OPEN ACCESS

GAVIN PUBLISHERS

International Journal of Clinical Pathology and Diagnosis

Case Report

Nair IR, et al. Int J Clin Pathol Diagn IJCP-128.
DOI: 10.29011/2577-2139.000028

Somatic Tumors Arising in Ovarian Teratomas-Experience from an Oncology Center in South India

Indu R Nair[1*], Rajanbabu Anupama[2], Prasad Chaya[3], Sreedhar Sarala[4]

Department of Pathology, Amrita Institute of Medical Sciences, India

Department of Gynecological Oncology, Amrita Institute of Medical Sciences, India

Department of Pathology, Amrita Institute of Medical Sciences, India

Department of Gynecology, Amrita Institute of Medical Sciences, India

[*]**Corresponding author:** Indu R Nair, Department of Pathology, Amrita Institute of Medical Sciences, India. Tel: +04842801234; Email: indurn@aims.amrita.edu

Citation: Nair IR, Anupama R, Chaya P, Sarala S (2019) Somatic Tumors Arising in Ovarian Teratomas-Experience from an Oncology Center in South India. Int J Clin Pathol Diagn IJCP-128. DOI: 10.29011/2577-2139.000028

Received Date: 17 December, 2018; **Accepted Date:** 04 January, 2019; **Published Date:** 11 January, 2019

Abstract

Background: Teratomas constitute 95% of ovarian germ cell tumors. Though somatic neoplasms have been reported to arise in teratomas,very few studies had attempted to analyze the incidence and associated risk factors.

Methods: We report the incidence of teratomas and the somatic neoplasms arising from them, over a 5 year period from January 2013 to December 2017,by analyzing the cases treated in our institute, which is an oncology center in South India.147 teratomas were encountered, of which,13 were immature teratomas.9 cases had somatic tumors arising in them, of which 2 were neuroectodermal tumors(one astrocytoma, one oligodendroglia) and 7 were carcinomas(5 squamous cell carcinomas,1 thyroid carcinoma and 1 mucoepidermoid carcinoma).We also attempted to study the associated risk factors.

Conclusions: All the carcinomas developed in women above 45 years; with tumor size more than 10cm and solid area more than 2cm.Hence we suggest that teratomas with these risk factors need to be thoroughly sampled to exclude associated carcinomas.

Introduction

Germ cell tumours constitute 20-25 % of all ovarian tumors. 95% of these are mature cystic teratomas[1].Secondary development of somatic tumours is a rare but well documented phenomenon in patients with ovarian teratomas. Malignant change occurs in 1% to 2% of teratomas, of which the most common is squamous cell carcinoma (75%). Studies have assessed the risk factors associated with such malignant transformation[2].Most of these are case reports, stating the isolated cases. We reviewed all the consecutive ovarian teratoma cases in our institute, over a 5-year period, which gave an estimate of the incidence of the somatic benign and malignant tumours, their clinicopathological features and the associated risk factors.

Materials and Methods

Records of all 840 ovarian neoplasms treated during the 5-year period from January 2013 to December 2017, in the departments of Gynaecology and Gynaecological Oncology in Amrita Institute of Medical Sciences, Kochi, India were retrieved. Tumours which had undergone torsion were excluded. Clinical data were collected from electronic medical records and the Pathology reports were reviewed for the relevant gross, microscopic and immunohistochemical findings.

155 germ cell tumours were encountered during this period, which constituted 17.5 % of all ovarian neoplasms, 147 of these were teratomas (95%). Among the rest eight, 5 were dysgerminomas and 3, yolk sac tumours. 13 of the teratomas were immature

teratomas, (twelve grade 1 and one grade 2, in the 3-tier grading system).2 cases of neuroectodermal neoplasms were present, one oligodendroglioma and the other, a low grade glioma, both in children less than 20 years. Seven cases of carcinomas arising in teratomas were seen.No skin appendage or melanotic tumors were encountered. (Table-1)The patients were in the age group ranging from 9 to 84 (mean age-34yrs).The mean age of patients with benign teratomas was 30 yrs. All the patients with immature teratoma were below 20 years of age (9-19 years, mean age -13 yrs.)

