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Malignant transformation of mature cystic teratoma an histological dilemma: Case report

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Abstract
Malignant transformation of mature cystic teratoma is a rare phenomenon and often a diagnostic challenge. We present a case of a 42-year-old female presenting with abdominal distension. CECT abdomen revealed a solid cystic tubo-ovarian mass in pelvis which was then resected. On histopathological examination of the resected specimen a diagnosis of Malignant transformation of MCT with the possibility of malignant component to be Squamous cell carcinoma or Clear cell carcinoma was given. On Immunohistochemical evaluation the malignant component was confirmed to be Squamous cell carcinoma.

Keywords: Malignant transformation, mature cystic teratoma, diagnostic challenge

Introduction
Mature cystic teratoma is a common benign ovarian tumor comprising approximately 40% of all ovarian neoplasms. It's the most common germ cell tumor of ovary. Malignant transformation of MCT's is rare and occurs in 1-2% of cases, most common of which is transformation to Squamous cell carcinoma (75%). We report a case of malignant transformation of MCT having histological features of both squamous cell carcinoma and clear cell carcinoma thus making it a diagnostic challenge on histology.

Case Report
A 42-year-old female patient presented with the complaint of abdominal distension. Serum tumor marker levels were carcinoembryonic antigen (CEA): 8.90ng/ml (normal <2.5), CA19-9: 1761.85 U/ml (normal < 30.9) and CA 125: 562.1 U/ml (normal < 30.2). On CECT abdomen a heterogeneously enhancing soft tissue mass was seen in pelvis extending to bilateral adnexa with solid cystic component. The mass also showed a heterogenous fat density lesion and few specs of calcification. The mass was abutting the uterus and the bilateral ovaries were not visible separately.
On exploratory laparotomy a large left tubo-ovarian cystic mass was identified which was densely adherent to the surrounding structures forming a jumbled mass. Right side ovary and fallopian tube were not visible due to dense adhesions. The mass was resected and 100-130 cc of clay colored fluid was drained. Omentectomy was also done.
The resected tubo-ovarian mass measuring 13x9x4.5 cm^3 was a unilocular cyst focally showing pultaceous material and a thickened portion. Outer surface was grey yellow to grey brown and had attached fallopian tube (Fig.1).

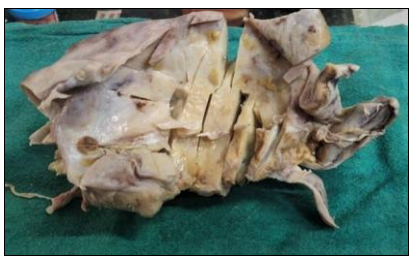

Fig 1: Gross specimen showing the solid area of the cyst wall

On microscopic examination the cyst wall was lined partly by stratified squamous and partly by glandular epithelium (Fig. 2). The subepithelium showed inflammatory infiltrate, adipose tissue, muscle fibres, melanin, mature neural tissue, focal dystrophic calcification and flakes of keratin, indicating MCT (Fig.3). Areas where the lining was absent showed marked foreign body giant cell reaction (most probably to the keratin). Sections from the solid area of the cyst showed tumor cells in glandular/ tubular and lobular arrangement, separated by thick hyalinized stroma (Fig. 4, 5). The glands were lined by single layer of tumor cells showing nuclear hob-nailing which is a characteristic of Clear cell carcinoma (Fig. 6). The tumor cells in lobular arrangement were polygonal, having small round and angular to large pleomorphic nucleus, hyperchromatic to vesicular chromatin, variably prominent nucleoli and abundant eosinophilic to clear cytoplasm. These features indicated squamous cell carcinoma with clear cell change. Also, similar lobular pattern is also seen in solid pattern of clear cell carcinoma. In view of these findings a diagnosis of malignant transformation of MCT was given, with the possibility of malignant component to be either Squamous cell carcinoma with clear cell change or Clear cell carcinoma. Immunohistochemistry (IHC) was advised for exact characterization.

