Case Report ISSN 2639-944X

Journal of Medical - Clinical Research & Reviews

Malignant Transformation Within an Ovarian Teratoma in A 34-Year Old Woman: A Case Report

DIAS DA MATA Thays Furtado[1*], CASOTTI Virginia Guidi[1], SCARDUA Eduardo Frizzera[1], FERREIRA Rodrigo Neves[2] and CHAMBÔ FILHO Antônio[1]

[1]Hospital Santa Casa de Misericórdia de Vitória. Vitória, Espírito Santo, Brazil.

[2]Pathology Laboratory, Hospital Santa Casa de Misericórdia de Vitória. Vitória, Espírito Santo, Brazil.

[*]Correspondence:
Thays Furtado Dias da Mata, Hospital Santa Casa de Misericórdia de Vitória, R. Dr. João dos Santos Neves 143, Vila Rubim 29025-023 Vitória, Espírito Santo, Brazil, Tel: +55 27 99738-4529.

Received: 16 October 2020; **Accepted:** 03 November 2020

Citation: Dias da Mata TF, Casotti VG, Scardua EF, et al. Malignant Transformation Within an Ovarian Teratoma in A 34-Year Old Woman: A Case Report. J Med - Clin Res & Rev. 2020; 4(8): 1-4.

ABSTRACT

Mature cystic teratoma of the ovary is the most common of the germ cell tumors, representing around 95% of cases. Malignant transformation within a dermoid cyst is a rare event, occurring in 1-2% of all cases and generally affecting postmenopausal women over 50 years of age. In cases of malignant transformation in a teratoma, squamous cell carcinoma is the most common finding (80-90%), followed by adenocarcinoma, carcinoid tumor, sarcoma and osteosarcoma. Since there are no specific screening tests, the identification of neoplastic cells occurs incidentally on histological examination of surgical specimens. However, in more advanced cases, patients may present with pelvic pain and a palpable abdominal mass at physical examination. Treatment is mainly surgical, involving total hysterectomy with pelvic lymphadenectomy. Chemotherapy can be used in some cases as an adjuvant treatment. Histopathology is critical to confirm diagnosis. This paper reports on a case of malignant transformation within a mature cystic tumor in a woman of reproductive age and describes the clinical and surgical management used.

Keywords
Malignant transformation, Mature cystic teratoma, Ovarian dermoid cyst.

Introduction

Mature cystic teratoma is the most common germ cell tumor of the ovary, representing 95% of all cases [1]. Although found predominantly in women in the second and third decades of life, it may occur in any age group [2]. The tumor involves a mixture of cystic components that originate from one or more of the three layers of germ cells: the ectoderm (skin, brain), mesoderm (muscle, teeth, fat, bone and cartilage) and endoderm (mucinous or ciliated epithelium, e.g. gastrointestinal and bronchial epithelium, and thyroid tissue) [3].

Teratomas have been classified into two groups: mature (benign, cystic/solid) and immature (malignant) [4]. The tumors most often grow in the gonads, but can also be found in the anterior mediastinum, retroperitoneum and gastrointestinal tract [5]. Ovarian teratomas grow slowly at a rate of 1.8 mm/year in premenopausal women and in rare cases may reach 30 to 40 cm [6,7].

There are no specific symptoms associated with a teratoma. Suspicion is raised following incidental findings, either when there is a palpable lump or as a serendipitous finding at vaginal ultrasonography, which is capable of detecting cystic tumors of differing densities. More advanced cases may present as a palpable abdominal lump, with abdominal distension and low pelvic pain. Acute abdominal pain may occur if there is rupture or torsion of the tumor [8-10].

The definitive diagnosis is reached by histopathology [9,10]. Malignant transformation of components within a dermoid cyst is a rare complication, occurring in 1-2% of cases. Squamous cell carcinoma (SCC) is the most common form of malignant transformation, occurring in 80-90% of cases, followed by adenocarcinoma, carcinoid tumor, sarcoma and osteosarcoma [11]. Malignant transformation generally occurs within a solid region of a mature teratoma referred to as a Rokitansky nodule [12].

