



## UNUSUAL HISTOPATHOLOGICAL FINDINGS AND MALIGNANT TRANSFORMATION IN MATURE CYSTIC TERATOMAS OF OVARY: A 2 YEAR STUDY WITH REVIEW OF LITERATURE

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### ABSTRACT

**Background-** Mature cystic teratoma is a benign most common tumor of the ovary occurring mostly in young and middle aged females. In this paper, we report and review 18 cases of mature cystic teratomas received in Department Of Pathology over a 2 year period with malignant transformation in 2 cases, which makes it very important for pathologist to thoroughly examine the entire specimen of mature cystic teratomas. **Material and Methods-** Eighteen reported cases of mature cystic teratomas received in Deptt. Of Pathology, BPS GMC Khanpur Kalan, Sonapat over a 2 year period from November, 2019 to October, 2021 were studied and reviewed retrospectively. Data regarding age, size, laterality, gross, morphological features and surgery performed was retrieved from pathological archives. **Results-** In our study, most common age of presentation was 30-40 year age group. Most common presenting complaint was fullness in abdomen or abdominal distension. Four out of 18 cases studied i.e. 22.2% cases presented with bilateral ovarian cysts. Tumor size ranged from 6 to 20 cm in diameter. Seven cases i.e. 38.9% cysts were greater than or equal to 10 cm in diameter. 2 cases (11.11%) showed malignant transformation. **Conclusion-** It is very important to thoroughly examine the contralateral ovary to rule out bilateral presentation. Furthermost thorough examination is advised in older females, in tumors of size > 10 cm and in tumors with solid areas to rule out any malignant transformation.

### KEYWORDS

Teratoma, ovary, malignant, transformation, bilateral, contralateral.

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### INTRODUCTION

Mature cystic teratoma is a benign most common tumor of the ovary occurring mostly in young and middle aged females. It is a germ cell neoplasm composed of well differentiated derivatives of three germ layers i.e. ectoderm, mesoderm and endoderm. Derivatives of atleast two germ layers must be present for diagnosis.<sup>1</sup> These tumors are unilateral in 88% cases and only provoke symptoms relating to the mass.<sup>2</sup> Grossly, mostly they are cystic with greasy content composed of keratin, sebum and hairs. Teeth may be present. Microscopically, skin appendages and neural tissue are extremely common followed by cartilage, respiratory tissue and gastrointestinal tract tissue. Other rarer tissues include thyroid, melanin containing tissues, anterior pituitary, prostatic, pancreatic tissue and cavernous blood vessels.<sup>2,3</sup> The most common complications of MCT are torsion, rupture and infection and rarely malignant transformation. These tumours are usually benign but occasionally they may undergo malignant transformation in one of its elements. The incidence of malignant transformation is 1 to 2 % and usually consists of squamous cell carcinoma in approximately 80% cases. Transformation to adenocarcinoma is extremely rare, accounting for just 6.8% cases. The age of patients with malignant transformation ranges from 19 to 88 years but is usually observed in postmenopausal age group. Prognosis for malignant transformation is very poor with a five year survival of just 15-30%.<sup>4,6</sup> This makes it necessary to diagnose them at the earliest to decrease the mortality and morbidity relating to the disease. In this paper, we report and review 18 cases of mature cystic teratomas received in Deptt. Of Pathology, BPS GMC Khanpur Kalan, Sonapat over a 2 year period from November, 2019 to October, 2021 with malignant transformation in 2 cases, which makes it very important for pathologist to thoroughly examine the entire specimen of mature cystic teratomas.

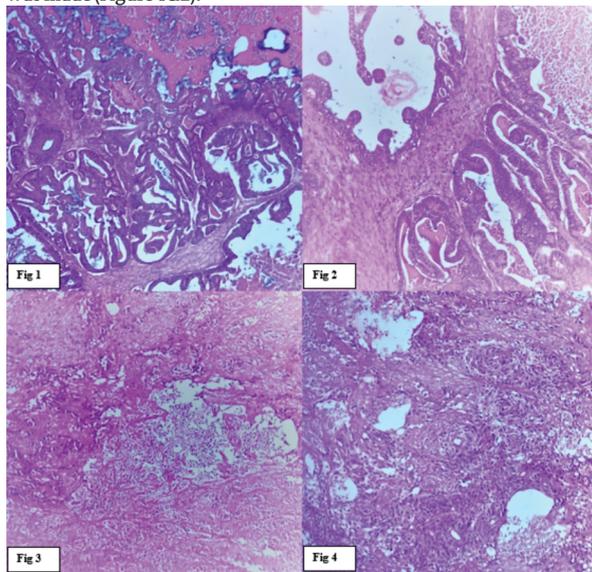
Eighteen reported cases of mature cystic teratomas received in Deptt. Of Pathology, BPS GMC Khanpur Kalan, Sonapat over a 2 year period were studied and reviewed retrospectively. Data regarding age, size, laterality, gross, morphological features and surgery performed was retrieved from pathological archives.

