Letter to the Editor

DOI: 10.5582/ddt.2024.01017

Metastasis to hypopharynx from epidermotropic metastatic malignant melanoma

Satoru Mizuhashi[1], Azusa Miyashita[1,*], Haruka Kuriyama[1], Toshihiro Kimura[1], Hisashi Kanemaru[1], Satoru Miyamaru[2], Sho Saeki[3], Satoshi Fukushima[1]

[1] Department of Dermatology and Plastic Surgery, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan;
[2] Department of Otolaryngology-Head and Neck Surgery, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan;
[3] Department of Respiratory Medicine, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan.

SUMMARY Previous reports proposed the concept and criteria of epidermotropic metastatic malignant melanoma (EMMM): (a) dermal involvement equal to or broader than the epidermal involvement, (b) atypical melanocytes within the dermis, (c) thinning of the epidermis, (d) widening of the papillary dermis with an epithelial collarette, and (e) vascular invasion of atypical melanocytes. However, it remains unclear whether EMMM also involves the mucosal epithelium. In this case, the patient was diagnosed with EMMM based on the histopathological findings of the patient's multiple skin lesions and clinical course. The patient also developed metastasis to the hypopharynx. Although histopathological findings of the lesion suggested the possibility of melanoma in situ, as the lesion included atypical melanocytes in the mucosal epithelium, the clinical course supported the diagnosis of hypopharyngeal metastasis from EMMM. This case suggests that EMMM may have epitheliotropic features not only in the skin but also in the mucosa.

Keywords metastasis to mucous membranes, epidermotropism, hypopharyngeal metastasis

Letter to the Editor,

Melanoma metastasis usually involved the dermis and subcutaneous tissue and less frequently involves the overlying epidermis (*1*). A previous report proposed the concept of epidermotropic metastatic malignant melanoma (EMMM) (*2*). It is often challenging to recognize EMMM because its histopathological appearance can mimic primary melanoma (*3*). Some reports have described the histopathological criteria for defining EMMM (*3,4*). However, it remains unclear whether EMMM also involves the mucosal epithelium. We herein report a case with an important finding of hypopharyngeal metastasis from EMMM.

A 50-year-old man presented with an upper lip melanoma at our hospital. The melanoma lesion was resected and reconstructed using a cross-lip flap. Right cervical lymph node dissection was performed, because metastasis was found in the sentinel lymph node. A BRAF mutation was not detected in the primary tumor sample. Two months after operation, a small pigmented macule developed in the hypopharynx (Figure 1a). Biopsy of the lesion revealed localized melanoma within the mucosal epithelium and in the subepithelial layer (Figures 1b and 1c). It was difficult to determine whether it was a new primary lesion or a melanoma metastatic to the mucosa at this point. Three months later, multiple pigmented macules were observed on the face and genital area of the patient (Figures 2a and 2b). At the same time, computed tomography (CT) revealed multiple frosted glassy shadows in the lungs (Figure 2c).

Skin biopsies were performed for several pigmented macules. Histopathologically, the patient's skin lesions exhibited some characteristic features of EMMM (Figures 2e-2h): the epidermal component was limited to the area above the dermal component; the epidermal and dermal components contained large atypical melanocytes; and angiotropic spread of atypical melanocytes was observed around the dermal blood vessels. Regarding pulmonary lesions, CT-guided biopsy revealed metastatic melanoma with lepidic growth (Figure 2d).

We diagnosed the patient with EMMM based on the histopathological findings of the patient's skin lesions and clinical course. Additionally, the clinical course supported the diagnosis of hypopharyngeal metastasis from EMMM. The lesions included atypical melanocytes in the mucosal epithelium, suggesting epidermotropism.