Tumor	Number	Percentage
Immature teratomas	**13**	**8.8**
Monodermal teratomas	**9**	**6.1**
Struma ovarii	7	
Pure carcinoid	1	
Stromal carcinoid	1	
Mature teratoma	**116**	**78.9**
Neuroectodermal tumours	**2**	**0.14**
carcinomas	**7**	**4.7**
Squamous cell carcinoma	5	
Thyroid carcinoma	1	
Mucoepidermoid carcinoma	1	
Total teratomas including those with somatic tumours	**147**	**100**

Table 1: Teratomas with and without somatic tumours.

All carcinomas were encountered in women above 45 years. (range 46-83, mean-56.4 yrs.) Most common clinical observation was abdominal pain and lower abdominal fullness. Grossly the tumour size ranged from 1.2 to 23 cms (mean diameter of 8.5cm), with a predominant cystic component in 89%.Benign tumours had a mean size of 7.2cm.Malignant tumours were larger than 10cms in size with a mean diameter of 11.4cm. All teratomas with somatic tumours had fleshy solid areas and all carcinomas had solid granular/friable areas more than 2cm in diameter (ranges from 2.4 to10.6 cm with a mean of 5.6 cm).

Cases

Neuroectodermal Tumours

First case of neuroectodermal tumour was of a 16year old girl with a 10 cm ovarian cyst showing mature teratoma with a solid nodule in the wall measuring 2.4cm in greatest dimension. On microscopy it showed sheets of cells with uniform oval nuclei and moderate cytoplasm arranged in a fibrillary background. Admixed were seen many large cells resembling ganglion cells, suggestive of a low grade glial neoplasm (figure-1). No mitosis/vascular proliferation/necrosis were seen. The tumour cells were positive for GFAP and p53 with a proliferation index of 8%. Adjuvant treatment was not given in view of the low grade disease and patient is doing well 24 months after completion of surgery. The oligodendroglioma was seen in the 11.2 cm sized ovarian cyst of an 11-year-old girl. Grossly it was seen as soft solid grey white area of diameter 7.4cm with a cerebriform appearance. Microscopy it showed a monotonous population of round, uniform cells with hyper chromatic nucleus and perinuclear halo with the classical fried-egg appearance. Also seen was a fine network of capillaries in the stroma. This was seen focally in an otherwise encapsulated mature teratoma with an area of immature teratoma, grade 2. The neoplastic cells showed S100 positivity confirming the diagnosis. Ki 67index was 10%. Owing to the presence of immature teratoma, she was treated with chemotherapy (6 cycles of Etoposide and platinum), and is now doing well 3 years post treatment completion.

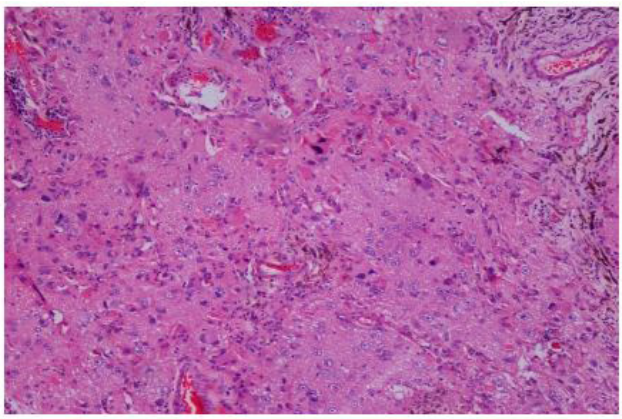

Figure 1: glioma in teratoma-Hand E-40X.

