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Case Report

Malignant transformation in mature cystic teratoma of ovary: Series of 4 cases

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ABSTRACT

Mature cystic teratoma is the most common benign ovarian tumour of germ-cell origin. Malignant transformation is rare in mature cystic teratoma. Here, we present a series of 4 cases showing malignant transformation in the form of squamous cell carcinoma, follicular carcinoma, and clear cell carcinoma in mature cystic teratoma. Our case series suggests that there should be suspicion of malignant transformation in mature cystic teratomas when they are present in perimenopausal and postmenopausal females.

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INTRODUCTION

Teratoma term was coined by Rudolf Virchow in 1863 from the Greek word “teras” meaning monster. Teratomas are the most common ovarian germ cell neoplasms. Different theories are given regarding the origin of teratomas. Origin from the primordial germ cell due to failure of meiosis I is the most accepted theory. Other theories originate from blastomeres segregated at an early stage of embryonic development or from embryonic cell rests.[1]Histologically, they are divided into mature teratoma, immature teratoma, and monodermal or highly specialised teratoma. Mature teratoma can be solid or cystic. They are composed of

mature tissue from ectoderm, mesoderm and endoderm. Mature cystic teratoma (MCT) is also known as dermoid cysts and is usually benign. Malignant transformation is seen in 0.17–2% of cases.[2] Malignant transformation is seen in older and postmenopausal females. It is rarely diagnosed preoperatively. Here, we present a series of three cases with malignant transformation in a MCTof the ovary that presented in our institute.

CASE REPORTS

 # CASE 1: A 49-year perimenopausal femalepresented with complaints of pain lower abdomen. On per abdominal examination, a mass arising out of the pelvis was felt on the left side of the abdomen. On CECT, a cystic adnexal mass was seen and the possibility of MCTwas kept. A totalabdominal hysterectomy with bilateral salpingo-oophorectomy was done. Intraoperative findings revealed a left ovarian cyst with an intact capsule and no adhesions were identified. The sample was submitted for histopathological examination. A cystic mass measuring 12x10.5x10cm was received with a smooth outer surface. The cut section revealed unilocular a cyst filled with sebaceous material and hair along with some solid and papillary areas. Sections were taken from solid areas and processed. Microscopic examination revealed keratinized stratified squamous epithelium lining, hair follicles, sebaceous glands, lobules of mature cartilage, glands lined by respiratory mucosa, skeletal muscle, and adipocytes along with tumour epithelial cells showing features of squamous cell carcinoma (fig. 1,2). Diagnosis of squamous cell carcinoma arising in MCTwas given.