We observed an important clinical characteristic of EMMM, which is epitheliotropic features in the hypopharynx. To our knowledge, this is the first report on the histopathological finding of hypopharyngeal

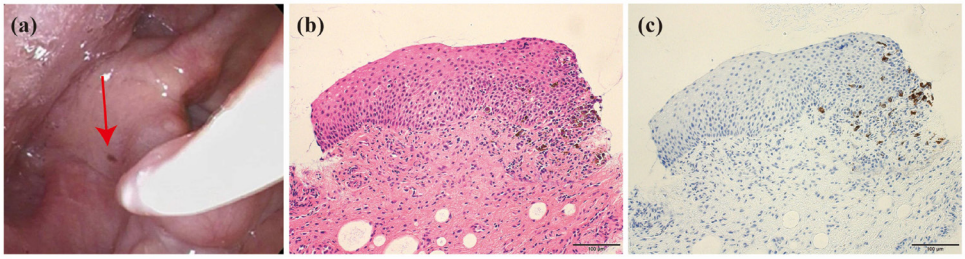

Figure 1. Histopathological findings of hypopharyngeal metastasis from epidermotropic metastatic malignant melanoma. (a) Clinical findings of the pigmented macule in hypopharynx. **(b)** Histopathological findings of the hypopharyngeal lesion (hematoxylin-eosin). Scale bar = 100 μm. **(c)** Immunohistochemical analysis with HMB-45 antibody (#M063401, Agilent, Santa Clara, CA, USA) and with Giemsa as a counterstain. Scale bar = 100 μm.

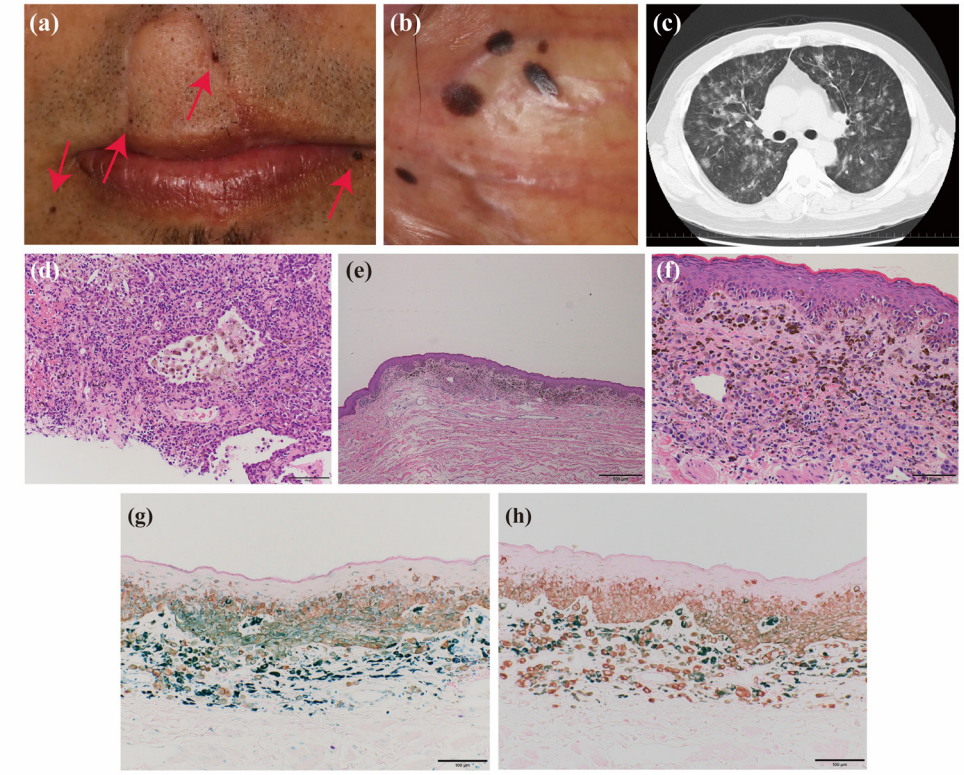

Figure 2. Clinical features and histopathology. (a,b) Clinical findings of multiple pigmented macules in the face and genital area. **(c)** Computed tomography findings of multiple frosted glassy shadows in the lung. **(d)** Histopathological findings of lung lesions (hematoxylin-eosin). Scale bar = 100 μm. **(e,f)** Histopathological findings of the skin lesion (hematoxylin-eosin). **(e)** Scale bar = 500 μm. **(f)** Scale bar = 100 μm. **(g)** Immunohistochemical analysis of the skin lesion with HMB-45 antibody (#M063401, Agilent, Santa Clara, CA, USA) and with Giemsa as a counterstain. Scale bar = 100 μm. **(h)** Immunohistochemical analysis of the skin lesion with MART-1 antibody (#413381, Nichirei Bioscience Inc, Tokyo, Japan) and with Giemsa as a counterstain. Scale bar = 100 μm.

metastasis from EMMM.

