Mycosis fungoides (MF) is the most common cutaneous T-cell lymphoma. Approximately 50% of all primary cutaneous lymphomas are MF. These lymphomas are comprised of epidermotropic collections of small- to medium-sized T lymphocytes with cerebriform nuclei. The neoplastic cell shows a mature CD3+, CD4+, CD45RO+, CD8– memory T-cell phenotype. However, rarely, MF with a CD4–, CD8+ cytotoxic T-cell phenotype has been reported.\(^2\) The World Health Organization (WHO)-European Organization for Research and Treatment of Cancer (EORTC) classification for cutaneous lymphomas describes three types of cutaneous lymphomas that express CD56: 1) subcutaneous panniculitis-like T-cell lymphoma, 2) extranodal natural killer (NK)/T-cell lymphoma, nasal type, and 3) CD4+/CD56+ hematodermic neoplasm (blastic NK-cell lymphoma).\(^1\) However, the report does not mention MF with CD56 expression. Earlier in 2003, a report by the EORTC cutaneous lymphoma task force workshop described cytotoxic/natural killer cell cutaneous lymphomas and divided them into eight categories.\(^6\) One of these categories was the CD56+, cytotoxic variant of MF. This report presents a rare CD8+, CD56+ variant of MF having the cytotoxic phenotype.

**CASE REPORT**

A 40-year-old male presented with a 5-year history of multiple round erythematous to dusky, brownish scaly patches with mild pruritus (Fig. 1). The skin involvement measured about 30% of total body surface. The lesions appeared first on the buttck and thigh, and lately on the upper arm. The skin lesions did not respond to topical corticosteroid treatment, at which time, he visited our hospital. A skin biopsy was taken from the thigh. The specimen showed a prominent band-like lymphocytic infiltration in the superficial dermis with epidermotropism (Fig. 2A). The epidermotropic lymphocytes were small- to medium-sized with an irregular nuclear membrane and coarse chromatin (Fig. 2B). The immunophenotype of the cells in the epidermis and a few cells in the superficial dermis were CD3+, CD4–, CD8+, CD56+, CD30–, and CD20– (Fig. 2C, D). The majority of lymphocytes in the superficial dermis were not atypical, in contrast to the epidermotropic lymphocytes, and were positive for CD4 and CD8. The neoplastic cells were positive for beta F1 (a marker of alpha/beta T lymphocytes) and granzyme B. An Epstein-Barr virus–encoded small non-polyadenylated RNA-1 (EBER-1) signal was not detected.

Lactate dehydrogenase was elevated to 432 IU/L (range, 200 to 400 IU/L). Laboratory blood tests revealed an elevated, total cholesterol level of 235 mg/dL (range, 125 to 220 mg/mL). Complete blood cell count and other results of blood chemistry were within the normal range. The chest X-ray and positron emission tomography–computed tomography revealed no abnormal findings and there was no lymphadenopathy. The patient was diagnosed as having the stage IB, CD8+, CD56+ cytotoxic immunophenotype variant MF. He was treated with narrowband ultraviolet B therapy and his condition was stabilized.

**DISCUSSION**

Prognosis of classic MF depends on stage, and, in particular, on the type and extent of skin lesions, as well as the presence of extracutaneous disease.\(^1\) Patients with limited patch/plaque-
stage MF have a similar life expectancy to an age, sex, and race-
matched control population. However, the prognosis of MF
with the cytotoxic phenotype, especially when it express CD56,
is not well established.

To date, there are 8 cases of CD56-expressing MF reported in
the current literature, and our case is the ninth case report. The
immunohistochemical and clinical characteristics of these cases
are summarized in Tables 1 and 2. Among the nine cases, six
cases co-expressed CD8 in a majority of the neoplastic cells, one
case co-expressed CD8 in a minority of neoplastic cells, and two were
negative for CD8. One out of nine cases was positive for CD4.
Age range was broad, from 6- to 85-years-old. Eight cases were
females and our case was the only male case. Poikiloderma was
the most frequent clinical feature at the time of diagnosis. Seven
cases showed good response to the therapy while two cases, in-
cluding our case, showed limited response. None of the cases,
including our case, had an aggressive clinical course. This result
suggests that CD56+ MF is a disease with good prognosis simi-
lar to classic MF.

Fig. 1. The skin lesions in the buttocks and both thighs are ery-
thematos to dusky brown.

Fig. 2. (A) The specimen shows a prominent band-like lymphocytic infiltration with epidermotropism. (B) The epidermotropic lymphocytes
are small- to medium-sized with an irregular nuclear membrane and coarse chromatin. These cells display the cytotoxic phenotype, showing
CD8 (C) and CD56 (D) immunoreactivity.
Several reports of MF with CD8+ and/or CD56+ expression have suggested that this variant would have no prognostic difference compared with classic MF.\(^2,3,5,7-10\) Massone \(\text{et al.}\)\(^9\) analyzed 73 biopsy specimens from 68 patients with early MF and divided them into four groups based on the immunophenotype. They stated that there was no statistical difference between the survival curves of the four groups, and therefore concluded that cytotoxic phenotype does not have any prognostic significance.