### RESULTS

A total of eighteen diagnosed cases of MCT were studied. Seven cases (38.9%) presented in the fourth decade. So, most common age of presentation was 30-40 year age group. Most common presenting complaint was fullness in abdomen or abdominal distension present in 55.5% cases. 44.4% cases presented with complaint of pain abdomen in which one of the women presented with acute pain abdomen and one had hydronephrosis on ultrasound. Four out of 18 cases studied i.e. 22.2% cases presented with bilateral ovarian cysts. Tumor size ranged from 6 to 20 cm in diameter. Most cysts (61.1%) were less than 10 cm in diameter. Seven cases i.e. 38.9% cysts were equal to or greater than 10 cm in diameter. On histopathology, skin appendages, neural tissue, cartilage, respiratory tissue, gastrointestinal tract tissue, thyroid tissue, melanin containing tissues were seen. Respiratory lining epithelium was seen in six cases, ganglion cells were seen in four cases. Thyroid follicles which are quite uncommon were seen in four out of 18 cases studied (i.e. 22.2%). Melanin containing tissues are also not so common but were seen in three of our cases (i.e. 16.7%). Two cases showed malignant transformation which is rare in mature cystic teratomas (Table 1). First case showed malignant transformation to papillary mucinous adenocarcinoma in a left side ovarian mature cystic teratoma in a 43 year old female who presented with pain abdomen and abdominal distension. On examination, abdominal lump was palpable measuring approximately 10x8 cm on left side of abdomen. CT scan of abdomen revealed a solid cystic mass measuring 15x10x13 cm with calcified and fatty components. Ovaries of either side could not be separated from

### MATERIAL AND METHODS

mass with surrounded mesenteric fat. A provisional diagnosis of ovarian dermoid was given. Hysterosalpingectomy and oophorectomy was done and specimen was sent to Deptt. Of Pathology in separate containers. Excised oophorectomy specimen measured 15x12x10 cm. On cut surface, the ovary was partially solid and partially cystic. Solid area measured 11x10x5 cm and was grey white, firm with mucoid areas. Cystic area showed presence of pultaceous material with embedded hair. Wall thickness of cyst was 0.2 to 0.3 cm. Uterus with cervix measured 9x5.5x4.5 cm. Endometrium and myometrium measured 0.2 cm and 2.0 cm in thickness respectively. Right and left fallopian tube measured 7.5 cm and 6.0 cm in length respectively. Right ovary measured 3x1.5x1.0 cm. on microscopic examination, the tumour displayed features of cystadenomatous pattern to borderline mucinous to frank invasive mucinous adenocarcinoma at different foci. At invasive foci, the tumour was arranged in complex cystic, papillary and tubular pattern. The tumour cells showed moderate nuclear pleomorphism with high n:c ratio, vesicular nuclei, prominent nucleoli and moderate amount of cytoplasm. Atypical mitosis and large areas of hemorrhage and necrosis noted. Sections examined from cystic areas showed histomorphological features of dermoid cyst. Diagnosis of papillary mucinous adenocarcinoma with dermoid cyst was made (Figure 1&2).



**Figure 1&2** (H&E;40x&200x): showing malignant transformation to adenocarcinoma. **Figure 3&4** (H&E;40x&100x): showing malignant transformation to squamous cell carcinoma in mature cystic teratoma of ovary.

