Metastatic malignant melanoma in an endometrial polyp

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Abstract

Melanocytic metastasis to gynecologic organs is rare with most metastases to the ovaries. Metastases to the uterus, or in this case report, a uterine polyp, is exceedingly rare with only 17 cases reported in the literature. Post-menopausal bleeding is the most common presentation of metastatic melanoma in the endometrium, followed by uterine bleeding or abnormal postnatal bleeding in the premenopausal population. We present an 81-year-old woman with metastatic melanoma confined to an endometrial polyp leading to the diagnosis of widespread dissemination of the patient's acral melanoma resected 6 years prior. Although rare, metastatic melanoma should be considered as a cause for abnormal bleeding, especially in the post-menopausal patient with a history of melanoma.

Keywords: acral melanoma, endometrial, metastatic, polyp

Introduction

Acral lentiginous melanoma is a rare form of malignant melanoma accounting for 4-6% of all melanoma diagnoses in Caucasian populations [1] . Patients with acral melanomas have a worse prognosis compared to melanoma in other locations. This may relate to delays in diagnosis and to more aggressive courses [2]. Acral melanoma is often equally overlooked in patients of higher Fitzpatrick skin types who are at lower risk for skin cancer but will be more likely to present with acral lesions. Typical metastases affect the local lymph nodes, brain, and liver. Melanoma metastases to gynecologic organs are rare, but mainly occur in the ovaries. Uterine metastases of other forms of cancer are usually a result of direct spread from the other pelvic organs and are manifestations of widespread dissemination [3, 4]. To our knowledge, only 17 cases have been reported describing melanoma metastases to a uterine polyp. In this case, the patient was diagnosed with metastatic melanoma after hysteroscopic polypectomy done for postmenopausal bleeding. The metastatic melanoma was confined to an endometrial polyp leading to the diagnosis of widespread dissemination of the patient's acral melanoma resected 6 years prior. The most common presentations of metastatic melanoma in the endometrium are abnormal postmenopausal uterine bleeding and abnormal postnatal bleeding in the premenopausal population [5].

Case Synopsis

An 81-year-old woman was referred to the gynecology department for post-menopausal bleeding with history of melanoma of the left heel 6 years prior treated by wide local excision with negative margins and negative sentinel lymph node biopsies (**Figure 1**). Final surgical stage was IIB (T4a, N0, M0) Breslow depth 4.1mm. She then underwent clinical surveillance every three months for the first year, every 6 months for three years, then yearly with no lesions of concern and negative chest radiographs every six months. She continued to follow with her primary care physician for her yearly examinations but did not establish care with a gynecologist as she was postmenopausal. At the time of presentation to the gynecology department she noted vaginal bleeding for two months that was

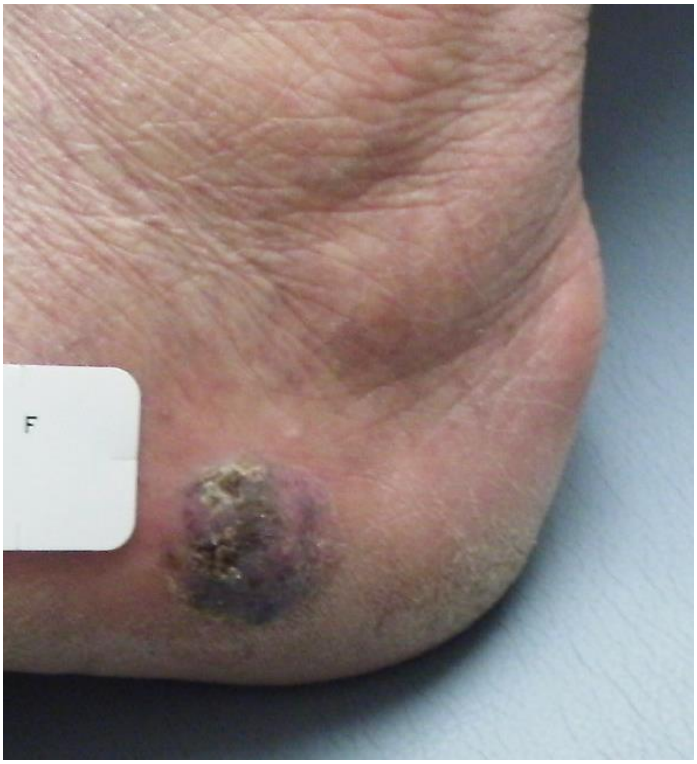

Figure 1. *Acral lentiginous melanoma at diagnosis.*

intermittently heavy; a transvaginal ultrasound suggested endometrial polyp.