Reaching a diagnosis of this disease prior to surgery is difficult, since no tumor marker or imaging test such as ultrasound or tomography is capable of providing a specific diagnosis. Serum carbohydrate determinant 19-9 (CA 19-9) levels may be high in around 50% of cases of dermoid cysts with malignant transformation. Consequently, an immature teratoma is generally discovered as an incidental finding [13].

Treatment of a teratoma with malignant transformation is mainly surgical (hysterectomy with bilateral adnexectomy and lymphadenectomy); however, benefits may be obtained from the use of adjuvant chemotherapy in more advanced stages [12]. Prognosis in cases of teratoma with malignant transformation is guarded; however, early detection is associated with better outcomes [14].

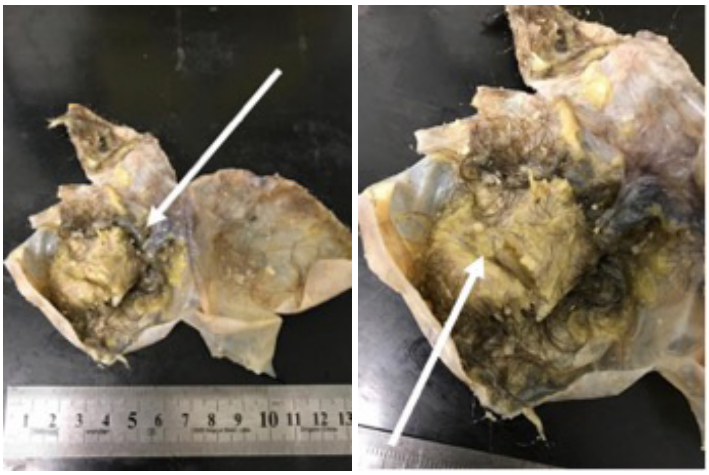
This paper describes the rare case of a patient of reproductive age in whom malignant transformation of an ovarian dermoid cyst was confirmed by histopathology. The internal review board of the *Santa Casa de Misericórdia* Hospital in Vitoria, Espírito Santo, Brazil approved the publication of this paper under reference CAAE 35712720.5.0000.5065. The patient signed an informed consent form giving her permission to publish this case report.

Case Report

A 34-year old nulligravida with regular menstrual cycles and no clinical comorbidities presented at this hospital's Gynecology Department with discomfort in the right iliac fossa that had begun around six months previously. The patient had no fever or any other associated symptoms. Physical examination of the abdomen revealed a moveable, palpable lump occupying the entire left iliac fossa and hypogastrium. Speculum examination showed no abnormalities in the vagina or cervix.

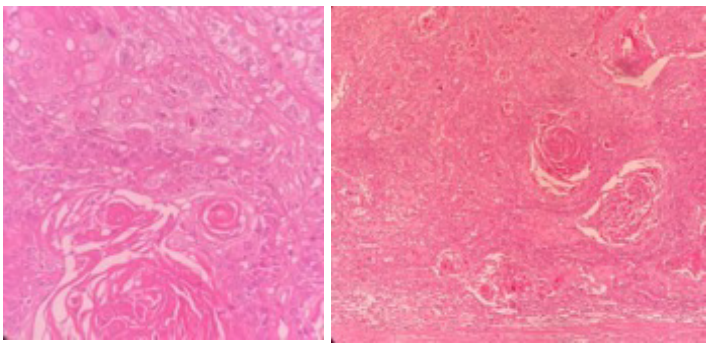
Transvaginal Doppler ultrasound revealed a uterus in normal position (anteflexed, anteverted) with volume of 194 cc, showing two echogenic and nodulated images on the posterior wall measuring 45 x 44 mm and 29 x 27 mm, respectively, suggestive of uterine fibroids. A clearly outlined, mixed, nodulated mass was seen to the right of the uterus, with dense cystic areas and solid echogenic areas, producing a posterior acoustic shadow and extending up to the mesogastric region, with a volume of 961 cc. There was a multi-septated left adnexal cystic mass with thick borders and a volume of 656 cc. Doppler flow imaging revealed the presence of blood flow only at the high-resistance borders. The tumor markers evaluated included: lactate dehydrogenase (LDH): 254 U/L, carcinoembryonic antigen (CEA): 2.17 ng/ml, CA 125: 30.30 U/ml, CA 19-9: 38.12 U/ml, and alpha-fetoprotein (AFP): 3.8 ng/ml. With the principal diagnostic hypothesis being mature teratoma, surgery was then indicated to respect the tumors.