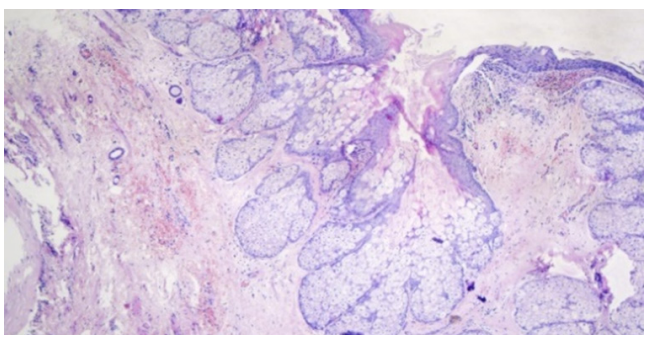

Figure 1: *Mature cystic teratoma*

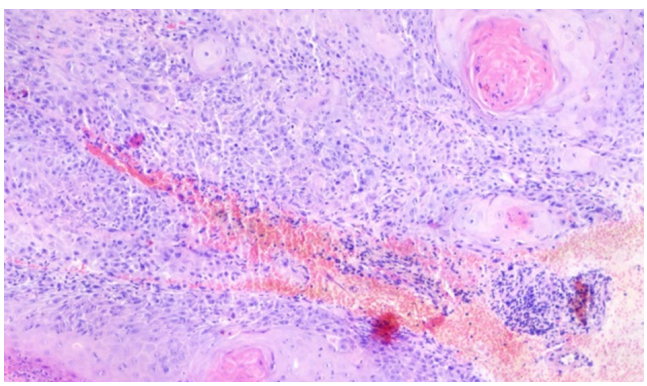

Figure 2: *Squamous cell carcinoma in mature cystic teratoma*

 # CASE 2: A 63-year female presented with complaints of heaviness of the abdomen for 20-25 days. On per abdomen, a mass was felt arising fromthe left side of the pelvis. Routine and specific examinations were done. On ultrasonography, a solid cystic mass was seen and the possibility of a dermoid/malignant tumour was kept. TAH with BSO was done. The intraoperative findings revealed a left ovarian mass with dense adhesions with omentum. The specimen was submitted for histopathological examination. Grossly a solid cystic tumour of 18.8x16x12 cm was received with an irregular outer surface. The cut section revealed a multinodular cyst filled with sebaceous and keratinaceous material and hair. A solid area with papillary excrescences was also identified. Microscopic examination revealed a tumour with histopathological features consistent with squamous cell carcinoma arising in MCT.

 # CASE 3: A 46-yearfemale presented with heaviness and pain lower abdomen for 15days. On per abdominal examination, a mass was notedfromthe pelvis tothe umbilicus. On ultrasonography, an abdominopelvic cystic lesion reaching up to the umbilicus with no septations/solid component was seen and the right ovary was not separately visualised. Exploratory laparoscopy with TAH with BSO was done and the sample was sent for histopathological examination. A cystic mass measuring 9 cm in diameter was received. The outer surface was smooth and shiny, on cut sections, small cystic spaces were identified, filled with brownish seromucinous material. No solid area was seen. Sections were taken and processed. Microscopic examination revealed a tumour comprising of mature thyroid tissue consisting of follicles of varying sizes, lined by a single layer of columnar to flattened epithelium, filled with colloid. In addition, the tumour showed crowded follicles and invasion into adjacent ovarian parenchyma (fig.3,4). Adipose tissue was seen focally. Diagnosis of strumaovarii with the possibility of follicular carcinoma thyroid was given, and close clinical follow-up was advised. The thyroid hormone profile of the patient was within normal limits. Post-operative CECT abdomen and pelvis revealed lytic lesions in vertebrae and iliac regions further confirming the diagnosis of follicular carcinoma arising from struma ovarii.

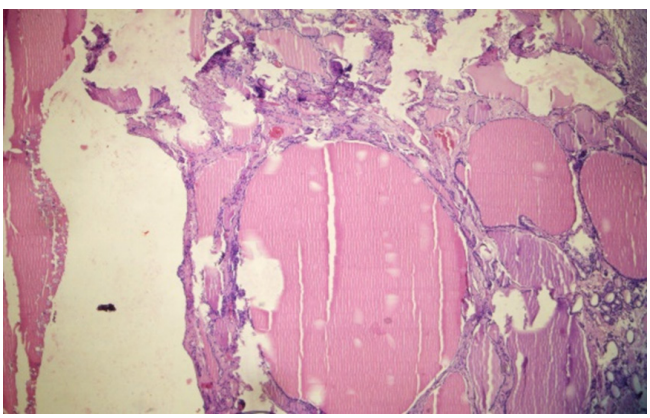

Figure3: *Thyroid follicles of varying sizes lined by columnar to flattened epithelium (HE stain X40).*

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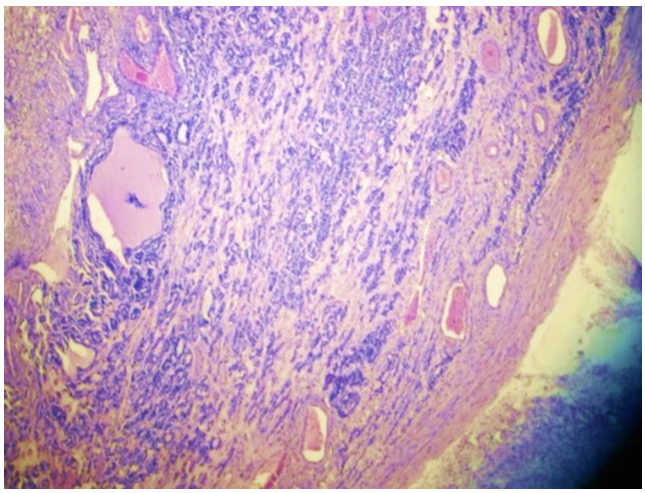