Carcinomas

Carcinomas constituted 4.7 % of germ cell tumours, of which 5 were squamous cell carcinomas. One of the struma ovarii had a differentiated thyroid carcinoma arising in it. The seventh was a mucoepidermoid carcinoma. All 5 cases of squamous cell carcinomas (figure-2) showed mature cystic teratoma. The clinicopathological characteristics were studied. (Table-2)Thyroid carcinoma was seen in a 83 year old lady with left ovarian cyst mea 17cm, with a solid granular nodule mea 7cm.Microscopy showed struma ovarii with a large partly capsulated nodule composed of closely packed follicles lined by cuboidal cells with moderate cytoplasm and uniform round vesicular nuclei. Nuclear features of papillary carcinoma were not seen. The follicles were invading the capsule, infiltrating into the adjacent area of fibrosis, adherent to the colon. With these microscopic features, a diagnosis of follicular carcinoma was made (figure-3). Owing to the advanced age and comorbidities, no further treatment was offered; she was kept on follow up and died 4 months after the surgery. Seventh carcinoma was in a 48-year-old lady with recurrent abdominal pain. She underwent right ovarian cystectomy, which showed a solid mass mea 10.6cm.A small cyst in the periphery showed lining by stratified

squamous cells with underlying appendages, suggestive of a mature teratoma. Solid areas showed mucinous and epidermoid cells along with nests of intermediate cells. The mucinous cells were positive for CK7 and CEA while the solid nests of epidermoid cells were positive for p63 andCK5/6, confirming the diagnosis of mucoepidermoid carcinoma, in a teratoma (figure-4). While on adjuvant chemotherapy (after 1 of 6 cycles of Paclitaxel, Carboplatin chemotherapy regimen), she was found to have a rectal wall mass suggestive of tumour recurrence at 4months. She was advised for surgery for removing the recurrent lesion.

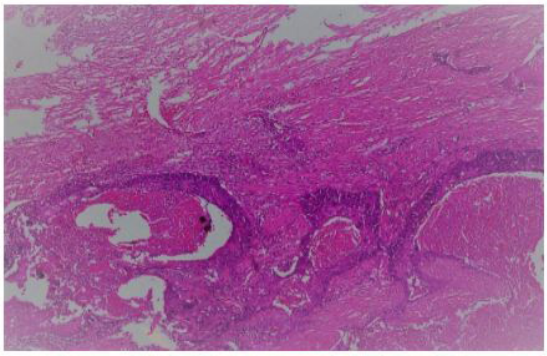

Figure 2: Squamous cell carcinoma in teratoma-Hand E-40X.

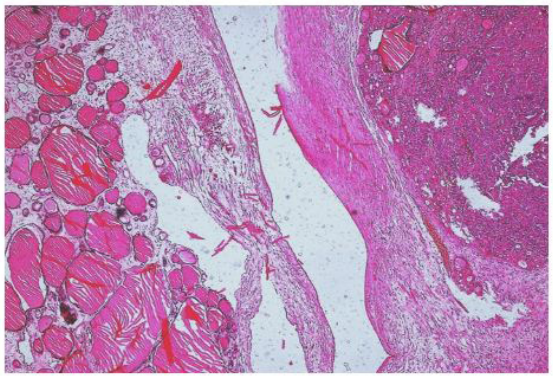

Figure 3: Thyroid follicular carcinoma in struma ovarii-H and E-40X.

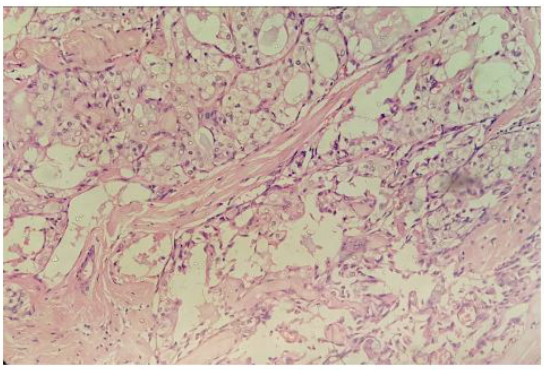

Figure 4: Mucoepidermoid carcinoma in teratoma-Hand E-40X.

