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Case Report

Pigmented Epithelioid Melanocytoma (Animal Types of Melanoma) on the Nose

Kentaro Ohuchi Taku Fujimura Yumi Kambayashi Hisayuki Tono
Eika Ohtake Akira Hashimoto Setsuya Aiba

Department of Dermatology, Tohoku University Graduate School of Medicine, Sendai, Japan

Keywords
Pigmented epithelioid melanocytoma · Prognosis · Tumor-associated macrophages · PD-L1 · CD163

Abstract
Pigmented epithelioid melanocytoma (PEM), also known as an animal-type melanoma, is a distinctive group of melanocytic tumors with a more favorable prognosis than conventional melanoma. Since tumor-associated macrophages (TAMs) extend in the premetastatic lymph nodes in several cancers, we hypothesized that the lower rate of lymph node metastasis in PEM might be correlated with the phenotypes of TAMs. Therefore, in this report, we further investigate the subpopulation of TAMs in PEM, revealing that the main population of TAMs in histiocytic lesion is CD163+CD206+PD-L1+ M2-polarized macrophages. In addition, since the PD-L1-expressing CD205+ dendritic cells are also detected in histiocytic lesions, the PD-L1-expressing TAMs and dendritic cells might suggest favorable prognostic factors in patients with PEM.

KARGER

Taku Fujimura
Department of Dermatology, Tohoku University Graduate School of Medicine
Seiryo-machi 1-1
Aoba-ku, Sendai 980-8574 (Japan)
E-Mail tfujimura1@mac.com

Introduction

Pigmented epithelioid melanocytoma (PEM), also known as an animal-type melanoma, is a distinctive group of melanocytic tumors with a more favorable prognosis than conventional melanoma [1–3]. The typical PEM contains an aggregation of histiocytes in the center of the tumor, which is useful for the differential diagnosis against nodular melanomas or cellular blue nevus [3–6]. As we previously reported, these aggregated histiocytes contain M2-like macrophages [7], which could be either positive or negative prognostic factors for skin cancers when stimulated by different cancer stromas [8]. Therefore, in this report, we further investigate the subpopulation of tumor-associated macrophages (TAMs) in PEM.

Case Report

A 60-year-old Japanese man visited our outpatient clinic with a 20-year history of a black nodule on the nose, which was histologically suspected to be a nodular melanoma. On his initial visit, physical examination revealed a blue-black, dome-shaped nodule, 10 mm in size, on the nose (Fig. 1a). A biopsy specimen from the nodule revealed the proliferation of epithelioid, pleomorphic, atypical cells with heavy pigmentation in the dermis and aggregation of histiocytes (Fig. 1b). Immunohistochemical staining revealed that these atypical cells were positive for HMB45 and Melan A. From the above findings, our diagnosis was PEM (animal types of melanoma) on the nose. We excised the tumor with a 5-mm margin.

The biological behaviors of PEM were reported to have a favorable prognosis compared to conventional nodular melanoma [1, 3], but little is known about the immunological microenvironment of PEM. Therefore, we employed immunohistochemical staining for CD163, CD205, CD206, and PD-L1, focusing on the profiles of tumor-infiltrating histiocytes, which are pathologically different from those of conventional nodular melanoma. The histiocytic area was composed of both CD163+ CD206+ M2-polarized macrophages (Fig. 2a) and CD205+ dendritic cells (Fig. 2b). In addition, most of these histiocytes highly expressed PD-L1 (Fig. 2c).

Discussion

PEM is a distinctive group of melanocytic tumors, which only rarely metastasize to regional lymph nodes compared to nodular melanoma [1, 3]. Since TAMs extend to the premetastatic lymph nodes in several cancers [9, 10], we hypothesized that the lower rate of lymph node metastasis in PEM might be correlated with the phenotypes of TAMs.

TAMs comprise an immunosuppressive microenvironment together with other suppressor cells, such as regulatory T cells, in the tumor-bearing host [11]. As Perry et al. [12] reported, reprogramming TAMs into inflammatory phenotypes by targeting CD40 and CD115 suppresses melanoma growth in vivo, suggesting that the phenotypes of TAMs could determine the progression of melanoma. Notably, PEM also possesses various TAMs, including CD163+ M2 macrophages [7], suggesting the importance of investigating the subtypes of TAMs. Since investigating the phenotypes of TAMs in skin tumors is important to estimate their biological behaviors [8, 13], in this report, we further determined the subpopulation of TAMs in PEM.

