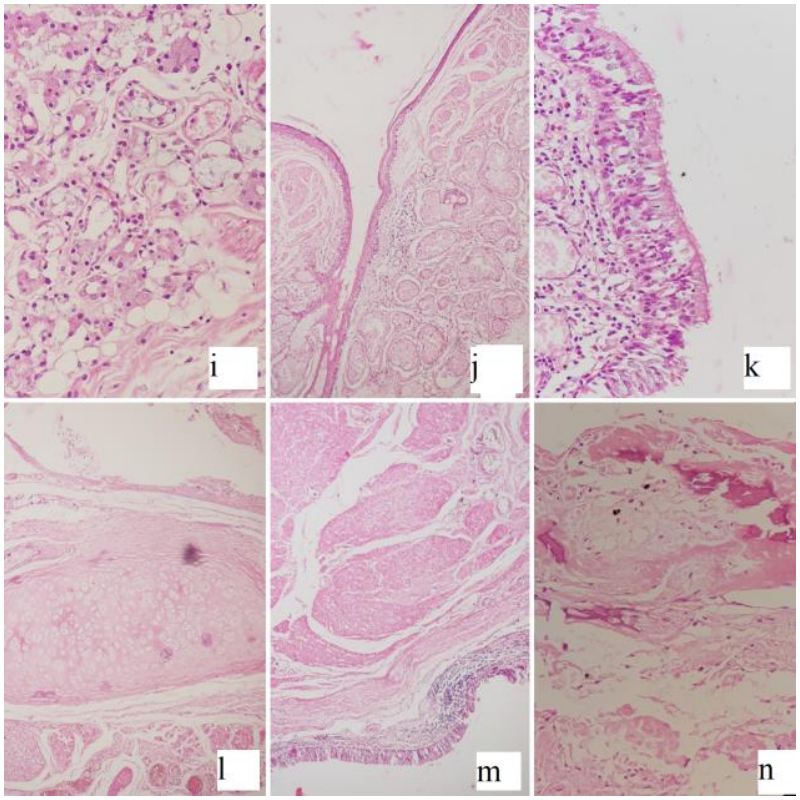

Figure 3: Microscopy of components seen in this case of teratoma (i. sebaceous glands, H&E, 400x; j. stratified squamous epithelium, H&E,100x; k. respiratory epithelium, H&E,400x; l. bony cartilage, H&E,100x; m. muscle tissue, H&E,100x; n. calcified tissue, H&E,100x)

DISCUSSION

Up to a quarter of ovarian masses originate from germ cells, and many of these are mature cystic teratomas. The secondary development of malignancy is a rare but well-known phenomenon in patients with ovarian teratomas. SCC in MCTO was mainly found in women aged more than 50 years, with high concentrations of squamous-cell-carcinoma antigen and cancer antigen CA125, and size more than 100 mm in size [5]. The clinical manifestations of SCC transformation in MCTO are not specific. At early stages, these tumors are often detected accidentally during routine physical examination or postoperative pathological examination, while symptoms like palpable mass, abdominal pain and fullness are often present in advanced stage. Acute abdomen may occur due to tumor torsion or rupture. Moreover, preoperative imaging investigation and laboratory tests are not specific either [6].

Pre-operatively, MCTO can be diagnosed based on various radiological clues including detection of bony tissues, teeth, bones and cartilages. However, the malignant transformation clues are difficult as this tumor cannot be readily differentiated from an uncomplicated MCT or other ovarian tumours [7]. Various risk factors have been identified that play a role in this transformation namely patient's age, menopausal status, tumor size, radiographical clues and serum markers. Hackethal *et al*., found the mean age of these patients around 55 years with raised serum markers (CA 125, CA 19.9 and CEA) in almost all the cases included in their analysis [5]. As per literature, the prognostic factors for ovarian carcinoma include capsular invasion, rupture, tumor dissemination, ascites, adhesions and additional invasive tumor types. Although prognosis seen in the study by Stamp *et al*., was very poor, as only five patients had tumor free period of 4 to 23 years while 18 survived for less than 12 months [8]. Patients with FIGO stage Ia tumours had better survival than those with more advanced disease.

