Letter to the Editor

DOI: 10.5582/bst.2022.01048

Analysis of microsatellite instability using Promega panel in dermatofibrosarcoma protuberans

Saki Maeda-Otsuka[§], Myangat Tselmeg Mijiddorj[§], Ikko Kajihara[*], Yuki Nishimura, Hisashi Kanemaru, Soichiro Sawamura, Katsunari Makino, Jun Aoi, Shinichi Masuguchi, Satoshi Fukushima

Department of Dermatology and Plastic Surgery, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan.

SUMMARY Dermatofibrosarcoma protuberans (DFSP) is a rare neoplasm derived from fibroblasts. Although the frequency of microsatellite instability (MSI) in skin cancer is reported to be less than 5%, there is only one report of the status of MMR in DFSP. The only analytical report of microsatellite stability in which Promega panel is not used, showed that the frequency of MSI-high, MSI-low and microsatellite stable (MSS) cases was 13.9% (5/36), 16.7% (6/36) and 69.4% (25/36), respectively. Thus, the aim of this study was to evaluate the status of MMR in 36 patients with DFSP diagnosed at Kumamoto University. MSI analysis using the Promega panel showed that all cases were MSS, which indicated the absence of MSI in DFSP. This result indicates that the status of MMR may not be useful for the potential therapeutic application of pembrolizumab and the pathogenesis of DFSP may not involve MSI.

Keywords microsatellite instability (MSI), dermatofibrosarcoma protuberans (DFSP)

To the Editor,

The deficiency of DNA mismatch repair (MMR) indicates good therapeutic response to immune checkpoint inhibitors (ICIs). There are several methods to evaluate microsatellite instability (MSI), and the frequency of MSI occurrence in skin tumors is generally less than 5% (*1*). Promega panel (Promega, Madison, WA, USA) is approved as a companion diagnostic reagent for the administration of ICIs. There are few reports about the status of microsatellite stability in skin tumors evaluated by Promega panel, and no MSI-high tumors were detected in cutaneous angiosarcoma (*2*) and extramammary Paget's disease (*3*).

The pathogenesis of dermatofibrosarcoma protuberans (DFSP) is characterized by a fusion gene between the α-helix domain of the collagen type-1 gene (*COL1A1*) and the platelet-derived growth factor-β gene (*PDGFB*) (*4*). The only analytical report of microsatellite stability in which Promega panel is not used, showed that the frequency of MSI-high, MSI-low and microsatellite stable (MSS) cases was 13.9% (5/36), 16.7% (6/36) and 69.4% (25/36), respectively (*5*). However, there was no case study about the occurrence rate of MSI using Promega panel in DFSP. Thus, we investigated the status of MMR in 36 patients with DFSP diagnosed at our hospital.

A total of 36 paraffin-embedded sections were collected from patients with DFSP [aged between 19 and 69 years, 24 men and 12 women, all cases without metastasis] diagnosed at our hospital between 2001 and 2018. Isolation of genomic DNA, capillary electrophoresis, and the evaluation of MMR were conducted as described previously (*2*). Institutional review board approval and written informed consent were obtained according to the Declaration of Helsinki.

Capillary electrophoresis showed all 36 tissues as MSS. Our study presented three major considerable findings. First, the occurrence rate of MMR-deficient tumors among skin tumors (*1*) is less than 5%, which is consistent with the results of our study. Second, the absence of MSI-high tumors in DFSP indicates that MSI may have little relevance to the pathological mechanism of DFSP. Third, we investigated the status of MMR in DFSP using the Promega panel to evaluate the possibility of applying pembrolizumab therapy because Promega panel is an approved companion diagnostic reagent for the administration of ICIs. Our results suggested that MSI might not be appropriate for the determination of the administration of ICIs in DFSP. Investigations of tumor mutation burden (TMB) in DFSP may be necessary because ICIs are also approved for TMB-high solid tumors by Food and Drug

Administration. In conclusion, our study revealed that the DFSP is an MSS tumor.

Acknowledgements

We thank Dr. Hironobu Ihn for his generous kindness and assistance over the years.

Funding: None.

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

References

1. Quinn AG, Healy E, Rehman I, Sikkink S, Rees JL. Microsatellite instability in human non-melanoma and melanoma skin cancer. J Invest Dermatol. 1995; 104:309-312
2. Maeda-Otsuka S, Myangat TM, Kajihara I, Sakamoto R, Yamada-Kanazawa S, Sawamura S, Makino K, Masuguchi S, Fukushima S, Ihn H. Status of microsatellite stability in angiosarcoma: Angiosarcoma is a microsatellite stable tumor. J Dermatol. 2021; 48:e368-e369.
3. Kashiwada-Nakamura K, Myangat TM, Kajihara I, *et al*. Absence of microsatellite instability in extramammary Paget's disease. Skin Health and Disease. 2021; 1:e37. doi.org/10.1002/ski2.37
4. Otsuka-Maeda S, Kajihara I, Kanemaru H, Sawamura S, Makino K, Aoi J, Makino T, Fukushima S, Ihn H. Retrospective study of COL1A1-PDGFB fusion gene-positive dermatofibrosarcoma protuberans in Kumamoto University. Clin Exp Dermatol. 2020; 45:1067-1068.
5. Takahira T, Oda Y, Tamiya S, Yamamoto H, Kawaguchi K, Kobayashi C, Oda S, Iwamoto Y, Tsuneyoshi M. Microsatellite instability and p53 mutation associated with tumor progression in dermatofibrosarcoma protuberans. Human Pathol. 2004; 35:240-245

Received February 8, 2022; Revised February 13, 2022; Accepted February 16, 2022.

[§]These authors contributed equally to this work.
**Address correspondence to:*
Ikko Kajihara, Department of Dermatology and Plastic Surgery, Faculty of Life Sciences, Kumamoto University, 1-1-1 Honjo, Kumamoto, Japan.
E-mail: kajiderma@gmail.com

Released online in J-STAGE as advance publication February 19, 2022