Inspection of the cavity revealed a cystic tumor of approximately 12 cm in size in the right adnexal region with thick yellow contents (fat and hair), as well as three cysts of 10 cm, 6 cm and 8 cm in diameter, respectively, in the left adnexal region. The thick contents of these cysts included fat and hair. Two nodules of uterine fibroids were found on the posterior wall of the uterus. Bilateral oophoroplasty was performed, as well as myomectomy of the nodules on the posterior wall. The macroscopic appearance of the surgical specimen is shown in Figures 1 and 2. The patient was discharged in good general condition and instructed to return for the histopathology results.



Figures 1 and 2: Macroscopic examination of a dermoid cyst removed from a 34-year old woman.
Note the presence of a Rokitansky nodule where an area of malignancy was later detected (white arrows).

Histopathology of the right adnexal tumor revealed a mature cystic teratoma (dermoid cyst). There were three teratomas on the left adnexal region, containing fat, hair and a solid portion. In the smallest tumor, malignant epithelial neoplasia was found, measuring 1.3 cm at the largest diameter, with differentiated squamous cells resembling skin keratinocytes, sometimes in keratin pearl formation. The nucleus was irregular, hyperchromatic, with moderate atypia and an evident nucleolus. The lesion was clearly differentiated, with no angiolymphatic invasion, and an expansive growth pattern. There was no sign of surface involvement. In accordance with the 2018 International Federation of Gynecology and Obstetrics (FIGO) staging system for ovarian cancer, the case was defined as IA (Figures 3 and 4).



Figures 3 and 4: Microscopic evaluation of a malignant epithelial neoplasm detected within a dermoid cyst.
Findings include cells with squamous differentiation similar to skin keratinocytes, sometimes in keratin pearl formation. The nucleus is irregular, hyperchromatic and with moderate atypia and an evident nucleolus. The lesion is well differentiated, with an expansive growth pattern

Complementary tests included tomography of the chest and abdomen, with results showing no secondary implants. Further surgery consisting of total abdominal hysterectomy, bilateral adnexectomy associated with pelvic and para-aortic lymphadenectomy and omentectomy was indicated to complete treatment. Surgery proceeded without complications. Histopathology showed no signs of malignancy in the surgical specimens or in the iliac and obturator lymph nodes. Cytology revealed transudate with no signs indicative of malignancy.

The patient progressed satisfactorily and was referred to the outpatient department for follow-up. Following clinical evaluation and assessment, it was decided that there was no need for any additional treatment due to the fact that the disease had been classified as surgical stage IA. The patient is currently being followed up at the gynecological oncology outpatient clinic at the Department of Gynecology, *Santa Casa de Misericórdia* in Vitória, with routine tests being all normal up to the present time (ten months following the second surgery).

Discussion

The incidence of mature cystic teratomas varies with age within the age bracket of 21-87 years, with the majority of cases occurring in women of reproductive age. On the other hand, malignant transformation in a dermoid cyst is a rare event, occurring in 1-2% of all cases and being more common in postmenopausal women. Squamous cell carcinoma is the most common type of malignant tumor involved in such cases [13].

The patient described here had two characteristics that differentiate this case from previous reports in the literature. First, she was 34 years old, hence younger than patients described in the other reports. This contrast is explained by the fact that the condition is indeed more common in postmenopausal women [13-15]. Second, the malignant transformation to squamous cell carcinoma was found in the smallest dermoid cyst (6 cm in diameter), whereas reports in the literature generally describe malignant transformation in association with larger cysts [14].

Dermoid cysts are encapsulated and their consistency may vary according to the tumor site. There is a solid protuberance on the internal surface of the capsule that is known as a dermoid plug or Rokitansky nodule, often containing sebaceous glands, sweat glands and hair follicles [13]. The ultrasound finding of this protuberance at various points may suggest a complex cyst [15]. One study reported that the majority of malignancies in dermoid cysts were found around solid portions such as in the present case [16].

