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Case report

Malignant melanoma arising in a mature teratoma: A case report with review of the recent literature

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ABSTRACT

Mature cystic teratomas constitute 10–20% of all ovarian neoplasms. Malignant transformation is very rare occurring in only 0.1–2% of mature teratoma cases. Malignant melanoma is among the least common transformations. Herein, we describe a case of young woman initially undergoing evaluation for infertility who was found to have malignant melanoma arising in a mature dermoid cyst. She subsequently underwent unilateral salpingo-oophorectomy with staging procedure with benign pathology. There was no need for adjuvant therapy and the patient is without disease to date (nearly 10-months in follow-up now). We reviewed the existing literature and this is one of only a few cases documented in the last decade.

1. Introduction

Although mature teratomas (MTs), also known as dermoid cysts, compromise 10–20% of ovarian neoplasms globally (Park et al., 2008), malignant transformation is very rare occurring in only 0.17–2% of MT cases (Hackethal et al., 2008). The most frequent malignancy arising in MTs is squamous cell carcinoma (88.3%) (Crouet et al., 1986), followed by adenocarcinoma, fibrosarcoma, carcinoid tumor and mixed tumors. Malignant melanoma is among the least common transformations, with estimated incidence of 0.2–0.8% (Mandal et al., 2010).

A review of 36 cases during 1901 to 2009 has been reported by Xu et al. (2011), showing only six patients surviving >2-years, while only one patient had no evidence of disease (NED) 5-years post-diagnosis. Another review by Ueng et al. (2010) discussed four cases of this tumor type. Prognosis was poor, with all dying 3, 17, 18 and 5 months, respectively, post-diagnosis. Herein, we describe a rare case of this tumor type and discuss various options for management/treatment.

2. Case presentation

A 35-year-old Hispanic female, G0, referred by her Reproductive Endocrinologist. While undergoing evaluation for infertility, pelvic ultrasound demonstrated a pelvic mass versus fibroid measuring 6.2 × 6.6 cm, midline to the left. The left ovary contained multiple follicles measuring 3.4 × 1.8 cm, and a dominant follicle measuring 2.4 × 1.8 cm. There was a contiguous mass, which measured 8.2 × 6.3 × 7.4 cm, present anteriorly, abutting the uterus and left ovary. The lesion was suggestive of a large hemorrhagic cyst or an endometrioma. She complained of pain in left lower quadrant that was crampy in nature.

The patient underwent surgical assessment in conjunction with Reproductive Endocrinology. Diagnostic hysteroscopy followed by laparoscopy was performed revealing a 10 cm mass apparently originating from right ovary and two pedunculated uterine fibroids, which measured ~2 cm and ~5 mm, respectively. Given the size of ovarian mass, the procedure was converted to laparotomy and the ovary was exteriorized. The right ovary was exteriorized from the abdominal cavity. During cystectomy, the cyst ruptured without evidence of intra-abdominal spillage. A myomectomy was also performed. Pathology revealed a unilocular cyst filled with sebaceous material and hair. A 1-cm Rokitansky nodule was present but no other nodules or papillations were identified. Microscopic examination of the ovarian cyst revealed a mature cystic teratoma containing 7 mm focus of melanoma, which was predominantly intra-epidermal; but contained a few

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small nests of invasive melanoma in the adjacent stroma, associated with a dense lymphocytic infiltrate (Figs. 1–3). No lymphatic invasion was identified and the melanoma did not involve surface of the ovary. Histologic sections were reviewed at Johns Hopkins Pathology Department with diagnostic concurrence.

For further assessment, CT scan was performed post-operatively. This showed a complex left ovarian cyst with a thickened wall, measuring 2.3 cm and a simple-appearing right ovarian cyst measuring 3.1 cm, and showed no evidence of retroperitoneal lymphadenopathy. PET scan was also obtained which showed no evidence of metastasis. The case was reviewed at our multi-disciplinary tumor board. Given the pathological findings of the malignant melanoma on initial surgery, recommendation was to perform right salpingo-oophorectomy and a staging procedure.

