

Ovarian malignant melanoma metastasized from skin mimicking a benign cyst: a rare case report and mini-review of the literature

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ABSTRACT

Malignant melanomas, often appearing on the skin, rarely metastasize to internal organs and the ovaries are the least affected site. A 45-year-old female patient presenting with a skin lesion on the right side of the neck and diagnosed with malignant melanoma through excision biopsy also appeared to have lung metastasis and a nonspecific ovarian cystic mass of 6 cm after PET-CT scan was performed. Examination revealed a mass with the widest diameter of 9 cm and a surgical decision was made due to the rapid growth pattern. Tumor markers appeared to be within the normal range. Laparoscopic right salpingoophorectomy was performed and frozen section biopsy was obtained. The result was found to be malignant and complementary surgery was performed. Pathological examination of the cystic mass, which was detected to have only nonspecific findings on radiological exam, revealed tiny solid areas in its capsule. The patient was started on postoperative Dabrafenib + Trametinib treatment by oncology and was followed up without recurrence until the 24th postoperative month. At month 24, the brain metastasis with no response to radiotherapy occurred and the patient was lost on the 15th day after decompression surgery. It is important to send adnexal masses to the frozen even if they appear to have a benign character. In patients with a known history of primary cancer, the possibility of the metastasis from the primary tumor site to the ovary should be considered in those whose peroperative frozen section result is in favor of malignancy. Our case is the first case of ovarian malignant melanoma metastasis with a completely cystic and septa-free character in the literature.

Keywords: Metastasis, ovarian malignant melanoma, ovary cyst, survey

Malignant melanoma (MM) is a malignant tumor of melanocytes with the skin being the most important site of localization [1]. Rarely, eye mucosa and internal organ involvement can also be seen. This type

of cancer is known to have the most rapidly increasing incidence worldwide. Genetic mutations such as CDKN2A, PTEN, TP53, and ARID2, atypical/dysplastic nevi, overexposure to UV and sunlight, FAMM



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(Familial atypical multiple mole melanoma syndrome), and immunosuppression are among the risk factors [2, 3]. Gynecologically, the most common site of metastasis is the endometrium; much more rarely, it is seen to metastasize to the ovary [4]. Female genital tract MM constitutes 3% of all melanomas [5]. MM of the ovary may be a metastasis of a melanoma originating from the skin or elsewhere, as well as it may be a primary site of disease [6]. Primary ovarian malignant melanoma is a rarely seen presentation. Although generally originated from mature cystic teratoma, it appears to be a rare malignant transformation of this tumor [6]. Clinically, it usually appears as a solid ovarian mass, although additional metastases may be seen during the operation [7]. MM may spread via lymphatic and hematogenous routes, and metastases often occur to regional lymph nodes, lung, liver, central nervous system, bone, and more rarely other visceral organs [8].

In this report it was aimed to present our experience of management for malignant melanoma case metastasize to ovary without any signs of malignancy. A 45-year-old female patient with a prior skin excision biopsy-confirmed diagnosis of malignant melanoma, with lung metastases detected on PET-CT is presented. In the same PET-CT session, a right ovarian cyst of 6 cm, which was considered to show physiological uptake, was reported, and further referral to obstetrics and gynecology was made. The patient, whose lung lesion was also surgically removed, was operated on after the ovarian cyst progression to 12 cm, and the final pathology result was reported as malignant melanoma for both sites.

CASE PRESENTATION

A 45-year-old climacteric period female, gravida 1, parity 1, was referred to our clinic after a 6 cm non-specific cystic mass originating from the right ovary was detected on PET-CT performed in an external medical center. There was no known history of chronic disease, she has been smoking ½ pack/day (5 packs/year) for 10 years and had a lateral neck mass of 1.5 × 1.5 × 0.8 cm excised at external center 5 months ago; as a result, a diagnosis of malignant melanoma was established. Immunohistochemical examination was focally positive for HMB45 genemed,

positive for vimentin clone V9 genemed, while microscopic examination showed poorly differentiated malignant tumoral infiltration. Following the diagnosis, a PET-CT scan revealed masses each one the size of 1 cm in the apical region of the right lung upper lobe and the middle lobe; therefore, wedge resection of the upper and middle lobes was performed. The pathology results were reported to be compatible with malignant melanoma metastasis; she was followed up by a thoracic surgeon.

