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Carcinoma arising in a mature cystic teratoma of the ovary - A rare case report

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ABSTRACT

Mature cystic teratoma (MCT) makes up almost 20% of all ovarian neoplasms. They are unilateral in 88% of cases and bilateral in about 10 % of cases. Malignant neoplasm is an uncommon event in MCT. It occurs in approximately 2% of cases. Most common malignant change in MCT is Squamous cell carcinoma, followed by carcinoid tumour, adenocarcinoma, malignant melanoma, sarcoma of various types, carcinosarcoma and malignant tumour of neural tissue. In this study we present a case of 38 years old woman presented with complains of pain and lump in the abdomen. She was evaluated clinically and biochemically. Investigation by ultrasound showed a left ovarian cystic mass with mixed echo pattern suggestive of Dermoid cyst with solid area. Her CA 125 was high. She underwent a hysterectomy with bilateral salpingo-oophorectomy for the removal of ovarian mass. On gross as well as on histopathology examination tumor shows features of Dermoid cyst with area showing highly cellular, spindle shaped cells with features of anaplasia and increased abnormal mitotic activity suggestive of poorly differentiated malignant tumor. Immunohistochemical study (IHC) shows strong positivity for cytokeratin confirms poorly differentiated (Sarcomatoid) Carcinoma arising in a mature cystic teratoma of the ovary. This rare type of malignant transformation should be kept in mind when faced with a dermoid cyst, especially in older patients, or in patients with larger than usual cysts.

INTRODUCTION

Mature cystic teratoma (MCT) is not a rare occurrence, accounting for about 20% of ovarian tumors, but malignant transformation of MCT is infrequent. Reports vary, but the risk of transformation is estimated to be around in 2% of cases and this most commonly occurs in postmenopausal women. [1] As expected, any component of the MCT can undergo malignant transformation, but most common malignant change in MCT is squamous cell carcinoma. It accounts for 80% of secondary malignant transformations of ovarian teratomas. [2] Preoperative diagnosis of malignant transformation is very difficult clinically, because this tumour cannot be readily differentiated from an uncomplicated MCT or other ovarian tumours. Serum tumour markers, patient age and tumour size are useful factors in distinguishing malignant transformation in mature cystic teratoma. We report one such rare case of poorly differentiated carcinoma arising in a peri-menopausal woman which seems to be worthy of review.

CASE REPORT

A 38-year-old female presented with history of pain and swelling of abdomen of about one month duration. Patient had normal menstrual cycle. Obstetric history was P2 G2.Her Hemoglobin was 9.9.Gm./dl. And CA 125 was 85 IU. (High). Other lab investigations were within normal limit. Ultrasound examination showed a well-outlined mass in the left adnexa with a mixed echo pattern consisting of cystic and solid components. A clinical diagnosis of the left ovary teratodermoid was made. The patient underwent total hysterectomy with bilateral adnexectomy. During surgery left ovary showed cystic as well as solid areas. It was adherent to the intestine and lateral pelvic wall. Biopsy from left Pelvic wall was also taken.

Gross examination: - Uterus with Cervix and both fallopian tubes were found normal. Left ovary was measuring 17x11x9 cm. and weighing 300 gms surrounded by greyish white capsule. On cut section it showed two different components cystic and solid with little demarcation. Cystic space was filled with cheesy

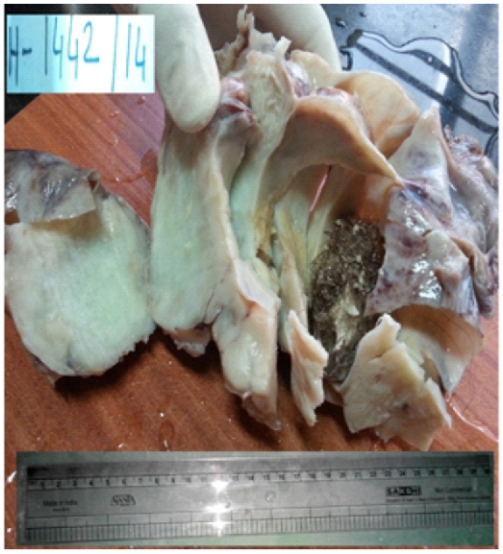

Figure 1: (The ovarian tumourmeasuring17x11x9 cm. On the right unilocular cystic space filled with hair and cheesy material. Adjoining whitish solid mass measuring 6 cm in diameter.)

