

# Amelanotic Metastasis of Melanoma Mimicking Ovarian Cancer: A Case Report and Review of the Literature

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**Abstract.** Ovarian manifestation of metastatic amelanotic melanoma is exceptionally rare and can lead to the clinical and even histological misdiagnosis of ovarian cancer. We report on a 35-year-old female patient who presented with bilateral adnexal masses, as well as massive ascites. She underwent laparascopy and multiple biopsies were taken. She was histologically diagnosed with malignant ovarian tumour and was referred for radical surgery. Postoperative final histological examination and immunohistochemical staining of the tumour revealed an amelanotic epithelioid melanoma. Despite the variety of this case, clinicians should be aware of this differential diagnosis when treating ovarian cancer. This report discusses the differential diagnosis and clinical management of both metastatic amelanotic malignant melanoma of the ovary and epithelial ovarian cancer.

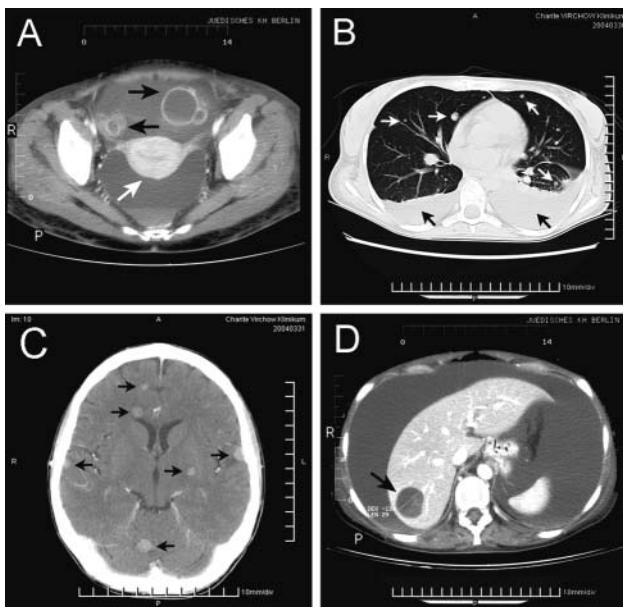
There are two types of malignant ovarian tumours: primary neoplasm and metastasis of other primary sites, the latter being the more common presentation. Ovarian manifestation of malignant melanoma (MM) is very uncommon in the gynecological setting. It is not easily diagnosed by clinical and macroscopic appearance, but can usually be identified by conventional histopathology supplemented with melanin staining. A rare subtype of melanoma can be devoid of pigment, thus making this amelanotic form very difficult to diagnose with conventional histopathological techniques. This amelanotic form represents about 2% to 8% of all malignant melanoma (1). This paper discusses a rare case of malignant melanoma with bilateral ovarian metastases imitating ovarian cancer.

## Case Report

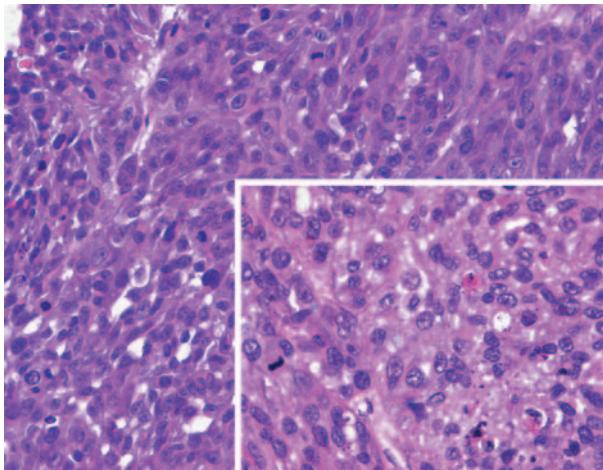
A 35-year-old female patient with progressive multiple sclerosis developed massive ascites and abdominal pain. A CT scan showed bilateral adnexal masses (Figure 1, panel A, black arrows; uterus, white arrow). A diagnostic laparoscopy with multiple biopsies was performed. Examination of the fresh frozen section revealed a malignant ovarian tumour. The patient was referred to our hospital for radical surgery, where she developed symptoms of bowel obstruction and underwent median incision laparotomy. Massive ascites were found and all small bowel segments were dilated with evidence of peritonitis. The small and large intestine was covered with adhesive fibrinous material. Both ovaries were suspicious and enlarged (about 100x70x50 mm). The tumours were of greyish-beige colour and consisted of cystic, as well as solid parts. Necrotic material was visible on the surface of both ovaries. A bilateral salpingo-oophorectomy was performed and the material was sent for fresh frozen sectioning. Histologically, the tumor was composed of solid groups of epithelioid melanoma cells lacking melanin pigment (Figure 2). Numerous mitotic figures could be identified in the H and E stain, as well as red nucleoli in some nuclei and significant cytological atypia (Figure 2, inset). No papillary or glandular tumour aggregates, nor psammoma bodies, which are typical for serous ovarian carcinoma, were found. Therefore, an undifferentiated ovarian carcinoma was diagnosed. The patient underwent total hysterectomy, deperitonealisation and omentectomy as a result of the histology. Ten days post-operatively the patient complained of cough, dyspnea and fever. A chest X-ray showed new lesions in the left upper field and the subsequent CT scan revealed disseminated lung metastases with diameters ranging from 5 to 11 mm (Figure 1, panel B, white arrows), as well as pleural effusion (Figure 1, panel B, black arrows). Moreover hepatic metastases could be identified in the subsequent CT scan (Figure 1, panel D, black arrow).