In addition, on the PET-CT scan taken upon the diagnosis, a 6 cm mass structure with a mild FDG uptake in the right adnexal area suggesting a nonspecific ovarian cyst was distinguished, and a 3 cm mass suggesting physiological ovarian tissue with heterogeneous and minimal FDG uptake at the anterosuperior junction was observed. Referral to obstetrics and gynecology has been made and approximately 9 cm in length cystic mass was observed on gynecological examination on the right adnexal locus. On MRI the endometrium and uterine cavity appeared to be normal, a few fibroids of 1,5 cm was found in the uterus corpus and fundus; in the pelvic entrance, a 7 × 8 × 9 cm thin-walled cystic mass with a slight thickening on the anterior wall was observed. Surgical excision was recommended.

After the decision of the patient for the surgery, on the gynecological examination, performed 4 months after the initial PET-CT, the uterus and left ovary were normal, and a homogeneous cystic mass of 12 × 9 cm



Fig. 1. Ultrasonographic image of a homogeneous cystic mass of 12×9 cm without septa in the right adnexal locus.

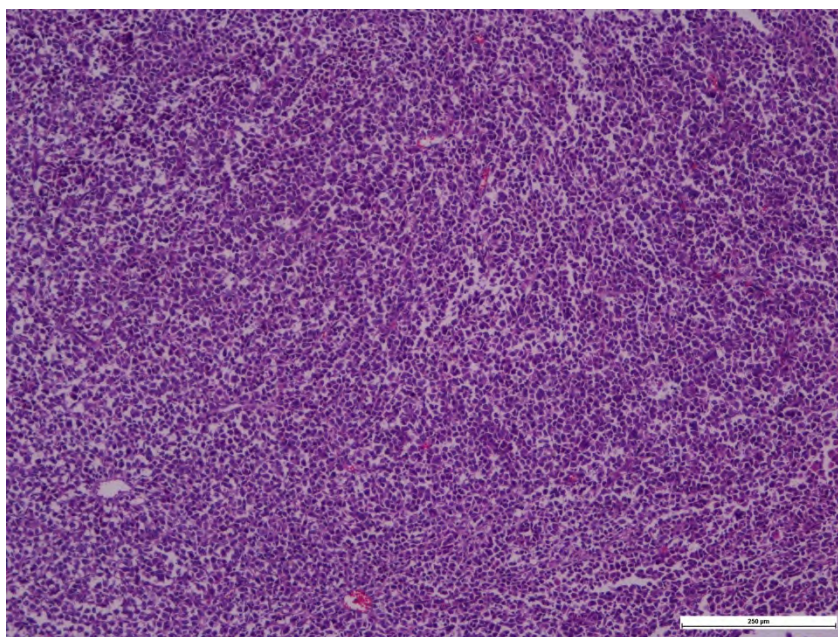


Fig. 2. Diffuse atypical proliferation of polygonal cells (H&E ×100)

without septa in the right adnexal locus was observed (Fig. 1). The patient in the climacteric period sees a period every 45 days; bleeding lasts for 4 days and changes 3-4 pads a day on average. Tumour marker levels were CA125 = 36.3- CA15.3 =14.1 – CA19.9 = 4.6 – CEA = 1.18 and considered normal. The cystic mass was considered benign in the foreground, and L/S right salpingo-oophorectomy was planned. Preoperative endometrial biopsy results were reported as irregular endometrial tissue fragments, and mammography was normal. During the operation, the cyst, approximately 13-15 cm in size, was taken into the endobag, and after the bag was mouthed out, it was ruptured and aspirated into the bag; the remaining material was taken out of the abdomen and sent to the frozen. It was observed that the aspiration fluid was slightly yellowish, attributed to the cyst's semitorision. After the frozen section result was reported as malignant, the patient was reopened with a median incision above and below the umbilicus, and complementary surgery was performed with hysterectomy, left salpingo-oophorectomy, bilateral pelvic/paraortic/obturator lymphadenectomy, omentectomy, and peritoneal biopsy; the patient was discharged on the 5th-day postoperatively with no complications. In the final pathology report, the cystic mass originating from the right ovary was described as 2 tissue pieces with macroscopic dimensions of $8.5 \times 6 \times 2$ cm and $10.5 \times 8 \times 1$

cm. On the larger piece of tissue, tiny solid areas were reported; the size was not specified. No metastasis was observed in the removed lymph nodes, and no adverse features were observed in the uterus, left ovary, left and right tuba. Immunohistochemical study was positive for S100, HMB45, Melan A, MART1; pan-cytokeratin and PAX were reported negative. In addition, after the BRAF mutation studied in the malignant mass sample was reported positive, the pathologic diagnosis of malignant melanoma metastasized to the ovary was established. Diffuse atypical proliferation consisting of polygonal cells (H&E × 100) is shown in Fig. 2, and a cross-section (× 100) in which positivity was detected in atypical cells with Melan A immunostain is shown in Fig. 3.

