

Primary Malignant Melanoma of the Ovary: Case Report and Review of the Literature

Overin Primer Malign Melanomu: Olgu Sunumu ve Kaynakların Gözden Geçirilmesi

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ABSTRACT

Ovarian malignant melanomas are extremely rare tumors. Most of them are secondary tumors and disseminated metastases are recognized at the time of diagnosis. Primary tumors are even more rare and usually associated with a teratoma. A 67-year-old female had a pelvic mass that was recognized on ultrasonography (USG) and physical examination. Intraoperative pathological consultation was reported as "pigmented solid ovarian tumor, probably compatible with malignant melanoma". Paraffin sections, and histochemical (Masson Fontana and Prussia blue) and immunohistochemical examination (S-100 and HMB-45) were also consistent with "malignant melanoma". This case was accepted as "Probably primary ovarian malignant melanoma" in lack of any other tumor focus on detailed clinical and radiological investigation, skin biopsies or pigmented lesions in medical history. It is reported for being an extremely rare tumor and its distinctive characteristics for differential diagnosis are emphasized.

Key Words: Malignant melanoma, Ovary, Histopathology

ÖZ

Overin malign melanomları son derece nadirdir. Çoğunluğu metastazlardan oluşmakta ve tanı sırasında yaygın tümör varlığı görülmektedir. Primer malign melanom olgularının çok daha nadir olduğu ve çoğunlukla teratom zemininde geliştiği rapor edilmiştir. Ultrasonografi (USG) ve fizik inceleme ile "pelvik kitle" tanısı konularak opere edilen 67 yaşındaki kadın hastada frozen inceleme sırasında "Pigmente solid over tümörü (Büyük olasılıkla malign melanom)" olarak değerlendirilmiştir. Parafin kesitlerde, histokimyasal (Masson Fontana ve Prusya mavisini) ve immünohistokimyasal (S-100, HMB45) inceleme sonucunda "malign melanom" olarak rapor edilmiştir. Hastanın daha önce geçirilmiş biyopsi ve melanom öyküsü olmaması, ayrıntılı fizik inceleme ve sistemlerin değerlendirilmesinde başka odak saptanmaması, tümörün tek taraflı olması nedeniyle "Overin olası primer malign melanomu" olarak kabul edilmiştir. Tümörün son derece nadir görülmesi ve ayırıcı tanıda dikkat edilmesi gereken özelliklerin vurgulanması amacıyla sunulmaktadır.

Anahtar Sözcükler: Malign melanom, Ovaryum, Histopatoloji

INTRODUCTION

Only 3% of melanoma cases are found in female genital organs (1). An ovarian malignant melanoma is more rare and is usually seen during the reproductive years, carrying an unfavorable prognosis (2). They are usually metastatic. Primary malignant melanomas are even more rare and most are reported to develop on a background of teratoma (3,4).

CASE REPORT

A 67-year-old female presented with a swollen abdomen and a mass was found on physical examination. Pelvic USG revealed 118x77 mm mass containing solid and cystic areas

that originated from the left adnexial area. The patient was operated on and the left ovarian resection material sent for frozen examination.

The macroscopic evaluation revealed a dark brown-black mass 14x12x6 cm in size and 612 gr in weight, with a smooth and lobular surface and a 6 cm-long tuba uterina attached. The section showed a mostly dark brown lobulated appearance with a smooth cyst 3 cm in diameter at one corner in the inner surface.

Microscopic examination showed tumor cells with large nuclei and wide cytoplasm that formed solid sheets. The frozen section interpretation was reported as "pigmented solid ovarian tumor, probably malignant melanoma" as

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there was widespread brown pigment in the cytoplasm of the cells (Figure 2).

Paraffin sections showed tumor tissue that formed solid nests within the sinusoidal vessel network containing dense brown pigment with black granules in their cytoplasm. Tumor cells with large cytoplasm containing prominent nucleoli and large central nuclei could be discerned where the pigmentation was less dense (Figure 3, 4). The histochemical tests revealed a positive reaction with Masson fontana stain and negative reaction with Prussia blue stain at the pigmented areas. Immunohistochemical (IHC) evaluation showed a diffuse strongly positive reaction for HMB45 and S100 in the tumor cells and the case was reported as malignant melanoma (Figure 5).

No sign of teratoma was seen in the tumor despite obtaining many sections.

Other resection materials received for the patient showed endometrial senile cystic atrophy, an endocervical polyp in the cervix, fibrous obliteration of the appendix and chronic signet ring cholecystitis in the gallbladder. The right ovary, right tuba, omentum and intestinal mesentery looked normal. Systemic investigation revealed a nevoid lesion in the pubic region. The histopathological analysis result was intradermal nevus. The patient had a cataract in the left eye. There was no systemic pathology other than a chronic renal failure history for the past 10 years.

The case was accepted as “probable primary malignant melanoma of the ovary” as there was no previous melanoma



Figure 1: The left adnexial mass has a smooth lobulated surface and occasional cystic appearance on macroscopy (A) while the section (B) is darkly pigmented, lobulated and mostly solid.