Hysteroscopic polypectomy was performed. Upon hysteroscopy a large sessile polyp was noted with increased vascularity and irregular appearance/color concerning for necrosis versus hyperplasia or malignancy (**Figure 2**). Histological examination revealed endometrial curettings composed of endocervical and endometrial lining epithelium with blood clots and diffuse infiltration by a poorly differentiated malignant tumor with a nested growth pattern (**Figure 3**). Immunohistochemical stains showed strongly positive staining for SOX10, HMB45, and Melan-A. However, tumor cells are negatively staining for AE1/3 and PAX8 (**Figure 3**). This biopsy specimen was consistent with her prior melanoma specimen done at the same facility. PET/CT was then performed and showed widely metastatic disease; brain MRI showed at least four enhancing lesions in the CNS. Recommendations were for gamma knife surgery targeting her intracranial metastatic disease, radiation therapy to lumbar spine lesions, and ipilimumab and nivolumab therapy. *BRAF* mutation was noted.

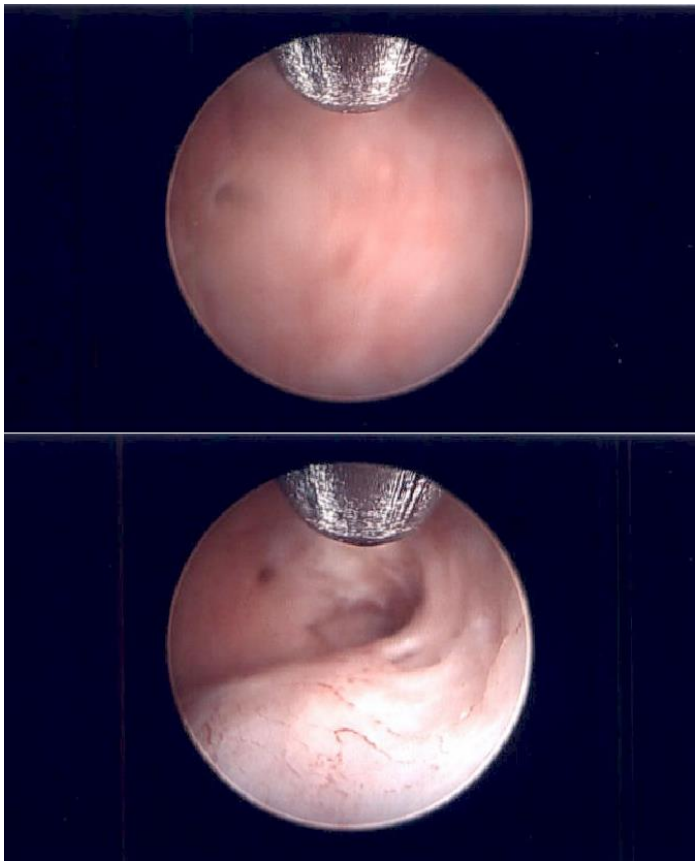

Figure 2. *Images at time of hysteroscopy for postmenopausal bleeding and endometrial polyp.*

However, the patient survived less than 7 weeks after diagnosis.

Case Discussion

Metastatic melanoma in the gynecologic tract is an exceedingly rare entity. Primary melanoma of the uterine cervix and vagina is more common but still accounts for only 3-7% of all melanoma cases [6]. In this case, metastatic disease of her previously resected acral melanoma was found during evaluation of post-menopausal bleeding and was located in a sessile endometrial polyp. This highlights the truly unpredictable nature of melanoma and unfortunately portends a poor prognosis for patients in which spread to non-lymphatic organs is present.