The patient then underwent robotic-assisted laparoscopic right salpingo-oophorectomy, right pelvic and aortic lymphadenectomy, omental biopsy, intra-peritoneal biopsies and left ovarian cystectomy. All pathology was benign. The right tube and ovary showed no evidence of residual melanoma.

Post-operatively, the patient did well and is without disease to date (nearly 10-months in follow-up now). The case was again discussed at tumor board and no further treatment was recommended, other than close surveillance.

3. Discussion

Mature cystic teratomas (MCTs) constitute 10–20% of all ovarian neoplasms. They tend to present in young women, around the age of 30-years. MCTs are composed of well-differentiated derivations from at least two of the three germ cell layers (i.e., ectoderm, mesoderm, and endoderm). They contain developmentally mature skin complete with hair follicles and sweat glands, sometimes luxuriant clumps of long hair and pockets of sebum, blood, fat, bone, nails, teeth, eyes, cartilage and thyroid tissue. MTs are usually benign, but undergo malignant transformation in <0.2% of cases, and reported incidence of 1–3% by Rim et al. (2006). Several malignancies may develop from any of the three germ-cell layers, such as adenocarcinoma, malignant thyroid struma, carcinoid tumors, melanomas and a variety of soft tissue sarcomas (Rim et al., 2006). The most common malignant evolution is squamous cell carcinoma (SCC) from ectoderm (Rim et al., 2006). Malignant melanoma arising within MCT is extremely rare, with an estimated incidence of <1%.

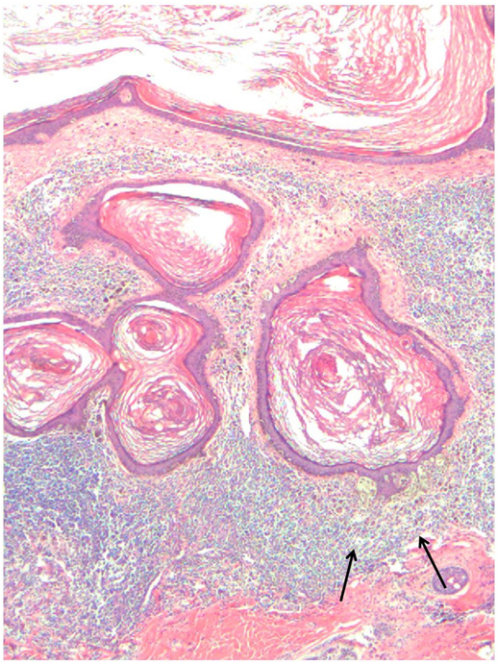

Fig. 1. Mature squamous epithelium in the ovarian teratoma contains numerous junctional nests of atypical melanocytes. Arrows mark an area shown at higher power (H&E stain, 4×).

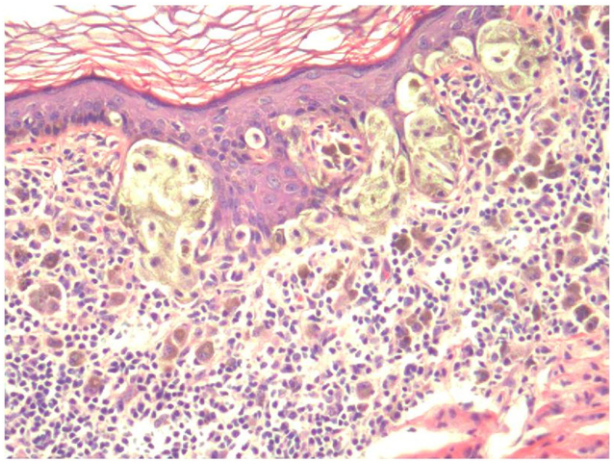

Fig. 2. Nests of melanoma in situ are present at the epithelial-stromal junction and invasive melanoma is present in the stroma accompanied by a prominent lymphocytic reaction (H&E, 20×).