No	Age	Size of tumour(cm)	Size of solid area(cm)	Recurrence	Follow up(months)
1	46	11.5	3	nil	26
2	53	13	4.5	8 months	10
3	59	14.5	7	6 months	7
4	54	15	2.4	nil	24
5	52	18	3.5	9 months	12(expired)

Table 2: Clinicopathological features of Squamous cell carcinomas in teratomas.

Discussion

Majority of the germ cell tumours were mature cystic teratomas. Among the monodermal teratomas, struma ovarii was the most common, as stated in literature.Of the 2 cases of neuroectodermal tumours; one was a low grade glioma in a mature teratoma and the other an oligodendroglioma, in an immature teratoma. Though studies have reported neuroectodermal tumours, they are very rare (less than 50 cases) and include the primitive, differentiated and anaplastic types[3].Majority of the previously reported cases were astrocytomas, though occasional high grade tumours like glioblastomas are also described. These were found to arise mostly in mature teratomas; only7 cases are reported to have developed in immature teratomas.Oligodendrogliomas arising in teratomas are extremely rare, and to the best of our knowledge, only less than 10 cases are reported so far with only one case in childhood[4]. Though dysgerminomas are described as the most common malignant tumours in literature [1], we found a higher incidence of immature teratomas, mostly of grade 1 type. In a study from Orissa India, by Pradhan et al, both teratomas and dysgerminomas contributed equally to the malignant ovarian germ cell tumours [5].The incidence of immature teratomas were slightly more than dysgerminoma in paediatric patients in Kerala, as stated by Rajeswari and co-workers [6].The difference in incidence could be attributed to geographic variation. All immature teratomas occurred in age group less than 20 years, in concordance with other studies[4].

Malignancies in germ cell tumours can be malignant germ cell tumours like embryonal carcinoma or somatic malignancies arising in teratomas, like carcinomas or sarcomas[1]. In observed patients, all the seven malignancies were carcinomas, no cases of sarcoma or melanoma were encountered. We also encountered a higher number of carcinomas than mentioned in the literature(4.7 % vs. 1-2%).This may be attributed referral bias, as our institute being a gynecological oncology centre, suspected malignancy cases are referred from outside hospitals. Squamous cell carcinomas were the commonest, in concordance with the findings described by Kedar et al. from Indian population[7].Other carcinomas described in literature are adenocarcinoma (7%) and sarcomas of

different types, like leiomyosarcoma and angiosarcoma followed by rare tumours like melanoma, which is often metastatic than primary [8].The pathogenesis of squamous carcinomas in teratoma is not yet clear. An in situ carcinomatous change similar to skin suggests squamous epithelial origin in most of the tumours. Three of our cases showed full thickness dysplasia of the cyst wall squamous epithelial lining, favouring this theory[7]. Iwasa et al. had suggested the origin to be from metaplastic columnar epithelium, supported by the IHC expression of CK18 more than CK10 similar to that seen in lung and cervix squamous carcinomas where metaplastic origin is proved [9] However, we have not done the differential cytokeratins in any of our cases.

5-10% of struma can harbour thyroid carcinomas, most of which are papillary carcinomas, with the characteristic nuclear features[1].No definite criteria are described for follicular carcinoma, as mostly the capsule seen around the tumour might be ovarian tissue or capsule. Also, well established criteria for diagnosis are absent because of the rarity of cases [7].As high as 37% of cases of struma ovarii can show malignancy, with metastasis in around 23% [10]. The possible criteria proposed are the presence of infiltration by tumour cells into the surrounding ovarian tissue, or lymphovascular emboli or metastasis. The most acceptable feature of malignancy is extra ovarian spread, into the adjacent tissues or organs but most of the reported cases have not shown aggressive behavior[11].