The second case of malignant transformation was a 45 year old female who presented with abdominal distension. On ultrasound, bilateral ovarian cysts were seen. On gross examination, right sided tumor was solid cystic measuring 17x11x3 cm. Cut section of cystic areas showed multiple loculations with pultaceous material along with grey white to brown solid areas. Left sided tumor was mostly cystic measuring 9x6x3 cm which on cutting open, showed pultaceous material. On microscopy, larger cystic piece from right side showed a cyst lined by squamous epithelium and transforming into typical squamous cell carcinoma. The wall tumor cells were arranged in sheets and clusters alongwith areas of necrosis and calcification. Thus, squamous cell carcinoma arising in mature cystic teratoma was diagnosed on right side and the left sided ovarian cyst was diagnosed to be mature cystic teratoma (Figure 3&4). One case showed collision tumor i.e. mature cystic teratoma associated with mucinous cystadenoma in a 29 year old female who presented to Department Of Gynecology with complaint of abdominal distension for past 9 months with regular menstrual cycle. On physical examination, per abdomen was soft and left adnexal mass was felt. On ultrasonography, bilateral ovarian tumours were seen, right measuring 6.2x4.9x1 cm and left measuring 19.8x12x7.2 cm. Right ovarian mass was mostly cystic and left appeared cystic with some solid areas. Bilateral salpingo-oophorectomy was done. On gross examination, right tumour revealed loculated cyst measuring 6x5x1 cm filled with pultaceous material, with some hair shafts. Left ovarian cyst revealed multilocular cystic cavities filled with mucin alongwith pultaceous material, hair

and fatty tissue. Sections examined from right ovarian tumour revealed mature cystic teratoma. Sections from left ovarian cyst showed cyst lined by columnar epithelium and teratoid component showed hair shafts, melanin pigment, fibroadipose tissue, thyroid follicles and muscular tissue. Thus, diagnosis of collision tumour i.e. mature cystic teratoma associated with mucinous cystadenoma was made.

## DISCUSSION

Mature cystic teratomas are one of the most common tumours in women of reproductive age group. Peak incidence of teratomas is in reproductive age group i.e. 20-40 year owing to the hypothesis that in this age group they develop from single primordial germ cells, which has completed meiosis I and meiosis II is suppressed.<sup>7</sup> In our study, age ranged from 24 to 50 years. Peak incidence was in 20-40 year age group and median age was 39.5 years which is in concordance with studies done by Comerci Jr et al<sup>8</sup> and Ayhan A et al<sup>9</sup> in whom median age was 30 years and 35 years respectively. In our study, 44.4% cases were left sided and 33.33% cases were right sided. 22.2% cases were bilateral. This was in concordance with study done by Khan et al<sup>3</sup> who found more incidence on left side (64% cases) than on right side. This was in contrast to study done by Ismail RS et al<sup>10</sup> in which incidence was 72.2%. Bilaterality was seen in 22.2% cases which is quite high as compared to studies done by Rathore et al,<sup>11</sup> Ozgur et al<sup>12</sup> and Ayhan et al<sup>13</sup> in whom bilateral cases were 8.9%, 10% and 13.2% respectively. Most patients in our study presented with complaints of abdominal distension i.e. 55.5% cases followed by complaint of abdominal pain (44.4%). None of the cases were asymptomatic. Most studies show that most common presenting symptom is abdominal pain, but in our study, the most common symptom was abdominal distension as study done by Rathore et al.<sup>12</sup>

Tumor size, in our study, ranged from 6 cm to 20 cm in diameter with 61.1% cysts being < 10 cm in diameter which was in concordance with studies done by Ismail et al,<sup>11</sup> Peterson et al<sup>14</sup> and Rathore et al<sup>12</sup> in whom most tumors were < 10 cm in diameter.

Collision tumors are defined by the histological admixture at interface of the two tumours. In various studies, 2-11% of mature cystic teratomas are associated with mucinous tumours and most of these are likely of germ cell origin. These tumours may show a wide spectrum of histological patterns ranging from cystadenomatous pattern to proliferative tumours with architectural complexity and epithelial stratification resembling borderline mucinous tumour of surface epithelium to a frankly malignant tumour though the latter combination is distinctly uncommon. Teratoma can also be associated with Granulosa cell tumour, serous adenocarcinoma and steroid cell tumours.<sup>15,16</sup> One case of collision tumor was also reported in our study in which mucinous cystadenoma was associated with mature cystic teratoma in a 29 year old female who presented with abdominal distension and bilateral ovarian cysts were seen on ultrasound.