Literature review does not demonstrate an optimal route of surveillance for uterine spread or management beyond the management of metastatic melanoma itself. However, if metastases

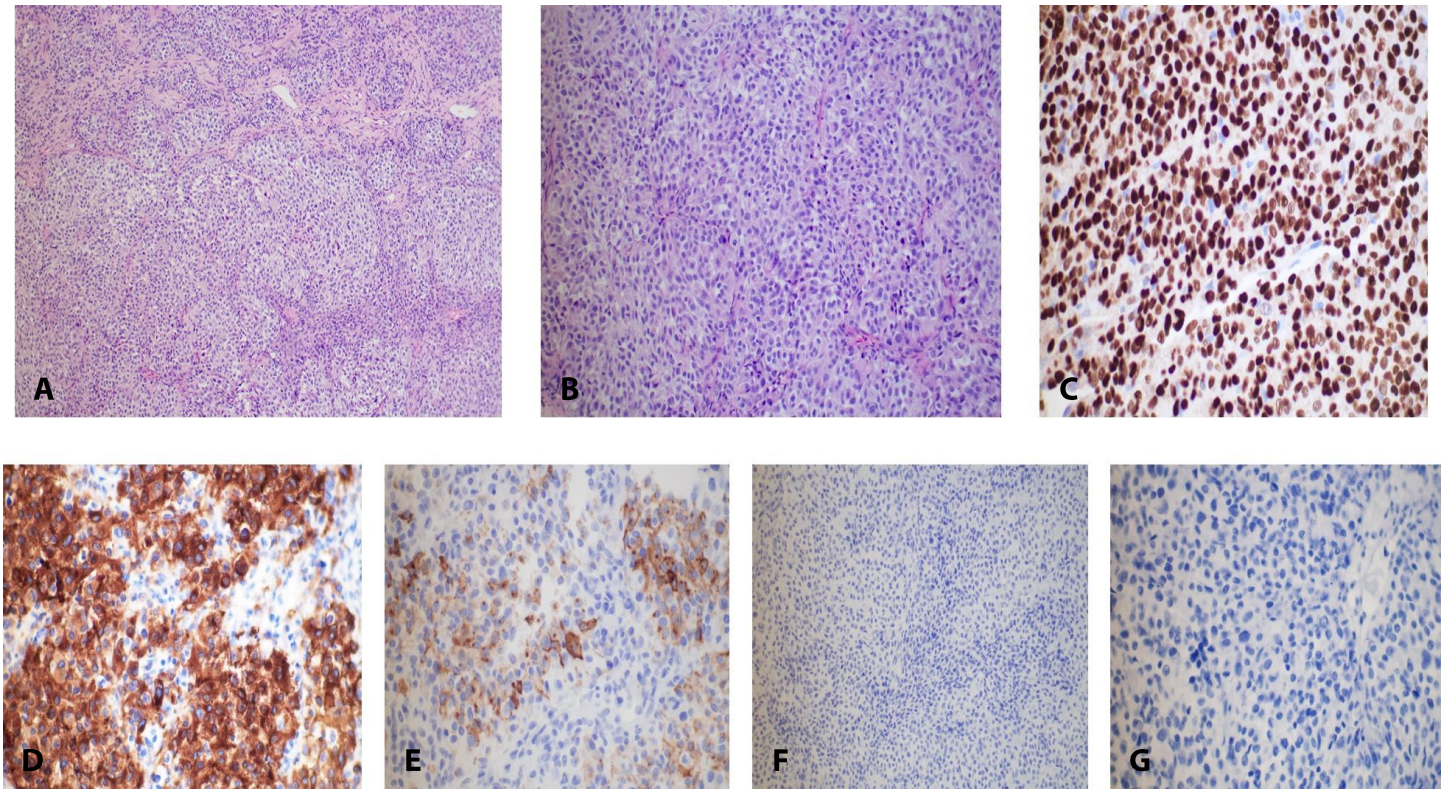

Figure 3. *Pathology specimen of endometrial polyp. H&E, **A)** 10×; **B)** 20×. Tumor cells demonstrate diffuse, strong tumor cell expression of CD10 and cyclin D1, with strong focal expression of desmin and smooth muscle specific alpha. Tumor cells are positive for **C)** SOX10, 20×, **D)** melanA, 20×, and **E)** HMB45, 20×, immunostains. Tumor cells show focal membranous expression of ckit. Tumor cells lack expression of androgen receptor, BCOR, creatine kinase 5/6, DOG1, estrogen receptor, napsinA, P16, P40, progesterone receptor, **F)** cytokeratin AE1/AE3, 10×, and **G)** PAX8, 20×. Tumor cells show wild pattern of staining with p53 immunostain.*