In our present case, the histiocytic area was mainly composed of CD163+CD206+ M2-polarized macrophages and CD205+ dendritic cells, both of which could express PD-L1 by the

stimulation of cancer stromal factors to induce an immunosuppressive microenvironment at the tumor sites [11, 14]. Notably, since the expression of PD-L1 on TAMs was associated with high levels of CD4+ and CD8+ tumor-infiltrating lymphocytes [15], the PD-L1-expressing TAMs and dendritic cells might suggest favorable prognostic factors in patients with PEM. Since we present only a single case, further cases are needed to gain additional insight into the pathomechanisms of PEM.

Statement of Ethics

The patient gave written informed consent.

Disclosure Statement

The authors have no conflicting interests to declare.

References

1 Bax MJ, Brown MD, Rothberg PG, Laughlin TS, Scott GA. Pigmented epithelioid melanocytoma (animal-type melanoma): an institutional experience. J Am Acad Dermatol. 2017 Aug;77(2):328–32.
2 Zembowicz A, Carney JA, Mihm MC. Pigmented epithelioid melanocytoma: a low-grade melanocytic tumor with metastatic potential indistinguishable from animal-type melanoma and epithelioid blue nevus. Am J Surg Pathol. 2004 Jan;28(1):31–40.
3 Mandal RV, Murali R, Lundquist KF, Ragsdale BD, Heenan P, McCarthy SW, et al. Pigmented epithelioid melanocytoma: favorable outcome after 5-year follow-up. Am J Surg Pathol. 2009 Dec;33(12):1778–82.
4 Moscarella E, Ricci R, Argenziano G, Lallas A, Longo C, Lombardi M, et al. Pigmented epithelioid melanocytoma: clinical, dermoscopic and histopathological features. Br J Dermatol. 2016 May;174(5):1115–7.
5 Ogata D, Arai E, Taguchi M, Ohara K, Saida T, Tsuchida T. Case of pigmented epithelioid melanocytoma affecting the thumbnail. J Dermatol. 2017 Nov;44(11):1322–3.
6 Ito K, Mihm MC. Pigmented epithelioid melanocytoma: report of first Japanese cases previously diagnosed as cellular blue nevus. J Cutan Pathol. 2009 Apr;36(4):439–43.
7 Sadayasu A, Fujimura T, Haga T, Kambayashi Y, Furudate S, Aiba S. Pigmented epithelioid melanocytoma: immunohistochemical profiles of tumour-infiltrating histiocytes. Acta Derm Venereol. 2013 Jul;93(4):481–2.
8 Fujisawa Y, Maruyama H, Furuta J, Ishii Y, Kawachi Y, Fujimoto M. Case of pigmented epithelioid melanocytoma with lymph node metastases. J Dermatol. 2014 May;41(5):452–3.
9 Go Y, Tanaka H, Tokumoto M, Sakurai K, Toyokawa T, Kubo N, et al. Tumor-Associated Macrophages Extend Along Lymphatic Flow in the Pre-metastatic Lymph Nodes of Human Gastric Cancer. Ann Surg Oncol. 2016 Feb;23(S2 Suppl 2):S230–5.
10 Chen XJ, Han LF, Wu XG, Wei WF, Wu LF, Yi HY, et al. Clinical Significance of CD163+ and CD68+ Tumor-associated Macrophages in High-risk HPV-related Cervical Cancer. J Cancer. 2017 Oct;8(18):3868–75.
11 Fujimura T, Kambayashi Y, Fujisawa Y, Hidaka T, Aiba S. Tumor-Associated Macrophages: Therapeutic Targets for Skin Cancer. Front Oncol. 2018 Jan;8:3.
12 Perry CJ, Muñoz-Rojas AR, Meeth KM, Kellman LN, Amezquita RA, Thakral D, et al. Myeloid-targeted immunotherapies act in synergy to induce inflammation and antitumor immunity. J Exp Med. 2018 Mar;215(3):877–93.
13 Fujimura T, Kakizaki A, Furudate S, Kambayashi Y, Aiba S. Tumor-associated macrophages in skin: how to treat their heterogeneity and plasticity. J Dermatol Sci. 2016 Sep;83(3):167–73.
14 Clavijo-Salomon MA, Ramos RN, Crippa A, Pizzo CR, Bergami-Santos PC, Barbuto JA. Monocyte-derived dendritic cells reflect the immune functional status of a chromophobe renal cell carcinoma patient: could it be a general phenomenon? Cancer Immunol Immunother. 2015 Feb;64(2):161–71.
15 Mattox AK, Lee J, Westra WH, Pierce RH, Ghossein R, Faquin WC, et al. PD-1 Expression in Head and Neck Squamous Cell Carcinomas Derives Primarily from Functionally Anergic CD4+ TILs in the Presence of PD-L1+ TAMs. Cancer Res. 2017 Nov;77(22):6365–74.