We reviewed nine recent cases of malignant melanoma arising in a mature cystic teratoma reported during 2011–2015 (Table 1). The ages of the patients ranged 24–75 years, with an average of 51.1 years. Initial diagnosis was an ovarian mass in most cases. Four of nine patients had evidence of metastatic disease. The standard treatment for these patients was surgery, specifically unilateral salpingo-oophorectomy (USO) or total abdominal hysterectomy with bilateral salpingo-oophorectomy +/− staging procedure. Six of nine patients received adjuvant chemotherapy, while three patients additionally received immunotherapy. Like our case, two received no adjuvant therapy. Four patients had distant metastases, all of whom died of disease (DOD) at the time of publication. Out of five patients without metastasis, two were reported with NED and the follow-up for the other two was unknown (Table 1). From this, we can conclude distant metastasis plays a significant role in prognosis in a tumor of this type. Therefore, evaluation of the patient for metastases is of paramount importance, and either surgical staging or PET imaging should be considered in these patients. The possibility of a melanoma arising at another site, such as skin, central nervous system, eye and gastrointestinal tract with secondary involvement of the ovary tract, needs to be excluded.

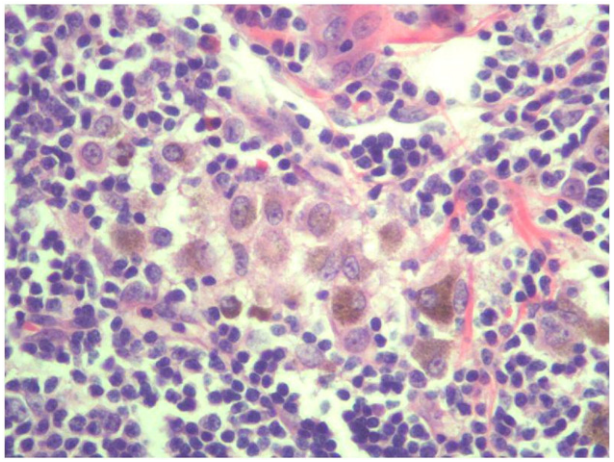

Fig. 3. Invasive melanoma (H&E, 40×).

Table 1
Demographics and patient characteristics of malignant melanoma arising in a mature cystic teratoma reported in the peer-reviewed literature during the years 2011 to 2015.

Authors	Year	Age (years)	Initial diagnosis	Tumor size (cm)	Procedures performed	Surgical staging	Adjuvant therapy	Distant Mets	Prognosis
Lee, et al.	2011	71	Pelvic cystic mass	15 × 12 × 11	BSO, total hysterectomy, Oment, left adrenalectomy, and Append	Yes	Chemotherapy (cisplatin-dacarbazine-vincristine)	Yes	Died 5 months after initial diagnosis
Menci	2011	24	Right ovarian mass	15 × 9 × 8	RSO, sampling of right and left pelvic gutters, pelvic lymph nodes, bowel adhesions, bladder serosa, omentum	Yes	Chemotherapy, immunotherapy (interferon), taxol	Yes	Died 7 months after initial diagnosis
Xu, et al.	2011	33	Right ovarian cystic mass	8 × 7 × 5	Right ovarian cystectomy, hysterectomy, BSO	No	Chemotherapy (dacarbazine), immunotherapy (interferon)	No	NED at 26 months
Godoy, et al.	2012	64	Right-sided pleural effusion, an ovarian mass, ascites	Un-known	Laparotomy, hysterectomy, BSO, omentectomy, resection of diffuse tumoral implants	No	Chemotherapy (temozolamide)	No	Unknown
Hyun & Mun	2013	75	Pelvic mass	20 × 14	LTH, BSO, partial Oment, cholecystectomy	No	Chemotherapy, immunotherapy (interferon)	Yes	Died 17 months after initial diagnosis
Lee, et al.	2014	38	Left adnexal mass	12 × 13	Left salpingo-oophorectomy	No	None	No	Unknown
Genc, et al.	2015	54	Right ovarian cyst	14	TAH, left salpingo-oophorectomy, PAL, appendectomy, Oment	Yes	Immunotherapy (interferon), radiotherapy	Yes	NED at 12 months post-surgery
Black, et al.	2015	45	–	20	TAH, BSO, PAL, Oment	Yes	None	Yes	Died 18 months post-surgery
Kudva, et al.	2015	56	Right ovarian mass	20 × 13 × 16	TAH, BSO, pelvic lymph node sampling, infra-colic omentectomy, Append	Yes	Chemotherapy	No	NED at last follow-up
Current case (Brudie, et al.)	2016	35	Left ovarian mass	10	RAL, right salpingo-oophorectomy, right PAL, left ovarian cystectomy	Yes	None	No	NED at 10-months