Malignant transformations may develop over the long term, although the reason for the emergence of malignancy remains to be clarified. Nonetheless, the presence of squamous metaplasia of the columnar epithelium may precede malignant transformation [16], while molecular studies have suggested P53 overexpression as being the causal factor [10]. The involvement of high-risk human papillomavirus (HPV) has also been suggested; however, further studies still need to be carried out in this respect [9,10,16].

The data associated with the detection of HPV in the malignant transformation of a dermoid cyst remain inconsistent. The detection of HPV in a mature teratoma is rare, suggesting that there may be no association between these benign tumors and HPV. Associations between HPV and vulvar, vaginal, perineal and some types of ovarian cancer have already been described; however, more data are still required on the possible association of this infection in cases of teratoma and malignant transformation [17,18].

Symptoms are non-specific. A tumor may be suspected at routine imaging such as transvaginal ultrasonography or may be detected at histopathology performed on a surgical specimen [16,19].

Tumor markers are important in the evaluation of malignancy in an ovarian tumor. Increased levels of the squamous cell carcinoma (SCC) antigen, of CA 125, CA 19-9 or CA 16-6 may be suggestive of malignant transformation in a dermoid cyst. CA 125 and SCC antigen were detected in cases reported in a study conducted by Chiang et al. and were also associated with poorer outcomes [17].

Rim et al. found that a combination of two factors, age ≥40 years and SCC antigen serum levels ≥2.5 ng/ml, was associated with malignant transformation, with specificity of 96% and sensitivity of 77% [16,20].

CA 19-9 serum levels are often elevated in patients with gastrointestinal cancer, particularly pancreatic cancer. Studies have reported that CA 19-9 levels may be elevated in over 50% of cases of dermoid cysts with malignant transformation [21]. In the case in question, CA 19-9 levels were within the normal range, as were the other markers investigated.

Due to the rarity of the disease, the ideal treatment is yet to be defined. The principal recommendation in the literature is bilateral salpingo-oophorectomy, total hysterectomy and comprehensive surgical staging (peritoneal washing, omentectomy, peritoneal biopsies and pelvic and para-aortic lymphadenectomy) in the initial stages of the disease, and cytoreductive surgery with chemotherapy at advanced stages of the disease. There are insufficient data to justify fertility-sparing surgery, even at initial stages of the disease [16].

The use of intraoperative frozen section is not well established in cases of cystic teratomas of the ovary; however, this procedure could be useful for diagnosis and intraoperative staging. It should be considered if the tumor has any characteristics of potential malignancy, thus avoiding a second approach to complete surgical treatment [16].

Prognosis is guarded and one-year survival for the various stages is between 60% and 69% [22,23]. In a study conducted in Taiwan, five-year survival was as high as 93% for cases classified as stage I [16]. For the more advanced stages of the disease (FIGO II-V), prognosis is better when surgery is associated with neoadjuvant chemotherapy. Characteristics such as the patient's age, tumor size, clinical stage, histological differentiation, capsular invasion

and the presence of vascular invasion may provide valuable information to help predict survival in these patients [16,23].

Conclusion

In view of the rarity of such cases, much has yet to be determined with respect to diagnosis and treatment. Further research is required to establish a protocol of care for these patients.