Mucoepidermoid carcinoma is a type of salivary gland tumour, which is the least common to arise in a teratoma. A literature search showed less than five reported cases so far[12]. It shows the typical morphology with mucinous, epidermoid and intermediate cell types, in varying combination, depending on the degree of differentiation. In our case all the 3 cell types were well appreciable. The absence of keratinisation in the epidermoid cells and the presence of well differentiated mucinous cells and intermediate cells excluded a more common adenosquamous carcinoma.

Studies have shown postmenopausal age group and tumour size more than 10 cm to be associated with the development of squamous cell carcinoma [2]We also found advancing age to be a risk factor for the development of carcinoma (risk ratio 44.5, P value 0.012).Tumour size is another potential indicator of malignant transformation of teratomas [13,14]. According to Kikkawa et al., who reviewed 277 cases from 64 studies, tumours with diameter larger than 9.9 cm or tumours demonstrating rapid growth were found to be associated with an increased risk for malignant transformation.All the carcinomas in our series had a tumour size of 10 cm or more, which was found to be a statistically significant risk factor for malignancy (Fischer's exact test value 0.0004, p value 0.013).But most of the bulk in these large tumours is contributed by the benign cystic component. Enlargement may also be due to the secondary changes like necrosis and haemorrhage. Hence, an assessment of the size and consistency of the solid areas were done.Teratomas with mono dermal components or other tumours arising in them had solid areas, which were fleshy in benign tumours like carcinoid and hemorrhagic, necrotic and friable in the malignant ones. All malignant tumours had friable or granular solid areas more than 2cm in size, unlike the benign ones, which were mostly cystic.Thus, size of fleshy solid area, more than 2cm was found to be another risk factor in our patients. (Fischer's exact test value 0.0006, p value less than 0.04). These findings are also in concordance with the risk factors observed by Park et al.[15]

Carcinomas arising in teratomas being very rare, there are no treatment guidelines established. Though several groups have suggested different chemotherapy regimen, the treatment must be tailored to the type of tumour[16]. The therapy proposed is multimodality treatment based on optimal cytoreduction, Cisplatin based adjuvant chemotherapy and radiotherapy for disease localized in the pelvis.It is recommended that after complete surgical staging, I A patients need only follow up. Suboptimal surgery and advanced stages are considered to be adverse prognostic factors. In our cases with squamous cell carcinomas, four patients underwent complete staging surgery, two of which had recurrence and other two were disease free. All carcinomas except the thyroid carcinoma case were offered 6 cycles of adjuvant chemotherapy, with cyclophosphamide and platinum.The patient with mucoepidermoid carcinoma developed recurrence after first cycle of chemotherapy .Out of the two squamous carcinoma patients who developed recurrence, one was at 8 months after completion of treatment whereas the other recurred at 6 months. Another patient had diagnosed with tumour recurrence at 9 months and expired in12 months(Table 2).

Conclusions

Somatic tumours arising in teratomas are rare; comprising 4.8%.Commonest malignancy was squamous cell carcinoma (4.7%).Risk factors associated with carcinomatous change in teratomas are age above 45 yrs, tumour size10cm or more and solid friable area, of size 2cm or more.

Suggestions

Though we encountered only seven cases of carcinoma, this proof-of-principle case study shows a significant association of carcinomatous growth with the gross size of the tumour as well as the solid area. In future, a study with a larger sample size might find a stronger association. We recommend that it might be worthwhile to sample extensively the solid areas in all teratomas occurring in the young, so as to ensure the absence of an immature component. Similarly, the friable or granular solid areas larger than 2cms, in large tumours(more than 10cm) occurring in women above 45 years may harbour carcinoma, hence needs to be thoroughly studied.

Source(s) of support: nil.