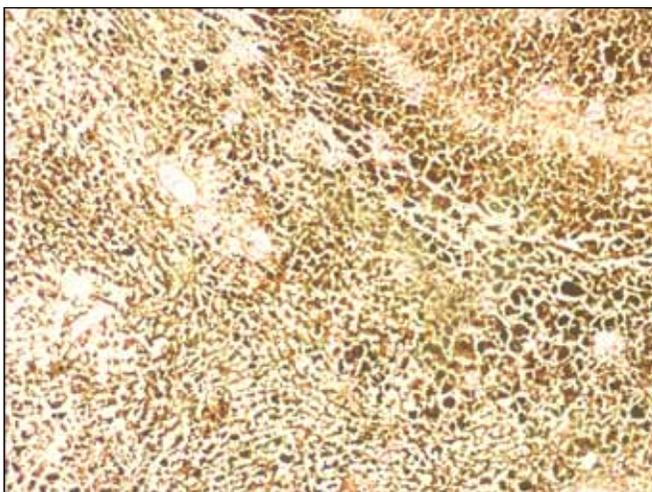


Figure 2: The frozen section shows solid tumor infiltration containing dense brown pigment (H&E; x100).

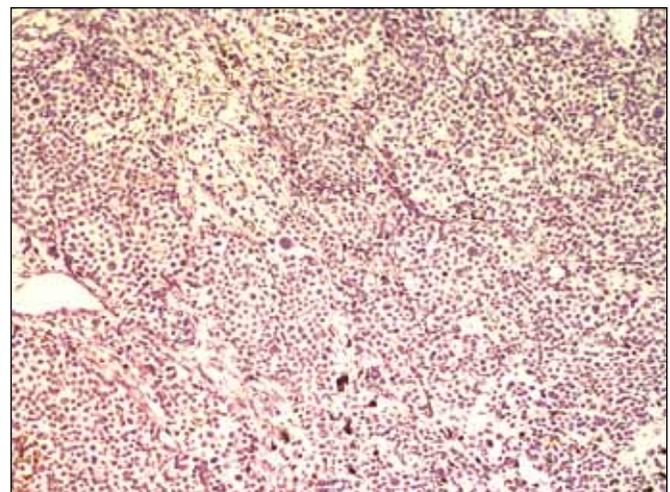


Figure 3: Paraffin sections reveal solid tumor infiltration consisting of epithelioid cells containing occasional melanin pigment and forming nests in pigment-poor areas.

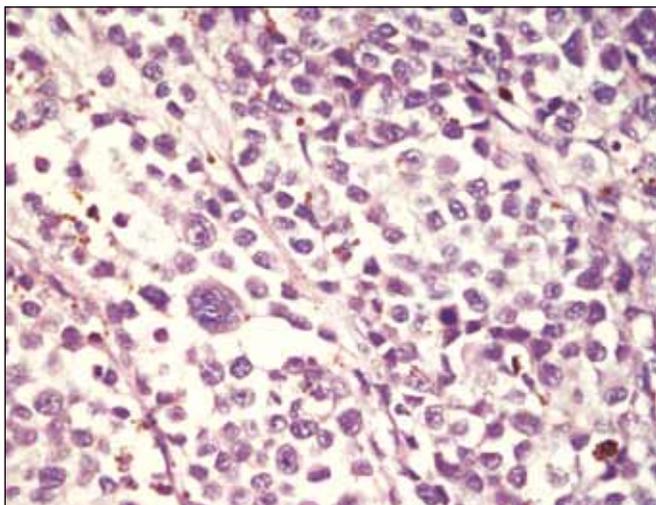


Figure 4: Large magnification shows frequent mitotic activity and dense brown pigment in tumor cells with large eosinophilic nucleoli and centrally located large nuclei.

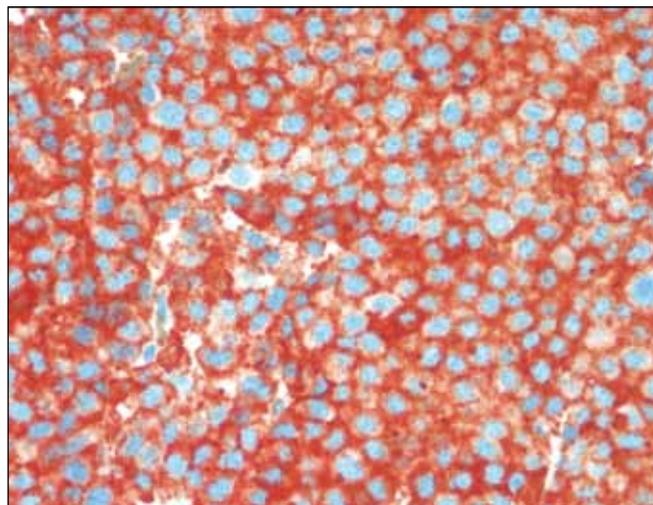


Figure 5: Immunohistochemical analysis showed diffuse strong cytoplasmic reaction with HMB45 in the tumor cells (HMB 45 400x).

history, no other melanoma foci were found during the physical examination and systemic evaluation and the tumor was unilateral (4).