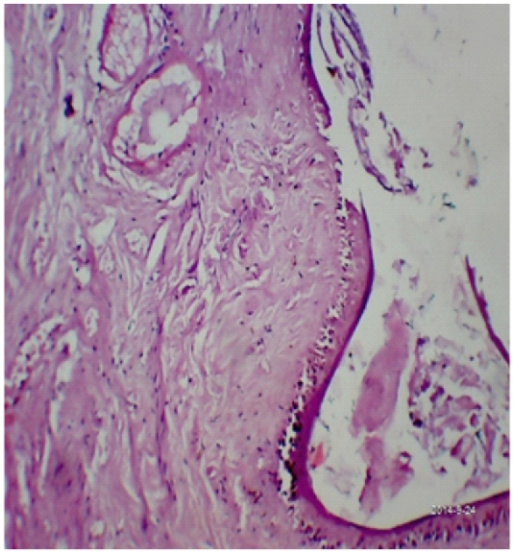

Figure 2: (H&E, 10X Cyst wall lined by stratified squamous epithelium with underlying area showing skin appendages.)

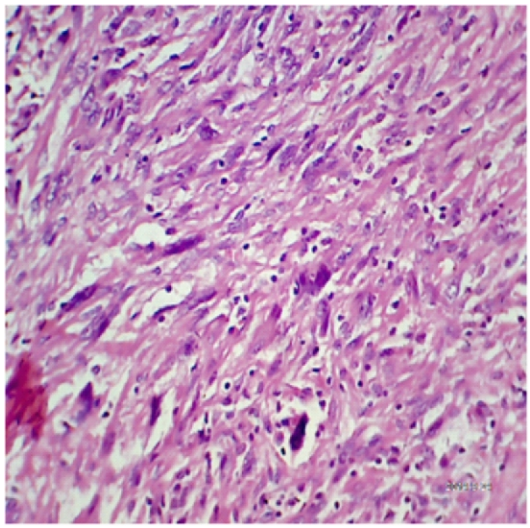

Figure 3: (40X, H&E shows mainly spindle shaped tumour cells with features of Anaplasia.)

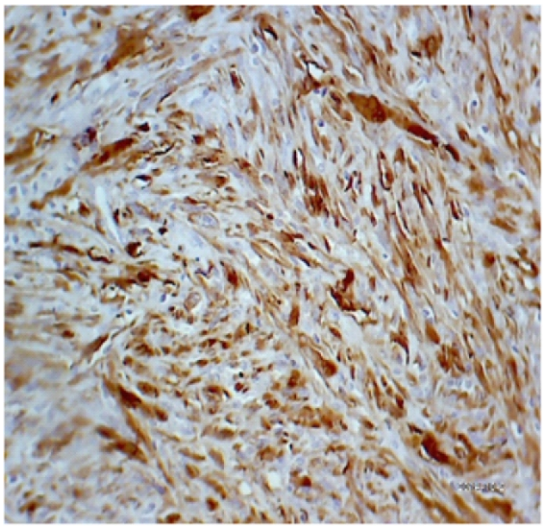

Figure 4: (40X, CK strongly positive in tumour cells)

material and hair follicles. Adjoining solid mass was whitish firm to hard in consistency with small foci of haemorrhage. (Figure 1) Rt. Ovary was normal in size with small cyst.

Microscopically on H&E stain, the cystic portion shows stratified squamous epithelium lining over the adnexal structures like sebaceous gland and hair follicles. Keratinous material was also seen on the surface. (Figure 2) No immature or neural tissue was identified. These findings were consistent with the diagnosis of mature cystic teratoma. Sections from the Adjacent solid area shows high cellularity of spindle shaped cells with storiform arrangement having features of anaplasia and high and abnormal mitotic activity. (Figure 3) Also present focal areas of haemorrhage and chronic inflammatory cells infiltrate. Features are in favour of poorly differentiated malignant tumor. Similar histology was also seen on pelvic biopsy. Various differential diagnoses like immature teratoma, Carcinosarcoma, Metastasis of tumour from intestine were considered. Immuno histochemical stains like Cytokeratin, Desmin, CD 117, DOG 1, H caldesmon and P 63 were done. Tumour cells showed strong positivity for Cytokeratin and focal positivity of Desmin. Other markers study was negative. Cytokeratin was strongly and diffusely positive in spindly tumour cells. (Figure 4) Based on our H & E and IHC findings, the tumour was diagnosed as Mature Cystic Teratoma with poorly differentiated (Sarcomatoid) carcinoma. Post-operative CT Scan showed infiltrative diffuse residual malignant mass in pelvis crossing midline adherent to pelvic small bowel loops and Sigmoid colon with metastatic bilateral internal iliac nodes. Liver appears normal.

DISCUSSION

Germ cell tumours account approximately for 30 % of all ovarian tumours. Mature cystic teratoma makes up almost 20% of all ovarian neoplasm. They are unilateral in 88% of cases and bilateral in about 10 % of cases. Malignant change is an

uncommon event in MCT. It occurs in approximately 2% of cases. [1] MCT accounts for 10 - 20 % of all ovarian tumours in females of reproductive age group is composed of well differentiated cell layers (ectoderm, mesoderm, endoderm).Most common malignant change in MCT is squamous cell carcinoma. It accounts for 80% of secondary malignant transformations of ovarian teratomas. [2] Others are Carcinoid tumour, adenocarcinoma, Malignantmelanoma, sarcoma of various types, Carcinosarcoma and malignant tumour of neural tissue. Sarcomatous transformation is even more unusual; only a few cases of leiomyosarcoma, chondrosarcoma,osteosarcoma, angiosarcoma, fibrosarcoma and malignantfibrous histiocytoma have ever been described. [3] Clinical signs and symptoms of malignant change in MCT are not much specific. The common symptom is abdominal pain followed by abdominal or pelvic mass, but the patients may be asymptomatic or have symptoms of abdominal distension or bloated abdomen, as those caused by benign cysts. [4]

In our case patient presented with pain and lump in abdomen of about a month duration.