Malignant transformation is rare but most common transformation is squamous cell carcinoma occurring in 75-83% cases. Adenocarcinoma occurring in mature cystic teratoma is extremely rare, accounting for just 6.8% cases. Patients developing malignant transformation are usually postmenopausal.<sup>17</sup> In our study, two cases showed malignant transformation. The ovarian masses with malignant transformation were quite large and long standing at presentation with maximum diameter of 17 cm and 20 cm in diameter respectively. Both the patients of malignant transformation were > 10 cm in diameter which was consistent with studies done by Shimada T et al<sup>18</sup> and Dos Santos et al.<sup>19</sup>

Distinguishing this malignant transformation from benign lesions is nearly impossible preoperatively as in our case. Although tumour markers such as Carcinoembryonic Antigen (CEA), CA125, CA19-9, AFP, LDH and hCG are important for diagnosis of malignancy in ovarian lesions but they are non specific and cannot be used for predicting malignancy preoperatively. Surface epithelial ovarian neoplasms show diffuse CK7 positivity with variable CK20 expression.<sup>20</sup> The papillary mucinous cystadenocarcinoma component in our case showed CK 20 positivity and CK 7 negativity. This can be explained by either a mucinous neoplasm arising from lower GIT type tissue present in ovarian teratoma or by a metastasis from lower GIT primary such as colorectum or appendix. To rule out primary malignancy from upper or lower gastrointestinal tract, extensive clinical and radiological

evaluation should be done. Serological evaluation of tumor markers also helps to diagnose primary neoplasm at any other site.<sup>21</sup> In our case also, evidence of a second tumor elsewhere was not found. Moreover, the tumor was CK20 positive/ CK7 negative which favoured the

diagnosis of mucinous adenocarcinoma arising in a mature cystic teratoma. A post operative follow up should also be done in such cases to look for recurrence or any second neoplasm which may have been missed earlier.

**Table 1: Clinical and histopathological findings in cases of mature cystic teratomas of ovary**

	Age	Presenting complaint	Site	Size	Histomorphological features
Case 1	43	Pain abdomen-abdominal distension	Left	15x12x10	Papillary mucinous adenocarcinoma, hemorrhage, necrosis
Case 2	32	Pain abdomen	Left	12x10x10	Glial, respiratory lining, ganglion cells
Case 3	39	Fullness in abdomen	Left	10x9x2	Colloid filled follicles
Case 4	50	Pain abdomen with hydronephrosis	Right	8x6x4	Respiratory columnar epithelium, leiomyoma in uterus
Case 5	40	Fullness in abdomen	Right	8x6x5	Glial tissue, skin appendages
Case 6	70	Fullness in abdomen	Bilateral	Right- 7x4x3.5 Left- 8x5x3.5	Cartilage, hair follicles
Case 7	70	Pain abdomen with left adnexal mass	Left	8.5x6x4.5	Cartilage, hair follicles
Case 8	34	Abdominal distension	Left	8x6x4	Cartilage, colloid filled follicles, respiratory lining, lymphoid follicles
Case 9	27	Acute abdominal pain	Right	7x5x3	Ganglion cells, cystic follicles, melanin pigment
Case 10	24	Pain abdomen	Right	8.5x7.5x5	Ciliated columnar, glial tissue, giant cell reaction,
Case 11	29	Abdominal distension	Bilateral	Right-6x5x1 Left-20x12x7	Melanin pigment, thyroid follicles, mucinous cystadenoma
Case 12	38	Fullness in abdomen	Left	9x7.4x4.2	Cartilage, hair, respiratory lining epithelium
Case 13	42	Pain abdomen	Left	7.4x4x3	Glial tissue, ganglion cells, hair follicles, git epithelium
Case 14	44	Fullness in abdomen	Right	9.4x6.2x3	Ganglion cells, cartilage, skin appendages
Case 15	36	Fullness in abdomen	Left	10x8x3	Hair follicles, respiratory lining epithelium
Case 16	32	Abdominal distension	Bilateral	R- 8x4x3 L- 7x6x4	Colloid filled follicles, hair follicles, cartilage
Case 17	68	Pain abdomen	Right	11x8x4	Glial tissue, neural tissue, melanin containing tissue
Case 18	45	Abdominal distension	Bilateral	Right-17x11x3 Left-9x6x3	Squamous cell carcinoma in mature cystic teratoma on right side Mature cystic teratoma on left side

## CONCLUSION

Mature cystic teratomas are the most common tumors of ovary occurring mostly in reproductive age group but they may also present in puberty and postmenopausal age group. Clinically, most of them present as abdominal distension. In our study, bilateral presentation was seen in 25% cases, so it is suggested that it is very important to thoroughly examine the contralateral ovary to rule out bilateral presentation. Furthermost thorough examination is advised in older females, in tumours of size > 10 cm and in tumours with solid areas to rule out any malignant transformation.

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