

# MALIGNANT TUMOUR ARISING IN MATURE OVARIAN TERATOMA

Haqaue WS<sup>1</sup>, Alam M<sup>2</sup>, Islam SMJ<sup>3</sup>, Karim MI<sup>4</sup>, Yeasmin S<sup>5</sup>, Ahmed I<sup>6</sup>

## Abstract

**Introduction:** Mature teratoma is a common ovarian tumour. They are predominantly cystic (rarely solid) composed exclusively by mature adult type tissues. Malignant transformation of the mature elements of mature teratoma is very rare, but malignant transformation may occur in any of the mature components of teratoma. Keeping in mind about this rare malignant transformation which often present as an incidental pathologic finding may allow early detection.

**Objective:** The objective is to observe prevalence of this rare form of tumour in Bangladesh and also to observe the pattern of malignant component of these malignant tumours.

**Methods:** This was a retrospective study carried out in Armed Forces Institute of Pathology (AFIP), Dhaka between the period February 2005 and January 2012. This study was based on retrieval of data of all cases with ovarian mature teratoma from surgical pathology register of Histopathology Department of the Institute. The Histopathology report and microscopic sections are reviewed with available clinical information for the purpose of the study.

**Results:** A total of 205 cases of mature teratoma of ovary were diagnosed at AFIP during the study period. Among these 205 cases only two cases were identified as malignant tumour arising on the top of mature ovarian teratoma.

**Conclusion:** Though rare, malignant transformations of mature teratoma should be

kept in mind for early detection which in turn is important for patient survival.

**Keywords:** Mature teratoma, malignant transformation, ovary, squamous cell carcinoma

## Introduction

Mature cystic teratoma is the most common ovarian tumour<sup>1</sup>. Predominantly cystic mature teratomas (MCT) are composed exclusively of mature adult type tissues. Mature teratoma consists of well differentiated derivatives of three germ layers with any type of combination of mature, adult type tissues<sup>2</sup>. Ectodermal tissue is the most abundant and typically manifests in the form of squamous epithelium, brain tissue, glia, retina, choroid plexus and/or ganglia. Adipose tissue, smooth and skeletal muscle, teeth, bone and cartilage are common mesodermal components. Endodermal tissue may form bronchial and gastrointestinal epithelium, thyroid glands and/or salivary glands. Monodermal teratomas consist of exclusively endodermal or ectodermal tissue types; struma ovarii is the most common monodermal teratoma of the endoderm. Malignant transformation of the mature elements of mature teratoma is very rare but that rare transformation may occur from any of the mature components of the teratoma. In this study we reviewed the reported cases of ovarian mature teratoma over last 7 years in Armed Forces Institute of Pathology, Dhaka with a search for components of malignant transformation.

## Methods

This is a retrospective study carried out in Armed

1. Major Wasim Selimul Haqaue, MBBS, MCPS, DCP, FCPS, Graded specialist in pathology, 71 Field Ambulance, Jessore cantonment; 2. Colonel Mahbulul Alam, MBBS, DCP, FCPS, Classified specialist in pathology, AFIP, Dhaka cantonment; 3. Lieutenant Colonel Sk Md Jaynul Islam, MBBS, MCPS, DCP, FCPS, Classified specialist in pathology, AFIP, Dhaka cantonment; 4. Major Md. Iqbal Karim, MBBS, MCPS, DCP, FCPS, Instructor Pathology, AMFC, Dhaka cantonment; 5. Major Shamoli Yeasmin, MBBS, MCPS, DCP, FCPS, Graded specialist in pathology, 31 Field Ambulance, Comilla cantonment; 6. Major Istiak Ahmed, MBBS, MCPS, DCP, specialist in pathology, 51 Field Ambulance, Sylhet cantonment.

Forces Institute of Pathology, Dhaka between February 2005 and January 2012 to find the malignant transformation of mature teratoma of ovary. This study is based on retrieval of data of all cases with ovarian mature teratoma from surgical pathology register of Histopathology Department of the Institute. The Histopathology report and microscopic sections were reviewed with available clinical information for the purpose of the study.

The diagnostic criteria of squamous cell carcinoma in ovarian mature teratoma are as usual detailed in other places of body as depicted by anaplastic squamous nest with invasion in the subepithelial tissue. Stromal invasion by malignant appearing epithelium should be used as definite criteria for categorizing MCT with malignant transformation. The diagnostic criteria for cases of papillary carcinoma are similar to those described in the cervical thyroid gland and are based primarily on nuclear and architectural features.