In 1978, Kornberg *et al*. (*2*) proposed the EMMM concept and criteria: (a) dermal involvement equal to or broader than the epidermal involvement, (b) atypical melanocytes within the dermis, (c) thinning of the epidermis, (d) widening of the papillary dermis with an epithelial collarette, and (e) vascular invasion of atypical melanocytes. Furthermore, some reports showed that the presence of angiotropism is suggestive of EMMM (*5-9*). In this case, the patient's multiple skin lesions exhibited some characteristic histological features of EMMM. The patient was diagnosed with EMMM based on the histopathological findings of patient's multiple skin lesions and clinical course.

A previous study indicated that gastric metastasis from EMMM may include atypical melanocytes in the superficial mucosa (*10*). However, little is known about the histopathological findings of hypopharyngeal metastasis of EMMM. In this case, atypical melanocytes were localized to the mucosal epithelium and in the subepithelial layer of the hypopharyngeal lesion. Although it was difficult to determine whether that is

a new primary lesion or a melanoma metastatic to the mucosa, the clinical course supported the diagnosis of hypopharyngeal metastasis from EMMM. This finding is similar to that of a previous report on gastric metastasis (*10*). These suggest that EMMM may have epitheliotropic features not only in the skin but also in the mucosa. However, further investigations are required to confirm the histopathological findings of mucosal metastasis from EMMM.

Acknowledgements

We would like to thank Chiemi Shiotsu for technical assistance.

Funding: None.

Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Plaza JA, Torres-Cabala C, Evans H, Diwan HA, Suster S, Prieto VG. Cutaneous metastases of malignant melanoma: A clinicopathologic study of 192 cases with emphasis on the morphologic spectrum. Am J Dermatopathol. 2010; 32:129-136.
2. Kornberg R, Harris M, Ackerman AB. Epidermotropically metastatic malignant melanoma. Differentiating malignant melanoma metastatic to the epidermis from malignant melanoma primary in the epidermis. Arch Dermatol. 1978; 114:67-69.
3. Skala SL, Arps DP, Zhao L, Cha KB, Wang M, Harms PW, Andea AA, Fullen DR, Chan MP. Comprehensive histopathological comparison of epidermotropic/dermal metastatic melanoma and primary nodular melanoma. Histopathology. 2018; 72:472-480.
4. Abernethy JL, Soyer HP, Kerl H, Jorizzo JL, White WL. Epidermotropic metastatic malignant melanoma simulating melanoma in situ. A report of 10 examples from two patients. Am J Surg Pathol. 1994; 18:1140-1149.
5. Gerami P, Shea C, Stone MS. Angiotropism in epidermotropic metastatic melanoma: another clue to the diagnosis. Am J Dermatopathol. 2006; 28:429-433.
6. Jang MS, Han SH, Kim JH, Lee KH, Park JB, Kim ST, Suh KS. Epidermotropic metastatic malignant melanoma. Korean J Dermatol. 2015; 53:53-57.
7. Yang HJ, Lee EM, Kim AY, Lee EJ, Hong IH, Huh SO, Jeong KS. Angiotropic metastatic malignant melanoma in a canine mammary gland. Lab Anim Res. 2011; 27:353-356.
8. Moreno A, Español I, Romagosa V. Angiotropic malignant melanoma. Report of two cases. J Cutan Pathol. 1992; 19:325-329.
9. Johnson CS, Ramos-Caro FA, Hassanein AM. Ultra-late erysipeloid angiotropic metastatic malignant melanoma. Int J Dermatol. 2001; 40:446-447.
10. Lestre S, João A, Ponte P, Peixoto A, Vieira J, Teixeira MR, Fidalgo A. Intraepidermal epidermotropic metastatic melanoma: a clinical and histopathological mimicker of melanoma in situ occurring in multiplicity. J Cutan Pathol. 2011; 38:514-520.

Received March 18, 2024; Revised April 5, 2024; Accepted April 13, 2024.

**Address correspondence to:*
Azusa Miyashita, Department of Dermatology and Plastic Surgery, Faculty of Life Sciences, Kumamoto University, 1-1-1 Honjo, Kumamoto, Japan.
E-mail: azusa-miyashita@kumamoto-u.ac.jp

Released online in J-STAGE as advance publication April 17, 2024.