Origin of SCC in MCTO can be either from epidermis or from columnar epithelium. The pathogenesis includes a continuous process of squamous metaplasia, atypical hyperplasia, carcinoma in situ, interstitial infiltration and invasive carcinoma [4]. Cooke *et al.*, also analyzed genomic alterations of 25 SCCs arising from MCTO and reported alterations of TP53, PIK3CA and CDKN2A [9]. Tamura *et al*., found genes associated with the PI3K-mTOR pathway, cell cycle pathway, protein kinase and epigenetic regulator were frequently altered [10]. They also found that XCL1 was overexpressed in cases with SCC in MCTO and was significantly associated with number of tumor infiltrating CD8 positive T cells and programmed death ligand-1 (PD-L1) expression on tumor cells, thus making it a promising biomarker for malignant transformation of MCTO into SCC and even a biomarker candidate of therapeutic response to anti PD-L1 therapy.

SCC arising from MCT is therefore a rare, albeit potentially lethal disease that warrants aggressive multimodal treatment approach. As the English literature falls short of such cases, a standard treatment plan has still to be devised. The scarcity of literature mandates that pathologists and physicians share their experience in diagnosing and treating this rare entity.

CONCLUSION

SCC in a setting of MCTO is a rare entity and various genomic alterations are seen to play an important role in its pathogenesis. A standard treatment plan is still to be devised for the treatment of such cases. Pathologists and physicians should therefore keep this rare type of tumor in mind when facing with a dermoid cyst, especially in older patients, or in patients with larger than usual cysts.

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Authors' Contributions:

Conceptualization: AK, VD, AK
Data curation: VD, AK, SN
Critical and intellectual evaluation: AK, VD, AK, SN
Drafting of manuscript: VD, AK, SN
Approval of final manuscript: All authors

REFERENCES

1. Höhn, A. K., Brambs, C. E., Hiller, G. G., May, D., Schmoeckel, E., & Horn, L. C. (2021). 2020 WHO classification of female genital tumors. *Geburtshilfe und Frauenheilkunde*, *81*(10), 1145-1153.
2. Kikkawa, F., Ishikawa, H., Tamakoshi, K., Nawa, A., Suganuma, N., & Tomoda, Y. (1997). Squamous cell carcinoma arising from mature cystic teratoma of the ovary: a clinicopathologic analysis. *Obstetrics & Gynecology*, *89*(6), 1017-1022.
3. Li, C., Zhang, Q., Zhang, S., Dong, R., Sun, C., Qiu, C., ... & Kong, B. (2019). Squamous cell carcinoma transformation in mature cystic teratoma of the ovary: a systematic review. *BMC cancer*, *19*(1), 1-12.
4. Pins, M. R., Young, R. H., Daly, W. J., & Scully, R. E. (1996). Primary squamous cell carcinoma of the ovary: report of 37 cases. *The American journal of surgical pathology*, *20*(7), 823-833.
5. Hackethal, A., Brueggmann, D., Bohlmann, M. K., Franke, F. E., Tinneberg, H. R., & Münstedt, K. (2008). Squamous-cell carcinoma in mature cystic teratoma of the ovary: systematic review and analysis of published data. *The lancet oncology*, *9*(12), 1173-1180.

6. Park, J. Y., Kim, D. Y., Kim, J. H., Kim, Y. M., Kim, Y. T., & Nam, J. H. (2008). Malignant transformation of mature cystic teratoma of the ovary: experience at a single institution. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, *141*(2), 173-178.
7. Mayer, C., Miller, D. M., & Ehlen, T. G. (2002). Peritoneal implantation of squamous cell carcinoma following rupture of a dermoid cyst during laparoscopic removal. *Gynecologic oncology*, *84*(1), 180-183.
8. Stamp, G. W. H., & McConnell, E. M. (1983). Malignancy arising in cystic ovarian teratomas. *BJOG: An International Journal of Obstetrics & Gynaecology*, *90*(7), 671-675.
9. Cooke, S. L., Ennis, D., Evers, L., Dowson, S., Chan, M. Y., Paul, J., ... & McNeish, I. A. (2017). The driver mutational landscape of ovarian squamous cell carcinomas arising in mature cystic teratoma. *Clinical Cancer Research*, *23*(24), 7633-7640.
10. Tamura, R., Yoshihara, K., Nakaoka, H., Yachida, N., Yamaguchi, M., Suda, K., ... & Enomoto, T. (2020). XCL1 expression correlates with CD8-positive T cells infiltration and PD-L1 expression in squamous cell carcinoma arising from mature cystic teratoma of the ovary. *Oncogene*, *39*(17), 3541-3554.