### Results

A total of 205 cases of mature teratoma of ovary were diagnosed at AFIP during the period from February 2005 to January 2012. The patient age ranged from 6½ years to 56 years with a mean age of 27.8±12.77 years. Examination of the cyst wall showed almost invariable presence of endodermal derived skin and adnexae. Thyroid tissue was present in 6% cases (Table I).

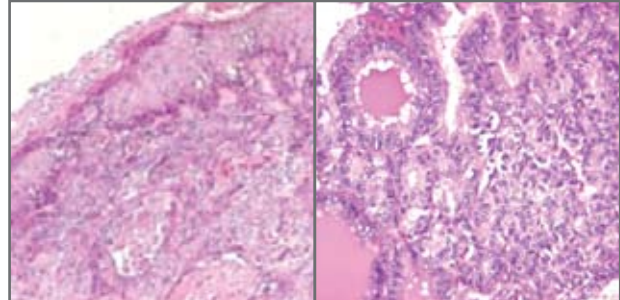
**Table -I:** Incidence of structures observed microscopically (n=205)

Malignant Component	Frequency	Percentage
Skin (Stratified Squamous epithelium)	204	99.5
Skin appendages	187	99.2
Fat	120	58.5
Cartilage	60	29.2
Nerve	40	19.5
Respiratory epithelium	30	14.6
Bone	24	11.7
Gastrointestinal epithelium	14	6.8
Thyroid	12	6.3
Tooth	04	1.9
Malignant component	02	1%

Among those 205 cases two cases identified as malignant tumour arising on the top of mature ovarian teratoma (Table II).

**Table -II:** Distribution of malignant tumour on mature ovarian teratoma(n=205)

Malignant component	Frequency	Age	Microscopic features
Squamous cell Carcinoma	1	36 yrs	Fig 1
Papillary thyroid carcinoma	1	52 yrs	Fig 2



**Fig I:** Anaplastic squamous nests showing microinvasion in the subepithelial tissue

**Fig II:** Neoplastic papillae are lined by overlapping crowded epithelial cell with optically clear nuclei

**MCT with malignant transformation into squamous cell carcinoma (SCC):** Fig I shows the microscopic section of a right ovarian cystic mass of a 36 yrs old 'Adibashi' woman. She reported to a NGO Hospital for her obstetrics care. Her USG report showed 13 weeks pregnancy with large right ovarian cystic mass (measuring 15.8 (L) x12.5 (D) x 15.5(W) cm) with small percentage of hyperechoic tissue. Gross inspection showed a unilocular cystic ovoid mass containing greasy sebaceous material and hair. External surface of the cyst was dull white and smooth. The cyst wall thickness was upto 5 mm. Histopathologic examination of sections from cyst wall showed features of MCT mostly lined by benign epidermis with underlying dermal adnexae. Squamous lining at places showed dysplastic changes with foci of invasion in the wall (Fig I) and diagnosed as a case of SCC. Mesodermal components like skeletal muscles were also noted.

**Malignant struma ovarii:** Fig II reveals a case of thyroid type malignancy in the background of struma ovarii. She was a 52 years old lady admitted in a military Hospital with complaints of occasional dull aching non-radiating pain and sense of heaviness in the lower abdomen for 3 months. On examination there was a non-tender, non reducible, firm, mobile, irregular mass in the right illiac fossa. Her USG examination detected a mass in right adnexal region measuring 7.4 x4.8 cm<sup>2</sup> with internal hypoechoic and echoic

component. Macroscopic examination revealed partly solid and partly cystic ovarian mass. Microscopic examination showed mature teratoma exclusively consisting of thyroid follicles filled with colloid containing multiple foci of papillary thyroid carcinoma. The branching neoplastic papillae are lined by crowded epithelial cell having optically clear nuclei (Fig II). Immediately after surgery, the patient's thyroid function, thyroglobulin and TPO level were measured which were found to be normal.

### Discussion

Twenty percent of ovarian tumours are mature teratoma<sup>1</sup>. Like other studies and standard text books, this study revealed various benign components in microscopic examination of cystic mature teratoma derived from three germ layers<sup>2,3</sup>. Malignant transformation of mature tissue of teratoma is rare. It occurs in less than 2% cases of mature of teratoma<sup>4,5</sup>. The most common malignancy is squamous cell carcinoma<sup>4,5,6</sup>. The reported other malignant tumours are adenocarcinoma<sup>7,8</sup> thyroid malignant tumour<sup>9</sup>, sarcoma<sup>10,5</sup> and melanoma<sup>11</sup>.

