Research Article ISSN: 2836-3647

American Journal of Pathology & Research

Ovarian Teratomas with Malignant Transformation at the Laboratory Department of the University Hospital Center / Joseph Ravoahangy Andrianavalona Madagascar

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Received: 02 Feb 2026; **Accepted:** 20 Feb 2026; **Published:** 28 Feb 2026

Citation: Volahasina Francine Ranaivomanana, Holy Tiana Andrianjafitrimo, Haingo Voahangy Rabetafika Ranaivoson, et al. Ovarian Teratomas with Malignant Transformation at the Laboratory Department of the University Hospital Center / Joseph Ravoahangy Andrianavalona Madagascar. American J Pathol Res. 2026; 5(2): 1-3.

ABSTRACT

Transformed teratomas represent a rare and aggressive form of germ cell tumor, characterized by the presence of a malignant somatic component within a typically mature teratoma.

This study aims to better understand the epidemiological, clinical, and histopathological characteristics of these atypical tumors.

Over a 13-year period, seven cases were included, as well as one case of carcinoid tumor, two cases of squamous cell carcinoma, and four cases of papillary thyroid carcinoma. Most of the patients were postmenopausal women presenting with large cysts.

The prognosis of transformed teratomas depends on early diagnosis, the nature of the transformed tissue, and the possibility of achieving complete surgical excision. Multidisciplinary management and rigorous follow-up are essential to improve survival in patients affected by this rare entity.

Keywords

Transformed teratoma, Malignant transformation, Mature cystic teratoma, Ovarian germ cell tumor, Somatic-type malignancy.

Introduction

A teratoma is a tumor composed of tissues derived from two or three embryonic germ layers: the ectoderm, mesoderm, and/or endoderm. Malignant transformation of one of its components is a rare occurrence, mainly affecting postmenopausal women. Its incidence remains low, estimated between 2% and 6% of germ cell tumors, but it has a significant prognostic impact due to its often aggressive behavior and relative resistance to conventional chemotherapy protocols.

Given the heterogeneity of transformation types and the lack of clear therapeutic consensus, a better understanding of transformed teratomas is necessary in order to optimize diagnostic and therapeutic strategies. This work aligns with that objective by analyzing clinical, histological, and follow-up data from documented cases in the literature as well as from the present study.

Patients and Methods

This is a retrospective and descriptive study of all cases of mature ovarian teratomas with malignant transformation of one of their components, over a 13-year period from January 2010 to December 2022, at the Paraclinical Unit for Training and Research

in Pathological Anatomy and Cytology of the University Hospital Center / Joseph Ravoahangy Andrianavalona.

Results

During the study period, 7 cases of mature teratomas with malignant transformation were recorded. The patients' ages ranged from 31 to 69 years, with a mean age of 57.28 ± 8.4 years. Tumor size ranged from 7 to 33 cm, and the contents varied depending on the tissue forming the mass. The cysts were multi-tissue in 3 cases and mono-tissue in 4 cases, including one case of dermoid cyst and three cases of struma ovarii.

Histologically, one case of malignant transformation into a carcinoid tumor, two cases into squamous cell carcinoma, and four cases into papillary carcinoma were observed (Table 1).

Discussion

Mature ovarian teratoma is a common tumor, accounting for 95% of ovarian germ cell tumors. Although benign in the majority of cases, malignant transformation of one of its components can occur in 0.17 to 2% of cases [1]. In this series, 7 cases of transformed teratomas were observed over a 13-year period.

A literature review conducted by Davila C in 2018 [2] identified clinical cases, case series, and meta-analyses involving transformed dermoid cysts published between 1902 and 2018, retaining 35 articles. Li C et al. [3], for their part, conducted a review focused solely on transformations into squamous cell carcinoma, identifying 45 case series and 54 clinical cases between 1977 and 2016. In the series by Hurwitz JL et al. [4], 14 cases of malignant transformation were reported.

From a pathophysiological perspective, the transformation of a mature teratoma component into squamous cell carcinoma may be associated with infection by high-risk human papillomavirus (HPV) and with molecular alterations such as mutations in the *p53* and *p16* genes. *p53* mutation has been correlated with a better prognosis. Other alterations, including those in *PIK3CA* and *CDKN2A*, have also been reported [5].

A study conducted by Noumoff JS et al. [6] highlighted significant cytogenetic differences between benign and transformed components of teratomas. In mature teratomas, cells exhibited a diploid karyotype (2n), ranging from 43 to 48 XX chromosomes, with numerical abnormalities including losses of chromosomes 4, 6, and 7, and gain of chromosome 20. The carcinomatous component shared some of these abnormalities, but additionally presented multiple copies of chromosomes 8 and 11, as well as translocations t(8;14) and t(11;14), associated with polyploidy, which was absent in the benign component.

The average age at onset of malignant transformation is higher than that of dermoid cysts, affecting mainly postmenopausal women, with a mean age of 52 years. This is consistent with the present study, where the average age was 57.28 years, ranging from 31 to 69 years. Li C et al. [3] observed a predominance of cases in patients over 45 years old (72.1%), while the series by Hurwitz JL et al. [4] reported a younger average age of 48 years, with a similar age range (27 to 69 years).