Figure4: *Crowded thyroid follicles showing invasion of ovarian stroma. (HE stain X 100).*

 # CASE 4: A 73-year female presented with heaviness in her abdomen. On per abdomen examination, an abdominopelvic mass was palpated. On ultrasonography, a left-sided solid cystic adnexal mass was seen and the possibility of a dermoid cyst was kept. TAH with BSO was done, and the sample was sent for histopathological examination. On gross examination, the left ovary was converted into a cyst measuring 16cm in diameter and it was filled with keratinaceous debris and hair. A solid area measuring 6X3X0.5 cm was identified. Sections were taken and processed. Microscopic examination revealed adenocarcinoma in the background of mature cystic teratoma. The malignant cells are arranged in papillae and clusters. These cells show a polyhedral shape with abundant clear cytoplasm and eccentric nucleus (fig. 5,6). Diagnosis of adenocarcinoma, possibly clear cell carcinoma arising in MCTwas given and immunohistochemistry was advised.

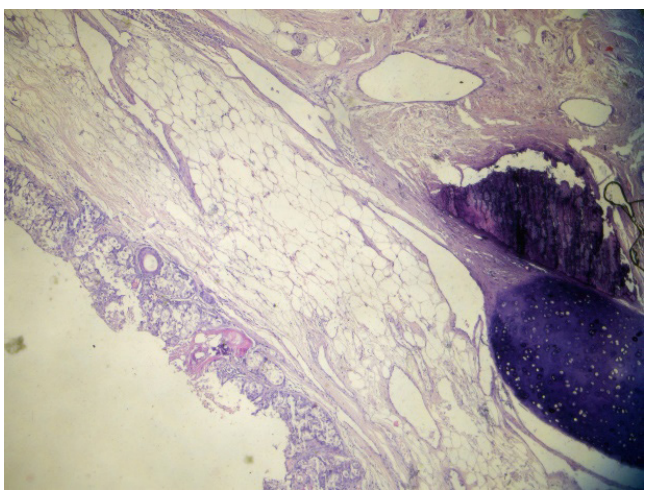

Figure5: *Tumour cells showing features of clear cell carcinoma in the background of mature cystic teratoma (HE stain, X40)*

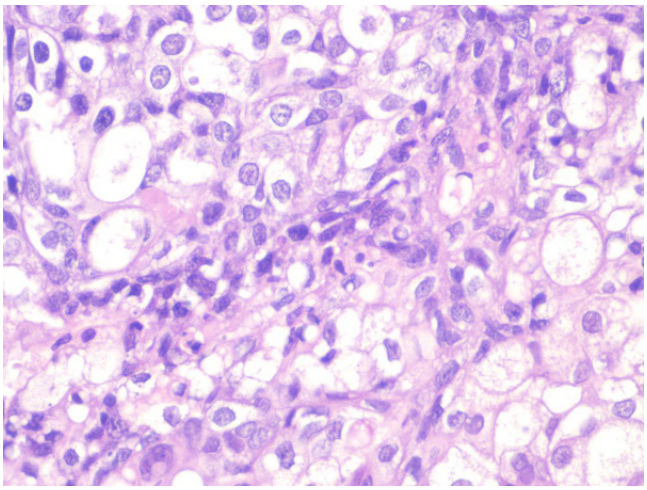

Figure6: *Tumour cells showing enlarged pleomorphic nuclei with clear cytoplasm (HE stain, X 100).*

DISCUSSION

MCTare one of the most common benign ovarian neoplasms, accounting for 10 to 20% of all ovarian tumours.[3] They can occur at any age, but the peak incidence is reported between 20 and 40 years of age.[4] Malignant transformation is rarely seen in MCT. The rarity of malignant transformation is seen in all age groups, but the chances of any of the components becoming malignant arehigher in perimenopausal and postmenopausal females. Malignant transformation in MCTis diagnosed with difficulty in the preoperative period due to a lack of specific signs and symptoms. The most common malignancy seen is squamous cell carcinoma, which represents about 75% of malignant transformations, other neoplasms, including adenocarcinoma, neuroectodermal tumours, sarcoma, and malignant melanoma, have also been reported.[5,6]

The mean age of presentation in our series is 56 years. Lesa dos Sentos et al in their study found amean age of 57 years.[7] The tumour was on the left side in two of our cases. The mean size of the teratoma in our study was 13.95 cm. Studies have reported that suspicion for malignancy should be raised when an MCT is larger than 9.9 cm.[8,9]Three out of four tumours in our study were multilocular. The contents comprised keratinaceous debris with hair in three cases while one case which was diagnosed as follicular carcinoma was filled with brownish seromucinous material.