Though malignant transformation is rare, SCC accounts for 80% of secondary malignant transformations of ovarian teratomas<sup>12</sup>. It is to be noted that squamous tissue is the most abundant component in mature teratoma. Cystic mature teratoma lined by epidermis known as dermoid cyst is the most common pattern of mature teratoma. First definitive description of dermoid cyst with illustration was found in literature more than 350 years ago<sup>13</sup>. The tumour in this study rose in the background of dermoid cyst. Squamous cell carcinoma is mostly reported in post-menopausal women (mean age 55 yrs)<sup>14</sup>. In this study the single case of squamous cell carcinoma developed at 35 yrs of age. Case Report<sup>15</sup> and study series<sup>4</sup> show squamous cell malignant transformation in an ovarian mature cystic teratoma in young woman with age range of 19-71 yrs. The mean size of a squamous cell carcinoma arising from a MCT measured more than 100 mm was seen in review of literature<sup>14</sup>. In our case the size of the tumour was 110 mm in greatest dimension. As SCC arising in MCT is

quite rare, one must exclude metastasis particularly from cervix.

Ten percent of ovarian teratoma contain thyroid tissue<sup>2</sup>. The presence of thyroid tissue in the ovary was first described by Böttlin in 1889 and the term "struma ovarii colloides" was coined by Meyer in 1903. Struma ovarii, a rare monodermal ovarian teratoma is defined when thyroid tissue is the predominant (>50%) or exclusive element and nearly 2.7% of ovarian teratomas are struma ovarii<sup>3</sup>. Five to ten percent of these Struma Ovarii are malignant<sup>16</sup>. The commonest type of malignant struma ovarii is papillary carcinoma which may be classical type or follicular variant of papillary carcinoma followed by follicular carcinoma; other forms of thyroid carcinoma occur only rarely<sup>17,18,19</sup>. Most of the patients were in their 40s to 50s at the time of diagnosis of malignant struma ovarii<sup>20,21</sup>. Thyroid type carcinoma can also be seen as a component of strumal carcinoid. Strumal carcinoid is a form of ovarian teratoma characterized by a mixture of thyroid tissue and carcinoid<sup>16,22</sup>. Immunohistochemistry using TTF-1 (thyroid transcription factor 1), thyroglobulin, and neuroendocrine markers, such as chromogranin or synaptophysin may assist in the diagnosis. Struma ovarii containing thyroid-type carcinoma must be distinguished from rare cases of papillary or follicular thyroid carcinoma metastatic to the ovary<sup>23,24</sup>. Again metastasis of malignant struma ovarii is also rare; site of metastasis noted in literature are adjacent pelvic structures, including the contralateral ovary and distant metastases to the lungs, bone, liver, and brain<sup>25,26</sup>.

### Conclusion

Malignant transformations of mature teratoma are often presented as incidental pathologic findings. Due to rarity of these tumours large scale prospective study is missing. The behaviour of malignant tumour is summarized basing on case report or small series of tumour. Prognosis and treatment largely depends on stage of the tumour. Though malignant transformation of MCT is rare, this condition should be kept in mind for early detection. Early detection is important for long term survival.