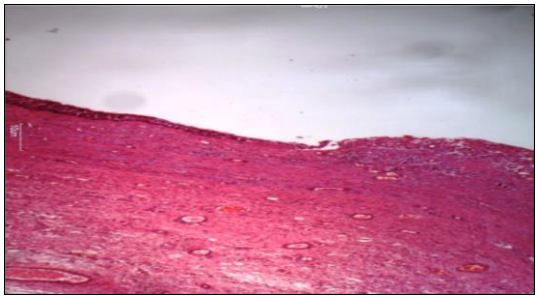

Fig 2: Microphotograph showing stratified squamous lining of the cyst

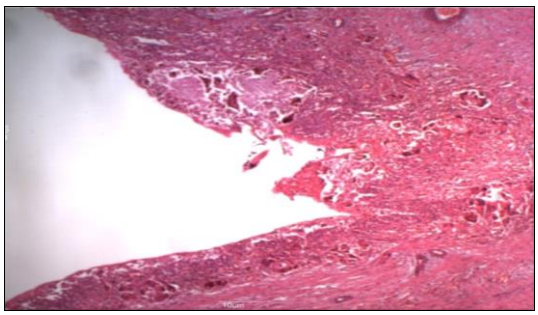

Fig 3: Microphotograph showing melanin pigment, blood vessels and muscle fibres in the cyst wall

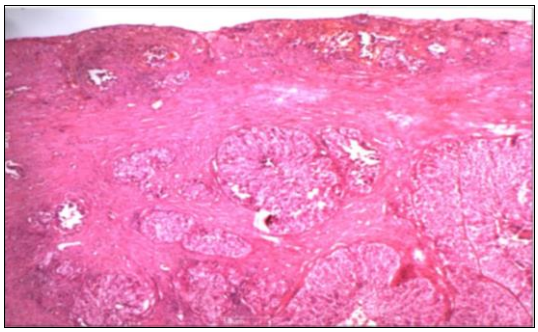

Fig 4: Microphotograph of areas showing tumor cells in solid nests and gland formation

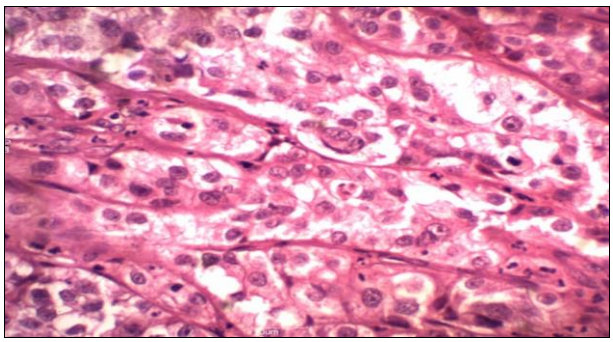

Fig 5: Microphotograph showing tumor cells with clear cell change

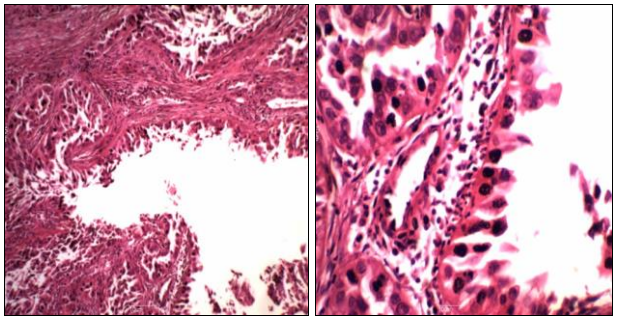

Fig 6: Low and high-power view of the tumor cells in gland formation and showing nuclear hobnailing

On IHC tumor cells showed positivity for p63 and focal positivity for CK5/6 confirming Squamous cell carcinoma. Other markers (Napsin A, PAX8, WT1, GATA3, CK7, CK 20, CEA, S100, SALL4, Synaptophysin) were all negative.