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*Key Words:* Amelanotic melanoma, ovarian metastasis.

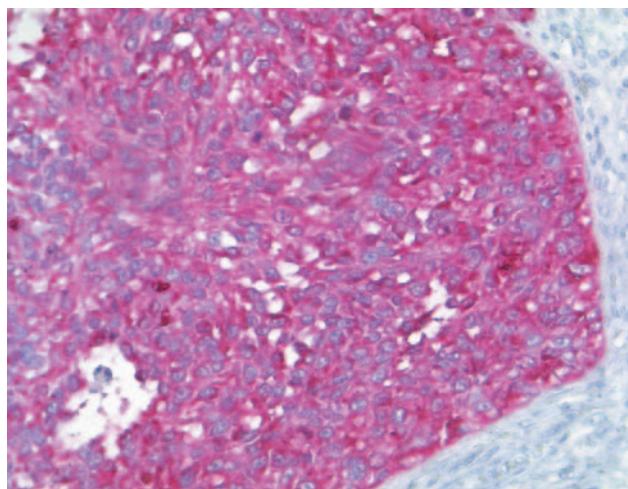


**Figure 1.** Axial computed tomography images of the head, thorax, and lower pelvic region. **A**, Bilateral tumor structures (black arrows) and uterus (white arrow). **B**, Multiple disseminated pulmonary lesions with diameters ranging from 5 to 11 mm (white arrows) and pleural effusion (black arrows). **C**, Multiple disseminated contrast-enhanced cerebral lesions. **D**, Hepatic lesion (black arrow).

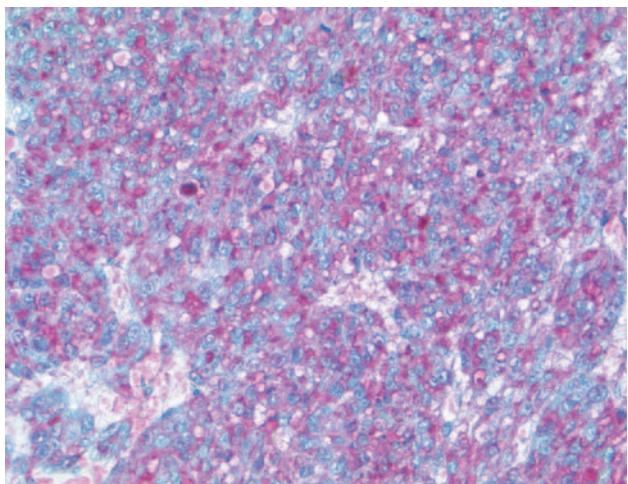


**Figure 2.** Photomicrograph showing tumor composed of epithelioid melanoma cells with a solid growth pattern lacking melanin pigment (*H* and *E* stain with original magnification of 200x). Inset: High-power photomicrograph showing epithelioid cells with high mitotic rate and pleiomorphic nuclei (*H* and *E* stain with original magnification of 400x).

Postoperative histology demonstrated the same tumor features as observed in the fresh frozen section. Immunohistochemical investigations were conducted with the paraffin-embedded tumor tissue to characterize and



**Figure 3.** Immunohistochemical staining with *Melan A* in the ovarian tumor tissue with original magnification of 200x. Note the positive staining in the cytoplasm of the melanoma cells.