After the final pathology report, the patient proceeded to oncology follow-up, and dual-targeted therapy (dabrafenib + trametinib) was initiated. Regression prevailed on the PET-CT performed at 6th month after surgery in contrast to the initial one, and routine follow-up continued.

Consecutive PET-CT scan taken at the 12th month postoperatively revealed hypermetabolic nodular formation in the upper inner quadrant of the right breast suggestive of malignancy (second primary?) and minimal hypermetabolic lymph node in the right upper axillary fossa, suggestive of metastasis. No hypermetabolic area was observed in the lungs and pelvis. On further

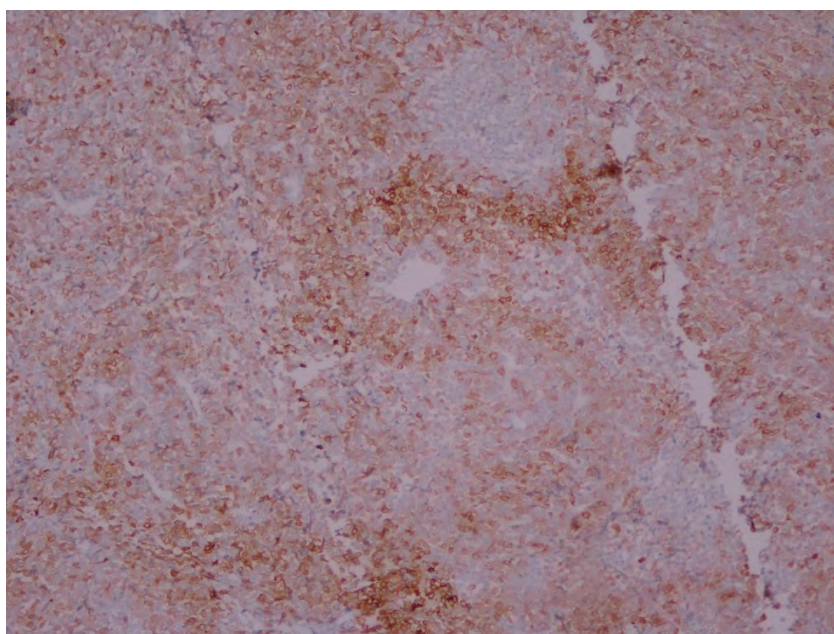


Fig. 3. Melan A immunostaining revealed positivity in atypical cells ($\times 100$).

investigation, no malignancy of the breast and axillary region was detected. Partial regression was observed in the hypermetabolic area of the breast on the 18th week postoperative PET-CT scan.

The patient was followed up with no recurrence till the 24th month. At the 24th month after surgery headache and convulsion attacks started to appear, and neurological follow up were initiated. Increased intracranial pressure and cerebral masses were seen on the MRI, and epilepsy was ruled out by neurology. Whole brain radiotherapy in 10 fractions was performed. Minimal regression of cerebral masses was observed on the control MRI after treatment. Convulsions recurred and intracranial pressure findings reappeared on the 27th month postoperatively. The neurosurgical evaluation took place and decompressive surgery was performed. The patient died on postoperative day 15 during the intensive care unit follow-up.

DISCUSSION

Ovarian metastases account for about 5% of all ovarian cancer cases, and usually, stomach, lung, and liver cancers metastasize to the ovary [8, 9]. Ovary metastasis from malignant melanoma is extremely rare [8].

Metastasis to the ovary occurs within an average

of 7 years after the diagnosis of primary malignant melanoma [9]. In our case, the patient was diagnosed with primary skin MM 5 months before referral, her treatment was completed and she was followed up for MM. From this perspective, in contrast to the time predicted in the literature, the time to ovarian metastasis in our patient was considerably shorter. According to the literature, the mean age of patients with MM metastasis in the ovary is 35.7 years, with extremities being the most common site of tumor spread [7]. Our patient is 45 years old and the primary tumor was detected in the left lateral part of the neck. In this context, our patient appears to be diagnosed with MM 10 years later than the predicted mean age of metastasis, and the localization is the neck - instead of the commonly seen extremities. It is known that malignant melanoma most commonly spreads to the lung and liver [10]. Consistent with the literature, the lung metastases were seen on PET-CT following the primary diagnosis, and the patient was under thorough follow-up after the tumor resection. Since the patient stated that she did not delay the visit to the doctor after the neck mass resection, it is clear that the tumor may have had an aggressive course in the patient. Thus, metastasis to the lung must have occurred at the time of the first diagnosis, and metastasis to the ovary was observed at the 5th month afterward.