## References

1. Secully RE. Dermoid cysts. In: Tumours of Ovary and maldeveloped gonades. Atlas of Tumour Pathology. Second series, Fascicle 16. Washington, DC; Armed Forces Institute of Pathology 1979:255-68
2. Rosai J. Ovary. In: Female Reproductive System. Rosai and Ackerman's Surgical Pathology. Philadelphia: Mosby 2004; 1687-1691.
3. Nogales F, Talerma A, Kubiki-Huch RA, Tavassoli FA, Devoussoux-Shisheboran M. Germ Cell Tumour. Tumour of the Ovary and Peritoneum. World Health Organization Classification of tumours: Pathology of Genetics of Tumour: Tumours of the breast and female genital organs. Loyn: France HRC Press 2003; 168-172.
4. Rim SY, Kim SM, Choi HS. Malignant transformation of ovarian mature cystic teratoma. Int J Gynecol Cancer 2006 Jan-Feb;16(1):140-4.
5. Peterson WF. Malignant degradation of benign cystic teratomas of the ovary: A collective review of the literature. Obstet Gynecol Surv 1957;12:793-830.
6. Gupta V, Sood N. Squamous cell carcinoma arising in a mature cystic teratoma. Indian J Pathol Microbiol 2009;52:271-3
7. Lee JM, Kim JW, Song JY et al. Adenocarcinoma arising in mature cystic teratoma: a case report. J Gynecol Oncol. 2008 September; 19(3): 199-201.
8. Kushima M. Adenocarcinoma arising from mature cystic teratoma of the ovary. Pathol Int 2004; 54: 139-43.
9. Salman WD, Singh M, Twaij Z. A Case of Papillary Thyroid Carcinoma in Struma Ovarii and Review of the Literature. Pathology Research International 2010; Article ID 352476, 2010. doi:10.4061/2010/352476
10. Ittyavirah AK, Krishnakumar AS, Sasidharan K, Ramachandran K. Osteosarcoma arising in a mature cystic teratoma of the ovary : A case report. Indian J Radiol Imaging 1999;9:65-7
11. Cronje H.S., Woodruff J.D. Primary ovarian malignant melanoma arising in cystic teratoma. Gynecologic Oncology, 98:12 (3):379-383.
12. Park JY, Kim DY, Kim JH, Kim YM, Kim YT, Nam JH. Malignant transformation of mature cystic teratoma of the ovary: Experience at a single institution European Journal of Obstetrics Gynecology and Reproductive Biology, 2008;141 (2):173-178.
13. Damjanov I. The pathology of human teratomas. In: Damjanov I, Knowles BB, Solter D, editors. The human teratomas: experimental and clinical biology. Clifton NJ: Humana press 1983.p. 23-54
14. Hackethal A, Brueggmann D, Bohlmann MK, Franke FE, Tinneberg HR, Münstedt K. Squamous-cell carcinoma in mature cystic teratoma of the ovary: systematic review and analysis of published data. The Lancet Oncology 2008; 9(12):1173-1180.
15. Prasad S, Ravindra BVS. Bilateral ovarian squamous cell carcinoma with an antecedent dermoid cyst in the left ovary. Journal of Obstetrics and Gynaecology Research 2011; 37: 1238-1240.
16. Navarro MD, Tan MAL, Lovecchio JL, Hajdu SI. Malignant Struma Ovarii. Ann Clin Lab Sci 2004 ; 34: 107-112
17. Devaney K, Snyder R, Norris HJ, Tavassoli FA. Proliferative and histologically malignant struma ovarii: a clinicopathologic study of 54 cases. International Journal of Gynecological Pathology 1993;12 (4):333-343.
18. Athanassiou K, Katsouli IL, Gogou L, Papagrigroriou L, Chatonides I, Kaldrymides P. Malignant struma ovarii: report of a case and review of the literature. Hormone Research 2002; 58(1): 34-38.
19. Makani S, Kim W, Gaba AR. Struma Ovarii with a focus of papillary thyroid cancer: a case report and review of the literature. Gynecol Oncol 2004;94:835-9.
20. Robboy S. Malignant Struma Ovarii: An Analysis of 88 Cases, including 27 with Extraovarian Spread. International Journal of Gynecological Pathology 2009; 28:405-422.
21. DeSimone CP. Malignant struma ovarii: a case report and analysis of case reported in the literature with focus on survival and I<sup>131</sup> therapy. Gynecol

Oncol 2003; 89: 543-548

**22.** Roth LM, Talerman A. The enigma of struma ovarii. Pathology 2007 Feb;39(1):139-46.

**23.** Young RH, Jackson A, Wells M. Ovarian metastasis from thyroid carcinoma 12 years after partial thyroidectomy mimicking struma ovarii: report of a case. Int J Gynecol Pathol 1994;13:181-5

**24.** Ruel, IF. Pulmonary Metastases of Struma Ovarii. A case report. Clinical Nuclear Medicine, 2010; 35(9): 692-694

**25.** Yassa L, Sadow P, Marqusee E. Malignant struma ovarii. Nature Clinical Practice. Endocrinology and Metabolism 2008; 4:469-472.

**26.** Song HJ, Xue YL, Xu YH, Qiu ZL, Quan-Yong Luo Rare metastases of differentiated thyroid carcinoma: pictorial review Endocr. Relat. Cancer 2011; 18: R165-R174.