Literature shows that the transformation of mature teratoma to squamous cell carcinoma is most common. Squamous cell carcinoma is considered to originate from a columnar epithelium (ciliated or non-ciliated) or a metaplastic squamous epithelium.[2] The pathogenesis of malignant transformation is still not clear. It is postulated that since 80% of mature teratomas are diagnosed during reproductive age, malignant transformation may develop due to the long-term presence of a non-removed teratoma.[10] Molecular studies conducted have shown overexpression of p53 in

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these cases.[11]

Approximately 5–20% of cases of mature teratoma contain thyroid tissue. The term "struma ovarii" is used when thyroid tissue is the predominant component containing 50% or more thyroid tissue. Struma ovarii is a monodermal variant of ovarian teratomas, which comprises 1% of all ovarian tumours and 2–3% of all mature ovarian teratomas [12], occurring in 5% of all. Thyroid tissue in strumaovarii is morphologically, and biochemically like that of the cervical thyroid gland. Hyperthyroidism appears clinically in 5–8% of the cases of struma ovarii, however, the thyroid hormone profile was normal in our case. Diagnosis of malignant transformation in struma ovarii, in the absence of typical nuclear features, is based on infiltration by tumour cells into the surrounding ovarian tissue, and involvement of the vascular system, or metastasis. Our case had an invasion of ovarian stroma along with metastatic lytic bony lesions. Malignant transformations that have been reported in struma ovarii are papillary carcinoma, follicular variant of papillary carcinoma and a few cases of follicular carcinoma. Struma ovarii with malignant transformation must be distinguished from thyroid carcinoma metastatic to the ovary by clinical examination and ultrasonography, which were normal in our case.

Clear cell carcinoma arising in mature cystic teratoma is extremely rare with only a few case reports. It is very important to determine whether the clear cell carcinoma coexists incidentally with MCTor whether the clear cell carcinoma arises from MCT. Three cases of the coexistence of MCT and clear cell carcinoma have been reported but only one case has been reported in which the clear cell carcinoma is seen arising from mature teratoma.[13,14]An extensive sampling of tumours was done in our case, but no focus on endometriosis was noted. Maeda et al have reported characteristic histological proof of transition from simple squamous epithelium via simple glandular epithelium to papillary change with atypiawhich is also seen in our case.[15] Preoperative serum markers (SCC antigen, CEA etc) are of less use as malignant transformation in mature cystic teratoma is a very rare occurrence and is often not suspected on radiological or clinical examination. Mori et al. concluded that a combination of the patient's age (above 40 years) with serum SCC antigen level (> 2.5 ng/ml) may be considered a suitable marker for diagnosis.[10] Some studies concluded that SCC antigen alone or in combination with other markers, such as macrophage colony-stimulating factor (M-CSF) and carcinoembryonic antigen (CEA), may be considered suitable markers for a preoperative diagnosis of MT in MCT.[16,17] In our study serum SCC levels were not determined in any of the cases, possibly due to the lack of a strong clinical and radiological suspicion of a malignant change.

Patient with mature cystic teratomas is given platinum-based chemotherapy post-operatively. Malignant transformation carries a poor prognosis due to chemoresistance to the therapy and makes the use of adjuvant treatment necessary. It is difficult to diagnose the malignant transformation preoperatively, however, a high index of suspicion based on the history and examination of the patient may give a clue towards the diagnosis. Patients with MCT may sometimes present with a rapidly enlarging tumour or may present with systemic symptoms suggestive of malignancy in an advanced stage of the disease.

CONCLUSIONS

There should be a high index of suspicion of malignant transformation in mature cystic teratoma in perimenopausal and postmenopausal females. The risk of malignancy increases with the increase in tumour size, age, and presence of mixed solid cystic components. Extensive sampling should be done in such cases as malignant transformation can lead to resistance to standard chemotherapy and poorer prognosis.

Conflict of Interest: None

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