No additional treatment was administered following the resection and the patient died with diffuse lung and bone metastases 7 months after the surgery.

DISCUSSION

Malignant melanoma of the ovary is very rare and usually metastatic. Primary ovarian malignant melanoma is even more rare and most primary cases are thought to develop on a background of cystic teratoma (3,4) (Table I). The presence of widespread melanosis areas in a “mature cystic teratoma” that we have found in the ovarian cyst resection material from a 25-year-old patient seems to support this view.

The differential diagnosis includes metastatic malignant melanoma and primary and secondary tumors of the ovary. It is also possible for a malignant melanoma that has regressed to have metastasized to the ovary. The metastases of the regressed tumor in various organs may be the first clinical sign in such cases.

The absence of history of malignant melanoma, pigmented skin lesions or excision, the inability to find another malignant melanoma focus despite systemic investigation and the unilateral tumor led us to diagnose this case as “probably primary malignant melanoma”.

Histology is important for ovarian malignant melanoma cases but most reports do not contain detailed histological

descriptions. The most common type is the epithelioid cell type with a diffuse or nodular pattern (2). The nodular or “nested” pattern is seen frequently in metastatic ovarian malignant melanoma (5). Metastatic cases are usually bilateral and can rarely be unilateral.

The differential diagnosis of primary ovarian malignant melanoma contains a vast variety of pathologies. Metastatic ovarian malignant melanoma should be differentiated from malignant lymphoma, undifferentiated carcinoma, PNET and malignant sex cord stromal tumors (5).

The carcinoma diagnosis is aided by findings such as rare psammoma bodies or a relationship with endometriosis in the presence of a glandular structure. However, it must be noted that epithelial markers such as cytokeratin and EMA can be positive in malignant melanoma and negative in carcinomas that have lost their antigenicity.

The presence of large epithelioid cells in malignant surface epithelium tumors of the ovary can lead to confusion. The oxyphilic variants of endometrioid clear cell carcinomas and hepatoid carcinomas should be considered in the differential diagnosis when large epithelioid cells have a dark eosinophilic cytoplasm. Transitional cell carcinoma of the ovary can contain small glands and small spaces and can look similar to pseudopapillary-pattern malignant melanomas with cystic degeneration. IHC helps to the differential diagnosis in such cases (5).

Ovarian sarcomas can also develop on a background of dermoid cyst besides malignant melanoma. The presence of epithelioid cells and melanin pigment helps in making

Table I: Definite and probably primary ovarian melanoma cases in the literature

Case	Age	Location	Maximum Size	Pigment	Cell type	Reference
1	21	RO	18 cm	No	SC	5
2	43	RO	6.5 cm	No	LEC	5
3	18	RO	23 cm	Yes	SC	5
4	72	LO	12 cm	Yes	LEC	5
5	50	LO	4 cm	Yes	SC	5
6	55	RO	8 cm	Yes	LEC	5
7	43	LO	9.5 cm	No	LEC	5
8	42	?	?	No	LEC	5
9	19	RO	0.2 cm	No	LEC	2
10	14	LO	4.8 cm	No	LEC	2
11	67	LO	14 cm	Yes	LEC	Current case

LEC: Large epithelioid cell, SC: Small cell, LO: Left ovary, RO: Right ovary.

the malignant melanoma diagnosis. Epithelioid or spindle-cell tumors that develop on a background of dermoid cyst are evaluated as carcinosarcomas. Carcinosarcomas give a positive reaction with epithelial markers and negative reaction with melanocytic markers (5).

Other tumors that are quite similar to ovarian melanomas are sex cord stromal cell tumors and steroid cell tumors. Both tumor cells have large eosinophilic cytoplasm. Steroid cell tumors are not mitotically active like malignant melanomas. They contain teratomatous elements. The presence of spindle cells and melanin pigment supports the diagnosis of malignant melanoma. Steroid cell tumors may contain lipofuscin pigment. Malignant melanoma cases can be confused with granulosa cell tumors when they consist of cells with a narrow cytoplasm. The luteinized areas of granulosa cell tumors may contain prominent nucleoli but these are usually characterized by pale vesicular nuclei. Granulosa cell tumors may also rarely be seen with a dermoid cyst. Sex cord stromal tumors are positive for inhibin and calretinin on IHC (2). Steroid cell tumors and sex cord stromal cell tumors are S-100 and melan-A negative. HMB45 is the most specific melanocytic tumor marker but one must not forget that it can also be positive in steroid cell tumors of the ovary (5). Dense melanin content helped in the differential diagnosis from stromal tumors in our case.

Other tumors to consider in the differential diagnosis are lymphoma, leukemia, dysgerminoma, neuroectodermal (NET) and primitive neuroectodermal tumors (PNET).

NET and PNET can be seen together with dermoid cyst and dysgerminomas can develop from a teratoma. Lymphoid and myeloid markers, PLAP, OCT-4, neuroendocrine markers, CD99 and FLI-1 are important for the differential diagnosis of these tumors in addition to melanocytic markers (5).

The dense melanin pigment of the tumor indicated malignant melanoma even at the intraoperative evaluation in our case. The typical morphology and immunohistochemical investigation provided the definite diagnosis.

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