Gross examination and on H&E section study of left ovary showed histology of Mature Teratoma with area showing poorly differentiated cells mainly of spindle type with features of anaplasia. Various differential diagnosis like Immature teratoma, Malignant mixed mullerian tumour (MMMT) fibrous histiocytoma and similar other stromal tumors and poorly differentiated carcinoma were considered. Extra uterine MMMT is usually seen in older age post-menopausal woman. Histologically in MMMT there is biphasic appearance i.e. Carcinomatous and sarcomatous elements. There is absence of skin appendages. IHC shows P53 positivity and CD10 Positive in sarcomatous area.In our case skin and its appendages are present and P 63 homolog of P 53 is negative hence diagnosis of MMMT was ruled out. Immature teratoma is present usually in children and adolescent age group. On histological examination there is presence of embyronal and adult tissue and primitive neural/glial tissue, which was absent in present case. In our case smooth muscle marker like H. Caldesmon was negative with focal Desmin positive but CK was diffusely strongly positive in tumour cells hence tumour of epithelial origin was considered and mesenchymal tumours were ruled out. Per operatively in our case tumour was adherent with intestinal loop so possibility of primary stromal tumour of intestine spreading in to ovary was also considered in differential diagnosis.IHC markers for GIST DOG1 and CD117 were done but are found negative. Finally diagnosis of Mature cystic teratoma with poorly differentiated (Sarcomatoid) carcinoma was offered.

The relationship between mature cystic teratoma and its secondary malignant change is yet to be established. Mature ovarian teratomas (MOT) are genetically homozygous tumors within heterozygous hosts. MOT may be associated with malignant tumors of a non-germ cell phenotype (so-called malignant transformation). Based on the presence of in situ changes, some cases have been hypothesized to arise from teratomatous tissue. However, other malignancies associated with mature teratomas, such as sarcomas, may originate from either teratomatous elements or preexisting somatic ovarian tissue. According to the study by Devouassoux-Shisheboran M et al eight cases of MOT containing various histologic types of malignancy, including four squamous cell carcinomas, two sarcomas, one thyroid carcinoma, and one carcinoid tumour, were selected for study. Using selective tissue micro dissection and PCR-based analysis of the extracted DNA, we compared the genotypic pattern of the mature teratomatous components to the associated malignant neoplasm with a random panel of highly informative genetic markers for different chromosomes. In all eight cases, genetic analysis of the malignant component revealed a homozygous genotype. In seven cases, the genetic profiles of mature teratomas and the associated malignant tumors were identical, suggesting a direct pathogenetic relationship between these lesions. In one case, the malignant component revealed homozygosity of different alleles compared with mature teratoma, suggesting independent teratomatous growth processes. This finding indicates that some ovarian malignancies of the non-germ cell phenotype arise in teratoma and fall into the spectrum of germ cell tumours. [5]

The prognosis of patients with malignant transformation in teratoma is very poor, Five-year survival is only 15 30%.with most women dying within 1 year. However, the prognosis is better if the tumour is limited to one ovary, with an intact capsule not adhered to adjacent structure and with uniform thickness of cyst wall. [6] Poor prognostic factors includes tumor grade, vascular involvement, ascites, spontaneous or accidental rupture, adhesions, and tumour type other than squamous cell carcinoma. [7]

CONCLUSION

Malignant transformation of mature teratoma is more common after the age of 50 yrs. but can occur in younger age patient. There are no particular signs or symptoms which are characteristic of malignancy arising in a dermoid cyst. Preoperative diagnosis of malignant transformation is very difficult clinically, because this tumour cannot be readily differentiated from an uncomplicated MCT or other ovarian tumours. **[8]** Serum tumour markers, patient age and tumour size are useful factors in distinguishing malignant transformation in mature cystic teratoma. Since MCT is a common ovarian neoplasm and is increasingly diagnosed as an incidental finding in patients, there has been growing emphasis on preoperative risk assessment of these tumours in order to optimize surgical management. Clinicians should keep this rare type of tumor in mind when faced with a dermoid cyst, especially, in older patients or in larger than usual cysts. Individual experiences with such tumors should be documented to optimize the diagnostic and prognostic criteria and to standardize therapy options for these patients. Histopathological typing plays an important role in deciding prognosis of patient.Better prognosis has been reported in cases of SCC compared with adenocarcinoma or sarcoma. [9]

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