Clinically, the solid component predominates in

malignant melanoma metastases, and they have an appearance suggestive of ovarian cancer on ultrasound [11]. First imaging is done with transvaginal ultrasound, though this modality only detects an ovarian mass, and it is not possible to detect clinical findings that would suggest malignant melanoma [12]. A pure cystic lesion with a maximum size of 12 cm was detected in the right adnexal area on the first transvaginal ultrasound examination performed in our patient, and since the tumor marker levels were within the normal range, the patient was initially considered to have a benign ovarian cystic mass. Among other imaging studies, PET-CT and MRI usually reveal nonspecific findings rather than those suggestive of MM [8, 12]. It is mentioned in the literature that ovarian malignant melanoma can be detected on MRI if the tumor contains melanin pigment, which may not always be present [9]. On the first PET-CT imaging of our patient, a nonspecific cyst of 6 cm and a 3 cm cyst suggestive of physiological ovarian involvement were detected, which was considered nonspecific, and consecutive MRI showed the cyst progression to $7 \times 8 \times 9$ cm. It is known from the literature that ovarian MM may have a partially cystic appearance, though a pure cystic lesion has not been shown in any case so far. It is known from the literature that ovarian MM may have a partially cystic appearance, nevertheless, a pure cystic lesion has not been shown in any case so far. In our case, no solid mass lesion was detected on any imaging modality, but tiny solid areas were found on the capsule on the paraffin section.

Patients may present with pain due to malignant metastases in the ovary, but the cases may also be asymptomatic, as is stated in the literature [4]. There was no pelvic pain in our case, and the patient appeared to be in an asymptomatic group in gynecological terms. Most cases are unilateral, with a minority of cases being bilateral [7, 13, 14]. In our patient, a cystic mass without septa, reaching a size of 12 cm, was seen in the right adnexal area, while the other ovary looked completely normal.

The diagnosis is made immunohistochemically according to proteins S-100, human melanoma black-45 and MART-1 positivity, and the absence of coexpression of the antibody vimentin: cytokeratins 8 and 18. Our case was diagnosed with MM by being reported positive for S100, HMB45, Melan A and MART1, and negative for pan-cytokeratin and PAX-8.

Although there is a common opinion that the treatment is surgical, there is no consensus on the type of surgery. As it is emphasized, surgery options are oophorectomy alone, TAH+BSO or, especially in advanced cases, pelvic and para-aortic lymphadenectomy with infracolic omentectomy in adjunction to TAH+BSO [9]. Since the findings suggestive of malignancy were insufficient in our patient, laparoscopic right salpingo-oophorectomy was performed first, and after frozen was found suggestive of malignancy, the operation was continued considering MM. Wide surgical excision, which is routinely applied to patients whose frozen results are found to be malignant, was also performed on our patient.

Survival remains poor despite new targeted treatments developed; even though there are cases reported with patients followed for as long as 96th month without recurrence after bilateral oophorectomy for ovarian metastasis was performed, the median overall survival is 2 years after metastasis [7]. Our patient died 27 months after ovarian metastasis was detected, which is consistent with these data.

CONCLUSION

Malignant melanoma has a worse prognosis compared to other ovarian cancers. As seen in our case, ovarian involvement is generally due to metastasis. In general, they manifest as solid lesions, but it should not be forgotten that they can also present as masses with a cystic appearance, as seen in our case. Our case is the first case of ovarian malignant melanoma metastasis with a completely cystic and septa-free character in the literature. It is important to evaluate adnexal masses histopathologically with frozen, even if they seem benign on ultrasonographic and radiological images. The possibility of tumor metastasis to the ovary should be kept in mind for patients whose frozen results are suggestive of malignancy if there is a known history of primary cancer.

Authors' Contribution

Study Conception: FKG; Study Design: FKG, BB; Supervision: SB; Funding: FKG, BB, HY, ZKUK; Materials: FKG, BB, SB; Data Collection and/or Processing: FKG; Statistical Analysis and/or Data Interpretation: FKG; Literature Review: FKG, BB, ZKUK;

Manuscript Preparation: FKG, BB, SB and Critical Review: FKG.

Informed Consent

Written informed consent was obtained from the patient for publication of this case and any accompanying images or data.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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