Abbreviations: BSO = bilateral salpingo-oophorectomy, RSO = right salpingo-oophorectomy, NED = no evidence of disease, TAH = total abdominal hysterectomy, PAL = pelvic-and-aortic lymphadenectomy, LTH = laparoscopic total hysterectomy, RAL = robotic-assisted laparoscopy, Oment = omentectomy, Append = appendectomy, Mets = metastasis.

In our patient's tumor, melanoma in situ was present in the teratoma, thereby confirming its origin, but post-operatively she also underwent dermatologic exam, and radiologic imaging with CT followed by PET to assess for distant metastasis. These were negative for metastasis. She ultimately had USO of the affected ovary with surgical staging which showed no residual melanoma. She is currently with NED, 14 months from time of surgical staging.

Pre-operative detection of malignant transformation of a MCT is difficult, thereby increasing the likelihood of tumor spread while reducing patient survival. When comparing data of MCT cases with those of malignant transformation, malignancy usually occurs in middle-aged women and the tumor diameter tends to be larger with malignant components, compared to tumors of pure benign nature. Gynecologic examination with pelvic ultrasound should be performed in women with a pelvic mass, as 80% of mature cystic teratomas are diagnosed during the reproductive age (Rim et al., 2006).

Due to the rarity of malignant melanoma within MT, there is a paucity of information in the literature regarding treatment or prognosis but multiple drugs have been shown to be efficacious. Multiple chemotherapy regimens have been offered in recent years to these patients. In recent reports, patients received chemotherapy consisting of dacarbazine, cisplatin and taxol. Extrapolating from treatment of cutaneous melanoma, immunotherapy alone or in combination with chemotherapy has also proven effective.

There may also be consideration of molecular/biological approaches in treatment of malignant melanoma. For example, BRAF is a serine/threonine protein kinase activating the MAP kinase/ERK-signaling pathway, and its mutations are seen in about 50% of melanomas (over 90% V600E). Compared to chemotherapy, BRAF inhibition targeted therapy has shown clinical benefits including progression-free survival, overall survival and objective response rate in patients with malignant melanoma, unrelated to the gynecologic tract. A recent study has shown BRAF inhibitor (dabrafenib), in combination with MEK inhibitor (trametinib), enhance tumor growth inhibition, delay acquired resistance and eliminate paradoxical activation of the MAPK pathway in pre-clinical models of melanoma. In addition, the combination of MEK inhibitors to the therapy removes the adverse effects of BRAF inhibitors alone, which include patient relapse around 7-months after targeted therapy and development of secondary cutaneous SCC and hyperkeratotic lesions within the first 2–3 months of therapy, seen in 14–26% of patients with metastatic melanoma.

Malignant transformations of MTs, especially those of malignant melanomas, are difficult to diagnose and treat. Based on the literature, prognosis of malignant melanomas arising in a mature teratoma is poor, with an overall 5-year mortality rate of 90%, although data is limited. Our review of recent reported cases shows different approaches including a combination of surgery, chemotherapy and/or immunotherapy (Table 1). Patient outcome is unpredictable even when favorable treatments are used. With more cases arising, establishing a successful therapy and improving mortality rate is becoming more likely.