Table 1: Summary of patient data from this study.

Age (years)	Side	Clinical Information	Size (cm)	Content	Microscopy	Diagnosis
69	Right	Painful pelvic mass evolving over 10 months	7	Sebaceous material with hair tufts and whitish nodule	Mature neural, glandular, and skin tissues + monomorphic cells, slightly atypical, arranged in nests, trabeculae, and cords	Carcinoid tumor arising in a mature teratoma
63	Right	Painful pelvic mass evolving over 3 months	17	Solid fleshy intracystic nodule (9 cm) with hair tufts	Mature skin, muscle + cohesive carcinomatous cells with keratin pearls	Squamous cell carcinoma arising in a dermoid cyst
67	Left	Painful pelvic mass	10	Bilocular cavity with sebaceous content and brown-black, budding nodules with colloid	Mature skin tissue, respiratory and thyroid epithelium + papillary tumor lined with cells showing papillary atypia	Papillary thyroid carcinoma arising in a mature teratoma
54	Left	Abdominopelvic mass	15	Mixed solid and cystic	Mature thyroid tissue + vesicular architecture tumor lined with cells showing papillary atypia	Papillary carcinoma arising in struma ovarii
53	Left	Menometrorrhagia with ovarian mass	33	Unilocular cavity with sebaceous content and solid area (11 cm), 50% necrosis	Mature skin tissue with pilosebaceous appendages + atypical carcinomatous cells with keratin pearls	Squamous cell carcinoma in dermoid cyst
64	Right	Right ovarian mass	8.6	Multiple cavities with gelatinous content and vegetations	Mature thyroid tissue + focus of papillary carcinoma	Papillary carcinoma arising in struma ovarii
31	Right	Right ovarian mass	9.6	Multiple cystic cavities with colloid content and vegetations	Mature thyroid tissue + well-circumscribed vesicular tumor with fibrous capsule and papillary atypia	Non-invasive papillary carcinoma of vesicular type arising in struma ovarii

The symptomatology associated with malignant transformation of a mature teratoma remains nonspecific. It generally presents as an abdominopelvic mass, pelvic pain described as a sensation of heaviness, menstrual disturbances, or may be discovered incidentally. A diagnosis of malignant transformation can only be made after histopathological examination of the surgical specimen. In the present series, the clinical presentation in all cases was an isolated pelvic mass, sometimes associated with other symptoms such as abdominal pain (3 cases) and metrorrhagia (1 case), occurring in postmenopausal women. Several authors have suggested that tumor size may be a predictive factor for malignancy. In this series, tumor sizes ranged from 7 to 33 cm, with an average of 14.3 cm, a result comparable to that reported by Li C et al. [3], who found an average of 14.8 cm. However, the series by Hurwitz JL et al. [4] reported a smaller average size of 9.6 cm, ranging from 5 to 15 cm.

The macroscopic appearance of the surgical specimen often provides clues for diagnosis. A mature teratoma typically reveals a yellowish fatty content that solidifies upon exposure to air, often accompanied by hair or even teeth. The Rokitansky protuberance helps to delineate the tumor from healthy ovarian tissue. In the presence of a malignant component, a solid, fleshy area of variable size is observed adjacent to the cystic cavities. In cases of struma ovarii, the specimen contains colloid or gelatinous material, and the malignant tumor component appears as intracytic vegetations.

Malignant degeneration most frequently occurs in the form of squamous cell carcinoma, which is explained by the predominance of cutaneous tissue in dermoid cysts. Other histological types have also been reported, including small cell carcinoma, papillary thyroid carcinoma, melanoma, sarcoma, and carcinoid tumor [7].

In the present study, one case of trabecular carcinoid tumor, two cases of squamous cell carcinoma, and four cases of papillary thyroid carcinoma were observed. Transformation into squamous cell carcinoma remains the most frequently reported form, typically occurring in women over 50 years of age. It is most often unilateral, with a size ranging from 3 to 40 cm.

Thyroid carcinoma arising in a tridermal teratoma or in struma ovarii is rare, with an estimated incidence of 0.1 to 0.3% [1]. Its diagnosis is based on the same histological criteria used for the thyroid gland. The most common forms are: papillary carcinoma (44%), follicular carcinoma (30%), and the follicular variant of papillary carcinoma (26%) [7]. In this study, thyroid carcinomas accounted for 57.1% of malignant transformations, of which 50% had a papillary architecture, 25% a follicular architecture, and 25% were classified as NIFTP (non-invasive follicular thyroid neoplasm with papillary-like nuclear features).

Finally, the carcinoid tumor observed in this series corresponded to a low-grade neuroendocrine carcinoma, composed of monomorphic cells arranged in solid structures, nests, trabeculae, or pseudoglands, consistent with the typical presentation of this tumor type.

Conclusion

The discovery of a large dermoid cyst in a postmenopausal woman should raise suspicion for possible malignant transformation. A thorough histopathological examination, with meticulous sampling of solid areas, is essential to rule out this possibility. Indeed, the prognosis and management differ significantly in cases of malignant degeneration.

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