References

1. Osório F, Franco A, Pedro A, et al. Ovarian Mature Cystic Teratoma with Strumal Carcinoid Transformation A Case Report. Acta Obstet Ginecol Port. 2008; 2: 203-206.
2. Comerci JT Jr, Licciardi F, Bergh PA, et al. Mature Cystic Teratoma a Clinicopathologic Evaluation of 517 Cases and Review of the Literature. Obstet Gynecol. 1994; 84: 22-28.
3. Outwater EK, Seigelman FS, Hunt JL. Ovarian Teratomas Tumor Types and Imaging Characteristics. Radiographics. 2001; 21: 475-490.
4. Falavigna A, Gandara C, Ferraz FA, et al. Sacrococcigeal Teratoma: Report of Three Cases. Arq Neuropsiquiatr. 2004; 62: 334-338.
5. Choi DJ, Wallace EC, Fraise AE, et al. Best Cases from the AFIP Intrarenal Teratoma. Radiographics. 2005; 25: 481-485.
6. Caspi B, Appelman Z, Rabinerson D, et al. The Growth Pattern of Ovarian Dermoid Cyst A Prospective Study in Premenopausal and Postmenopausal Women. Fertil Steril. 1997; 68: 501-505.
7. Tindal VR. Jeffcoate's Principles of Gynaecology. 5th edition. Oxford, UK Butterworth-Heinemann Elsevier Ltd. 1987; 466.
8. Hasanzadeh M, Tabare S, Mirzaean S. Ovarian Dermoid Cyst. Professional Med J. 2010; 17: 512-515.
9. Li C, Zhang Q, Zhang S, et al. Squamous Cell Carcinoma Transformation in Mature Cystic Teratoma of the Ovary A Systematic Review. BMC Cancer. 2019; 19: 217.
10. Rathore R, Sharma S, Agarwal S. Malignant Transformation in Mature Cystic Teratoma of the Ovary A Retrospective Study of Eight Cases and Review of Literature. Prz Menopauzalny. 2018; 17: 63-68.
11. Hurwitz JL, Fenton A, McCluggage WG, et al. Squamous Cell Carcinoma Arising in a Dermoid Cyst of the Ovary A Case Series. BJOG. 2007; 114: 1283-1287.
12. Barbosa CA, Soares AA, Lacerda AA, et al. Bilateral Mature Cystic Ovarian Teratoma. Rev Med Minas Gerais. 2003; 13: 218-221.
13. Takemori M, Nishimura R. MRI Findings of an Ovarian Dermoid Cyst with Malignant Transformation. Magn Reson Med Sci. 2003; 2: 105-108.
14. Kikkawa F, Nawa A, Tamakoshi K, et al. Diagnosis of Squamous Cell Carcinoma Arising from Mature Cystic Teratoma of the Ovary. Cancer. 1998; 82: 2249-2255.
15. Pedrosa IS, Alpendre FC, Sousa R, et al. Rare Case of Sarcomatoid Squamous Cell Carcinoma Arising in an Ovarian Mature Teratoma. Rev Bras Ginecol Obstet. 2019; 41: 628-632.
16. Chiang AJ, Chen MY, Weng CS, et al. Malignant Transformation of Ovarian Mature Cystic Teratoma into Squamous Cell Carcinoma A Taiwanese Gynecologic Oncology Group TGOG Study. J Gynecol Oncol. 2017; 28: e69.
17. Chiang AJ, Chen DR, Cheng JT, et al. Detection of Human Papillomavirus in Squamous Cell Carcinoma Arising from Dermoid Cysts. Taiwan J Obstet Gynecol. 2015; 54: 559-566.
18. Wu QJ, Guo M, Lu ZM, et al. Detection of Human Papillomavirus-16 in Ovarian Malignancy. Br J Cancer. 2003; 89: 672-675.
19. Espindola AP, Amorim VB, Koch HA, et al. Atypical Presentation of Mature Cystic Teratoma Floating Balls. Radiol Bras. 2017; 50: 206-207.
20. Rim SY, Kim SM, Choi HS. Malignant Transformation of Ovarian Mature Cystic Teratoma. Int J Gynecol Cancer. 2006; 16: 140-144.
21. Pradhan P, Thapa M. Dermoid Cyst and its Bizarre Presentation. J Nepal Med Assoc. 2014; 52: 837-844.
22. Tseng CJ, Chou HH, Huang KG, et al. Squamous Cell Carcinoma Arising in Mature Cystic Teratoma of the Ovary. Gynecol Oncol. 1996; 63: 364-370.
23. Dos Santos L, Mok E, Iasonos A, et al. Squamous Cell Carcinoma Arising in Mature Cystic Teratoma of the Ovary A Case Series and Review of the Literature. Gynecol Oncol. 2007; 105: 321-324.