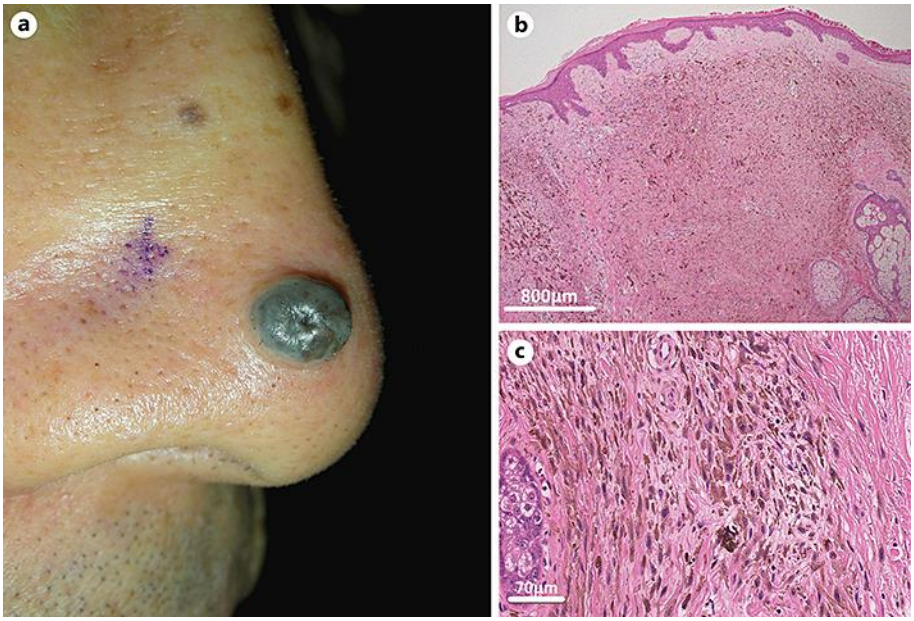

Fig. 1. **a** A blue-black, dome-shaped nodule, 10 mm in size, on the nose. **b**, **c** A proliferation of epithelioid, pleomorphic, atypical cells with heavy pigmentation in the dermis and aggregation of histiocytes. Original magnification: ×50 (**a**), ×400 (**c**).

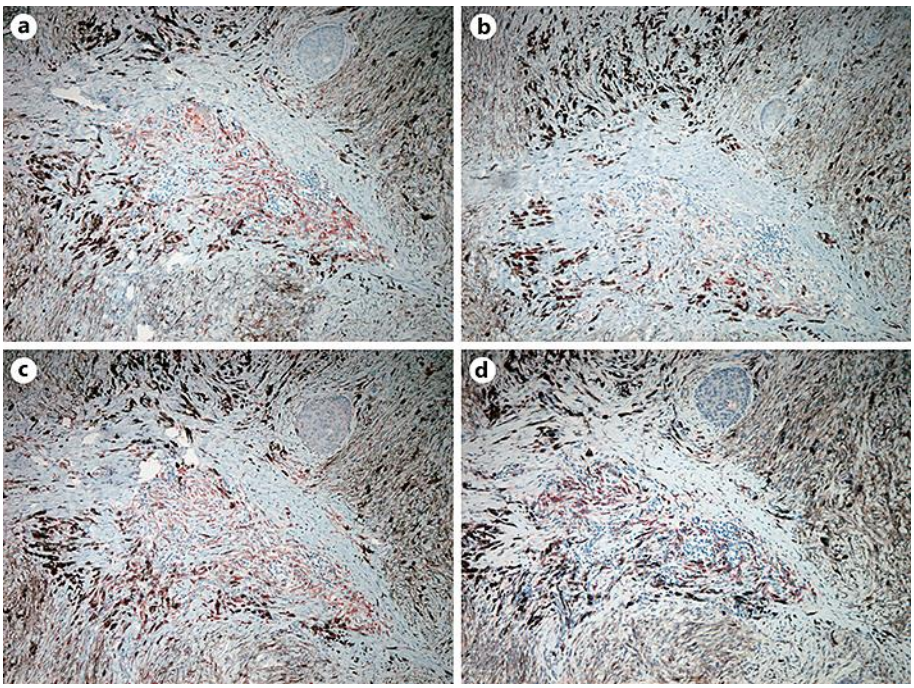

Fig. 2. Paraffin-embedded samples were deparaffinized and stained with anti-CD163 Abs (**a**), anti-CD205 Abs (**b**), anti-CD206 Abs (**c**), and anti-PD-L1 Abs (**d**). The sections were developed with liquid permanent red. Original magnification: ×200.