are limited to the gynecologic organs the gold standard of treatment remains surgical resection [7,8]. As this case demonstrates, abnormal bleeding in post-menopausal patients with a history of melanoma warrants an expeditious workup and endometrial sampling. Literature review also suggests that melanoma be considered in pre-menopausal patients with abnormal uterine bleeding as this was the second most common patient population diagnosed with metastatic uterine melanoma (Table 1).

Conclusion

Metastatic melanoma should be considered in patients with a history of malignant melanoma with postmenopausal bleeding or premenopausal abnormal uterine bleeding.

Potential conflicts of interest

The authors declare no conflicts of interests.

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Table 1. *Cases of metastatic uterine melanoma in available literature with age, presentation, primary lesion, diagnostic method and outcomes.*

Year	Author	Age	Presentation	Primary	Diagnostic Method	Outcome
1971	Weber [15]	26	Postnatal irregular bleeding	Leg 12 months prior	Endometrial biopsy	Not stated
1974	Casey and Shapiro [6]	31	Postnatal irregular bleeding	Scapula 8 years earlier	TAH BSO	Died 1 month later
1976	Jaffrey et al. [9]	45	Abnormal uterine bleeding	Back 2 years prior	Endometrial curettage	Died 7 weeks later
1978	Takeda et al. [14]	74	Postmenopausal bleeding	Back at time of diagnosis	Endometrial curettage	Died 5 months later
1978	Wood [16]	61	Post enopausal bleeding	Leg 2 months prior	Endometraial curettage	Alive at 4 months
1980	Scholz and Eckert [13]	75	Postmenopausal bleeding	Cheek 2 years prior	Endometrial curettage	Died 1 month later
1984	Bauer et al. [3]	73	Postmenopausal bleeding	Leg	Endometrial biopsy	Alive 2.5 years later
1989	Pommerenke and Tessmarin [12]	77	Postmenopausal bleeding	Diagnosed after death on leg	Endometrial curettage	Died 1 month later
1990	Nagy et al. [11]	38	Menorrhagia	Back 18 months earlier	Endometrial curettage	Lost to follow up at 6 months
1992	Glaubitz et al. [7]	65	Postmenopausal bleeding	Back 12 months prior	Endometrial curettage	Died 10 months later
1997	Luxman et al. [10]	60	Postmenopausal bleeding	Vulva 6 months prior	Endometrial curettage	Alive at 16 months
2001	Heinig et al. [8]	60	Postmenopausal bleeding	Hand 3 years prior	Endometrial curettage	Died 6 months later
2004	Berker et al. [4]	39	Abnormal uterine bleeding	Trunk 5 years prior	Endometrial curettage	Alive at 6 months
2006	McGettigan et al. [18]	54	Postmenopausal bleeding	Finger 4 years prior	Hysteroscopy and polypectomy	Died 4 months later
2006	Giordano et al. [19]	44	Abnormal uterine bleeding	Right should 4 years prior	Endometrial biopsy	Died 5 months later
2008	Fambrini et al. [20]	52	Abnormal uterine bleeding	Posterior right leg 11 years prior	Hysteroscopic polypectomy, dilation and curettage	Alive at 6 months
2018	Little and Braniff [17]	59	Postmenopausal bleeding	Brain 9 years prior	Hysteroscopic polypectomy, dilation and curettage	Alive at 4 months
2019	Song et al. [23]	67	Postmenopausal bleeding	Right Sole 2 years prior	Dilation and Curettage	Not reported
2020	This case	81	Postmenopausal bleeding	Left heel 6 years prior	Hysteroscopic polypectomy, dilation and curettage	Deceased 7 weeks later