Presentation at a meeting: nil.

Conflicting Interest: nil.

References

1. WHO Classification of Tumours of the Female Reproductive Organs (IARC WHO Classification of Tumours 4th Edition-2014
2. Goudeli C, Varytimiadi A, Koufopoulos N, Syrios J, Terzakis E (2017) An ovarian mature cystic teratoma evolving in squamous cell carcinoma: A case report and review of the literature.Gynaecologic Oncology Reports 18: 27-30.
3. Yousef R Badran, Fatima N Obeidat, Mazen A Freij (2014) Low-Grade Astrocytoma Arising in a Mature Ovarian Teratoma in an Adolescent. Clinical Ovarian and Other Gynaecologic Cancer 6: 62-64.
4. BetülÜnal, Faruk Güleç, Murat Sedele (2014) Oligodendroglioma Arising in Mature Cystic Teratoma. Case Reports in Oncological Medicine 3.
5. Hemanta Kumar Pradhan, Pratibha Singh, Ravikumar (2018) Study of risk factors and tumour markers in ovarian malignancy in western part of Odisha: a prospective observational study. Int J Reprod ContraceptObstet Gynecol 7: 1571-1578.
6. Rajeswari B, Nair M, and NinanA, Parukuttyamma K (2016) Ovarian tumours in children: 10-year experience from a tertiary care centre in South India. Indian J Cancer53:292-295.
7. Yasunaga M, Saito T, Eto T, Okadome M, Ariyoshi K, et al. (2011) Dedifferentiated Chondrosarcoma Arising in a Mature Cystic Teratoma of the Ovary: A Case Report and Review of the Literature. International Journal of Gynaecological Pathology 30: 391-394.
8. Rekhi B, Parikh P, Deodhar KK, Menon S, Maheshwari A, et al. (2015) Squamous carcinoma coexistent with teratoma of ovary: A clinicopathological study of 12 cases diagnosed over a 10-year period at a tertiary cancer referral center. Journal of Cancer Research and Therapeutics 11: 211-215.
9. Iwasa A, Oda Y, Kaneki E, Ohishi Y, Kurihara S, et al. (2007) Squamous cell carcinoma arising in mature cystic teratoma of the ovary: An immunohistochemical analysis of its tumorigenesis. Histopathology 51:98-104.
10. Selvaggi F, Risio D, Waku M, Simo D, Angelucci D, et al. (2012) Struma ovarii with follicular thyroid-type carcinoma and neuroendocrine component: case report.World Journal of Surgical Oncology 10:93.
11. Zhang X, Axiotis C (2010) Thyroid-type carcinoma of strumaovarii. ArchPathol Lab Med 134:786-791.
12. Momin YA, Kulkarni MP, Pandav AB, Sulhyan KR (2017) Mucoepidermoid carcinoma in a mature cystic teratoma-case report with review of literature. Indian Journal of Pathology and Microbiology 60: 117-118.
13. Hackethal A, Brueggmann D, Bohlmann MK, Franke FE, Tinneberg HR, et al. (2008) Squamous-cell carcinoma in mature cystic teratoma of the ovary: systematic review and analysis of published data. Lancet Oncol 9: 1173-1180.
14. Kikkawa F, Ishikawa H, Tamakoshi K, Nawa A, Suganuma N, et al. (1997) Squamous cell carcinoma arising from mature cystic teratoma of the ovary: a clinicopathologic analysis. Obstet Gynecol 89: 1017-1022.
15. Chan-Hong Park, Min-Hyung Jung, Yong-Il Ji (2015) Risk factors for malignant transformation of mature cystic teratoma. Obstet Gynecol Sci 58: 475-480.
16. Abhilasha N, Bafna UD, Pallavi VR, Rathod PS, Krishnappa S (2016) A review of squamous cell carcinoma arising in mature cystic teratoma of the ovary. Indian Journal of Cancer53:612-614.