Discussion

MCT is the most common germ cell tumor of ovary which usually arises during reproductive years. The tumor is composed of well-differentiated derivatives of the three germ layers–ectoderm, mesoderm, and endoderm – with ectodermal elements predominating.

In its pure form, mature cystic teratoma is always benign but occasionally it may undergo malignant change in any of its various elements. This malignant transformation occurs in 1-2% of MCT cases [17]. Transformation to Squamous cell carcinoma is most common, other transformations include adenocarcinoma, carcinoid tumor, melanoma etc. [1].

The diagnosis of malignant transformation of MCT is mainly done histologically. Lack of specific clinical signs, tumor markers and imaging features makes it difficult to diagnose MCT preoperatively. However, certain factors have been suggested by various studies which can indicate malignant transformation such as age (most of the malignant MCT are seen in post-menopausal women whereas MCT alone is usually seen in reproductive age women), size of tumor, solid cystic mass on imaging and elevated tumor markers such as SCC antigen, CA125, CEA and CA19-9[1-6].

Grossly the tumor is frequently larger than the average mature cystic teratoma. It may exhibit a more solid appearance, but differentiation usually cannot be made on gross examination [16].

Hackethal *et al*. study reported a mean age of 55 years and tumor size of 14.8 cm for malignant transformation of MCT[1]. Chen *et al*. reported a mean age of 55.0 ± 14.4 years and a mean size of 13.8 ± 5.7 cm [7]. In our case the patient age was 42 years and tumor size was 13.5 cm which is within the reported range by various studies.

Hackethal *et al*. reported elevation of serum markers in

malignant transformation of MCT. In their study high SCC antigen was seen in 86.5%, high CA 125 in 71%, high CA 19-9 in 77% and high CEA in 16% of patients. High SCC antigen and CA 125 were associated with poor outcome [1]. According to Mori *et al.* combination of patients age (>40years) and serum SCC antigen level (>2.5ng/ml) was 77% sensitive and 96% specific for malignant transformation. Elevated SCC antigen is usually seen when the transformation is to squamous cell carcinoma [5]. In our case the SCC antigen was not measured but the other three markers (CEA, CA125, CA 19-9) were elevated.

None of these factors are helpful in indicating the histological type of malignant transformation that has occurred in the MCT, except for serum SCC antigen level of more than 2.5 ng/ml which is mostly seen in case of transformation to squamous cell carcinoma [5].

Our case was a diagnostic dilemma as it showed histological features of both Squamous cell carcinoma and Clear cell carcinoma with MCT.

Squamous cell carcinoma is the most common malignant transformation in MCT (75% of cases) which are usually moderate to poorly differentiated [16].

Transformation of MCT to clear cell carcinoma is rare and to our knowledge only one case has been reported till now[10], while three reports of coexistence of MCT and clear cell carcinoma are also there [9, 11, 12].

Clear cell carcinoma as we know histologically displays several patterns which often occur together. These include papillary, tubulocystic and solid. Solid pattern shows sheets of polyhedral cells with abundant, clear cytoplasm separated by delicate fibrovascular septae or dense fibrotic stroma. Papillary pattern shows hyalinized or fibrotic papillae lined by clear cells showing atypia and hob-nailing and tubulocystic pattern shows tubules and cysts lined by clear cells [17].

The one case report of Clear cell carcinoma arising from MCT reported papillary and glandular lesions with hobnail like atypical cells.

Similar to this in our case too areas of tubule / glandular formation with hobnail like atypical cells were seen along with lobules of cells with clear to eosinophilic cytoplasm like the solid pattern of Clear cell carcinoma.

Identifying the correct histological type of transformation in MCT becomes important as transformation to squamous cell carcinoma has a relatively better prognosis than other histological types. Also, clear cell carcinoma of ovary shows resistance to platinum-based chemotherapy which is currently used in these tumors because of its known activity against epithelial ovarian carcinoma and squamous cell carcinoma of cervix [13-15].

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