**Figure 4.** Immunohistochemical staining with *HMB-45* in the ovarian tumor tissue with original magnification of 200x. Note the positive staining in the cytoplasm of the melanoma cells.

explore the ovarian origin. Expression of cytokeratin 7, CA-125 and hormone receptors could not be detected. Further immunostaining was performed and a strong expression of protein S100, melan A (Figure 3), HMB45 (Figure 4), KBA62 and vimentin was found in the malignant tissue of both ovaries. This profile is very atypical for ovarian cancer, however it is highly characteristic of malignant melanoma. The final diagnosis of an amelanotic epitheloid malignant melanoma was made due to these results and H&E stains being negative for melanin. Investigation of primary and

secondary sites for melanoma were initiated. There was no clinical evidence or previous history of malignant melanoma. The vulva and vagina were re-examined, with no detectable lesions. The examination of the eyes and choroid displayed only a small pigmented naevus of the lower eye lid and conjunctiva, but showed no malignancy confirmed with histology. CT staging was performed and revealed adrenal and cerebral metastases (Figure 1, panel C, black arrows) in addition to the previously identified hepatic and pulmonary lesions. A bone scan was negative for pathological findings. The melanoma was classified as Stage IV C according to the staging system of the American Joint Committee on Cancer (2). Massive pleural effusion was detected on CT and X-ray. The patient refused palliative therapy and died at home 40 days after surgery. Post-mortem inspection was not performed.

## Discussion

Malignant melanoma rarely appears in the female genital tract. These cases represent only 3% of all malignant melanomas (3). The most common site of genital manifestation is the vagina followed by the vulva (4). Ovarian involvement can be found in up to 18% of patients dying of MM at post-mortem inspection (5). Manifestation of MM in the ovary is a very uncommon diagnosis in clinical practice. Clinical manifestation of amelanotic malignant melanoma (AMM) in the ovary is extremely rare. Only four cases have been reported.

Two cases were primary occurrence in cystic teratoma of the ovary (6, 7) and the other two were ovarian metastases from AMM (8, 9). These women were 55-, 47- and 45-years-old respectively. Metastatic occurrence of MM in the ovary is supposed to be more common than primary manifestation. In this case report no primary site could be located. This could be due to possible regression of a cutaneous site or non-cutaneous primary site (*e.g.* lung) that was not picked up in the CT scans. It is also not clear if the primary tumour was an AMM, since amelanotic metastases can arise from AMM as well as MM. The bilateral appearance of the ovarian tumour strongly suggests a metastatic manifestation in this patient. Many authors have stressed the importance of immunohistochemistry for the correct diagnosis of AMM (10, 11). The lack of pigment and cell diversity can easily lead to misdiagnosis histologically. Several melanoma markers such as S100, HMB45 and KBA62 have been developed, which can secure the correct diagnosis even when no melanin granules can be detected. Gupta and Lallu (10) stated that no one single immunohistochemical marker is reliable and a panel of antibodies should be used to verify diagnosis. In this case, the malignant tissue showed a profile of expression that is highly typical of AMM with no detectable pigment in the

**Table I. Immunohistochemical profile of MM vs. ovarian cancer.**

Immunohistochemical marker	
Melanoma	Protein S100 HMB45 Melan A KBA62 Vimentin Cytokeratin 7 Estrogen receptor CA-125
Ovarian cancer	EMA

H&E stains. This profile can easily be distinguished from a typical antigen expression of ovarian cancer (Table I) and led to the final diagnosis in our case. The fresh frozen section was performed twice and examination was not able to reveal the correct diagnosis. The epithelioid appearance of the melanoma cells (without pigmentation) resembled an undifferentiated carcinoma and led to the misdiagnosis. Fresh frozen sections are known to have limited value in the diagnosis of malignant ovarian tumours. Stewart *et al.* have reported a specificity of 58.8% in this setting (12). These results show that immunohistochemistry is a vital diagnostic tool for ovarian neoplasia.

Currently there is no reliable preoperative method to discriminate between AMM and ovarian cancer. Even though about 80% of ovarian cancer patients have raised CA-125 levels, it is not a highly specific tool, because about 20% do not have (*e.g.* mucinous or clear-cell carcinoma). Secondary metastasis into the ovary should be excluded in case of bilateral adnexal masses, atypical tumour feature and a family or past medical history of malignant disease. This case demonstrates immunohistochemistry as being a valuable tool to provide accurate diagnosis of ovarian cancer: it is essential for the diagnosis of the disease and to avoid mismanagement.

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