Letter to the Editor

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Primary cutaneous lymphoma is a microsatellite stable tumor: An analysis of microsatellite instability

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SUMMARY: A deficiency in DNA mismatch repair (MMR) leads to microsatellite instability (MSI), which is associated with a favorable response to immune checkpoint inhibitors (ICIs), and the Promega MSI Analysis System is approved as a companion diagnostic tool for it. In this study, we investigated the MMR status in patients with primary cutaneous lymphoma (PCL) diagnosed at our hospital. MSI was found in 1 of the 29 patients (3.4%), an 87-year-old man diagnosed with subcutaneous panniculitis-like T-cell lymphoma. Only the NR-21 marker was present in both tumor and normal tissue, indicating that the MMR status was MSI-low, and he had a germline mutation of SLC7A8. Our study showed that most PCLs are microsatellite stable tumors. This study is a single-center small-sample investigation and requires validation in larger cohorts.

Keywords: DNA mismatch repair (MMR), Promega panel, mononucleotide markers

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A deficiency in DNA mismatch repair (MMR) leads to microsatellite instability (MSI) and indicates a favorable therapeutic response to immune checkpoint inhibitors (ICIs). The Promega panel (Promega, Madison, WA, USA) is approved as a companion diagnostic tool to guide ICI administration. According to previous reports on malignant lymphoma, MSI has been detected in 27% of mycosis fungoides (*1*), 41% of adult T-cell leukemia/lymphoma (not only primary cutaneous lymphoma [PCL]) (*2*), and 13% of diffuse large B-cell lymphoma (*3*). However, there have been no reports of using the Promega panel for MSI analysis in PCL. Therefore, we investigated the MMR status in patients with PCLs diagnosed at our hospital.

A total of 29 paraffin-embedded sections were collected from patients diagnosed with PCLs at our hospital between 2016 and 2024. The age, sex, and pathological diagnoses are summarized in Table 1. Genomic DNA isolation, capillary electrophoresis, and MMR evaluation were conducted as previously described (*4*). Five mononucleotide markers (BAT-25, BAT-26, MONO-27, NR-21, and NR-24) were used to determine the MMR status of each sample. Institutional Review Board approval and written informed consent were obtained in accordance with the principles of the Declaration of Helsinki.

MSI was found in 1 of the 29 patients (3.4%) (Table 1, case 29), an 87-year-old man diagnosed with subcutaneous panniculitis-like T-cell lymphoma. Only the NR-21 marker was present in both tumor and normal tissue in Supplementary Figure S1 (*https://www.ddtjournal.com/action/getSupplementalData.php?ID=263*), indicating that the MMR status was MSI-low, and he had a germline mutation of SLC7A8.

Our study is the first, to our knowledge, to investigate the occurrence rate of MSI in patients with PCL, and we identified two findings. First, the occurrence rate of MSI is < 5% among skin tumors (*5*), and our results are similar to those of several previous studies. However, they differ in that our rate is lower than that reported for MSI in malignant lymphoma (*1-3*). These differences may be owing to our analysis of various types of PCLs and our method of analysis using the Promega panel. Second, no significant correlations were found between MSI and other clinical features, as demonstrated in Table 1. The absence of MSI in PCL suggests that the pathogenesis of PCL may not involve MSI.

However, our study has several limitations. This was a single-center study, and the evaluation was conducted using only one Promega Panel as our primary goal was to explore the potential therapeutic indications of ICIs based on MSI frequency. Additionally, the number of samples analyzed was small, as PCL is a rare malignant tumor.

Table 1. Representative results of capillary electrophoresis for microsatellite instability in primary cutaneous lymphoma

Patients	Age, year	Sex	Pathological diagnosis	MSI
1	64	Male	Adult T-cell leukemia/lymphoma	stable
2	87	Female	Primary cutaneous diffuse large B-cell lymphoma	stable
3	65	Male	Mycosis fungoides	stable
4	42	Male	Primary cutaneous anaplastic large cell lymphoma	stable
5	50	Male	Mycosis fungoides	stable
6	78	Female	Mycosis fungoides	stable
7	82	Female	Adult T-cell leukemia/lymphoma	stable
8	66	Male	Adult T-cell leukemia/lymphoma	stable
9	67	Male	Adult T-cell leukemia/lymphoma	stable
10	89	Male	Primary cutaneous diffuse large B-cell lymphoma	stable
11	86	Male	Adult T-cell leukemia/lymphoma	stable
12	62	Male	Mycosis fungoides	stable
13	72	Male	Mycosis fungoides	stable
14	83	Female	Primary cutaneous follicle center cell lymphoma	stable
15	85	Male	Primary cutaneous diffuse large B-cell lymphoma	stable
16	65	Female	Mycosis fungoides	stable
17	78	Male	Primary cutaneous CD4+ small/medium T-cell lymphoma	stable
18	34	Female	Mycosis fungoides	stable
19	66	Female	Mycosis fungoides	stable
20	61	Male	Adult T-cell leukemia/lymphoma	stable
21	60	Female	Primary cutaneous marginal zone lymphoma	stable
22	56	Female	Mycosis fungoides	stable
23	76	Male	Mycosis fungoides	stable
24	84	Male	Mycosis fungoides	stable
25	80	Male	Mycosis fungoides	stable
26	94	Female	Primary cutaneous diffuse large B-cell lymphoma	stable
27	70	Female	Primary cutaneous peripheral T-cell lymphoma, not otherwise specified	stable
28	67	Female	Mycosis fungoides	stable
29	87	Male	Subcutaneous panniculitis-like T-cell lymphoma	low

In conclusion, our study showed that most PCLs are microsatellite stable tumors, which warrants further validation in larger cohorts in the future.

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