Conflict of interest statement

The author declares that there are no conflicts of interest associated with this manuscript.

Patient consent

This study was deemed exempt by our Florida Hospital Institutional Review Board.

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None.

References

Black, J.D., Roque, D.M., Pasternak, M.C., Buza, N., Rutherford, T.J., Schwartz, P.E., et al., 2015. A series of malignant ovarian cancers arising from within a mature cystic teratoma: a single institution experience. Int. J. Gynecol. Cancer 25, 792–797.

Crouet, H., de Ranieri, E., de Ranieri, J., 1986. Secondary cancers arising in mature benign cystic teratomas of the ovary (dermoid cysts). Review of the literature apropos of a new case. J. Gynecol. Obstet. Biol. Reprod. 198 (15), 1055–1066 (Paris).

Genc, M., Sivrikoz, O., Genc, B., Kurt, S., Celik, E., 2015. Synchronous primary endometrial carcinoma and metastatic melanoma in an ovarian cystic teratoma. Turk. Patoloji. Derg. 31, 215–218.

Godoy, H.E., Kesterson, J.P., Kasznica, J.M., Lele, S., 2012. Malignant melanoma arising in mature cystic teratoma of the ovary. Gynecol. Oncol. Rep. 2, 14–15.

Hackethal, A., Brueggmann, D., Bohlmann, M.K., Franke, F.E., Tinneberg, H.R., Münstedt, K., 2008. Squamous-cell carcinoma in mature cystic teratoma of the ovary: systematic review and analysis of published data. Lancet Oncol. 9, 1173–1180.

Hyun, H.S., Mun, S.T., 2013. Primary malignant melanoma arising in a cystic teratoma. Obstet. Gynecol. Sci. 56, 201–204.

Kudva, R., Ayachit, G.S., Ayachit, A., 2015. Malignant melanoma arising in an ovarian mature cystic teratoma: a rare entity. J. Clin. Diagn. Res. 9, 14–16.

Lee, S., Kim, J.H., Chon, G.R., Kim, A., Kim, B.-H., 2011. Primary malignant melanoma arising in an ovarian mature systic teratoma: a case report and literature review. Korean J. Pathol. 45, 659–664.

Lee, J., Magpayo, J., Panchari, C., Peng, S.-K., 2014. Primary malignant melanoma of the ovary asising in a cystic teratoma: case report and review of the literature. Dermatol. Online J. 20 (10), 1–7.

Mandal, S., Dhingra, K., Gupta, P., Khurana, N., 2010. Rare growth of a psammomatous meningioma in a mature ovarian teratoma: a case report. Pathol. Res. Pract. 206, 322–324.

Menci, D.W., 2011. Cytologic findings in two cases of dermoid cysts with malignant transformation. Diagn. Cytopathol. 39, 919–923.

Park, J.H., Whang, S.O., Song, E.S., Choi, S.J., Lee, W.Y., 2008. An ovarian mucinous cystadenocarcinoma arising from mature cystic teratoma with para-aortic lymph node metastasis: a case report. J. Gynecol. Oncol. 19, 275–278.

Rim, S., Kim, S., Choi, H., 2006. Malignant transformation of ovarian mature cystic teratoma. Int. J. Gynecol. Cancer 16, 140–144.

Ueng, S., Pinto, M., Alvarado-Cabrero, I., Lee, L., Tavassoli, F., 2010. Ovarian malignant melanoma: a clinic-pathologic study of 5 cases. Int. J. Surg. Pathol. 18, 184–192.

Xu, Q., Xie, R., Yang, L., Lin, Y., Chen, G., Ohara, N., Ying, M., 2011. Primary malignant melanoma arising in an ovarian dermoid cyst. Eur. J. Obstet. Gynecol. Reprod. Biol. 157, 117–119.