In our case, with the observed immunophenotype, we considered different diagnoses including primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma, primary cutaneous gamma/delta T-cell lymphoma, and extranodal NK/T-cell lymphoma, nasal type. We were able to rule out these different diagnoses based on the following: clinical course and presentation, beta F1 positivity, and EBER-1 negativity.

In conclusion, we present a case of a cytotoxic variant of MF with a CD8+, CD56+ immunophenotype. MF with cytotoxic immunophenotype is characterized by a typical clinical presentation, histology, and course of MF. Clinical presentation and course should be a primary consideration in diagnosis. We emphasize that it is important to recognize this rare variant of MF and to distinguish it from other aggressive cutaneous lymphomas to avoid aggressive treatment.

### Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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### REFERENCES

1. Willemze R, Jaffe ES, Burg G, \textit{et al.} WHO-EORTC classification for cutaneous lymphomas. Blood 2005; 105: 3768-85.
2. Nikolaou VA, Papadavid E, Katsambas A, \textit{et al.} Clinical characteristics and course of CD8+ cytotoxic variant of mycosis fungoides: a case series of seven patients. Br J Dermatol 2009; 161: 826-30.
3. Sawada Y, Sugita K, Kabashima R, \textit{et al.} CD8+ CD56+ mycosis fungoides with an indolent clinical behaviour: case report and literature review. Acta Derm Venereol 2010; 90: 525-6.
4. Shiomi T, Monobe Y, Kuwabara C, Hayashi H, Yamamoto T, Sada-hira Y. Poikilodermatous mycosis fungoides with a CD8+ CD56+ immunophenotype: a case report and literature review. J Cutan Pa-

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**Table 1. Immunohistochemical staining results of the reported cases**

| Author                   | CD3 | CD4 | CD8 | CD56 | Granzyme B | CD30 |
|--------------------------|-----|-----|-----|------|------------|------|
| Wain \(\text{et al.}\) \(\text{case No. 1}\) | +   | −   | +   | +    | –          | –    |
| Wain \(\text{et al.}\) \(\text{case No. 2}\) | +   | −   | −   | +    | +          | –    |
| Wain \(\text{et al.}\) \(\text{case No. 3, poikiloderma}\) | +   | −   | +   | +    | –          | –    |
| Wain \(\text{et al.}\) \(\text{case No. 3, tumor}\) | +   | −   | +   | +    | +          | –    |
| Sawada \(\text{et al.}\) \(\text{case No. 2}\) | +   | −   | −   | +    | +          | –    |
| Horst \(\text{et al.}\) \(\text{case No. 1}\) | +   | +   | +/− | +    | Not performed | Not performed |
| Nikolaou \(\text{et al.}\) \(\text{case No. 2}\) | +   | −   | −   | +    | Not performed | –    |
| Klekotka \(\text{et al.}\) \(\text{case No. 3}\) | +   | −   | −   | +    | Not performed | Not performed |
| Shiomi \(\text{et al.}\) \(\text{case No. 1}\) | +   | −   | +   | +    | −          | −    |

**Table 2. Clinical characteristics of the reported case**

| Author                   | Age (yr)/Sex | Clinical pattern      | Treatment                 | Clinical course | EBER-1 |
|--------------------------|--------------|-----------------------|---------------------------|-----------------|--------|
| Wain \(\text{et al.}\) \(\text{case No. 1}\) | 45/F         | Poikiloderma          | Radiotherapy and topical steroid | Limited response | Not performed |
| Wain \(\text{et al.}\) \(\text{case No. 2}\) | 6/F          | Hypo- and hyperpigmentation | Topical steroid and nUVB | Good response | Not performed |
| Wain \(\text{et al.}\) \(\text{case No. 3}\) | 37/F         | Poikiloderma, tumor   | PUVA, excision             | Good response   | Not performed |
| Sawada \(\text{et al.}\) \(\text{case No. 2}\) | 68/F         | Poikiloderma          | nUVB, oral PUVA           | Good response   | Negative |
| Horst \(\text{et al.}\) \(\text{case No. 1}\) | 85/F         | Erythroderma          | Topical steroid            | Good response   | Not performed |
| Nikolaou \(\text{et al.}\) \(\text{case No. 2}\) | 43/F         | Poikiloderma          | PUVA                      | Good response   | Not performed |
| Klekotka \(\text{et al.}\) \(\text{case No. 3}\) | 33/F         | Erythroderma          | Topical steroid and PUVA  | Good response   | Not performed |
| Shiomi \(\text{et al.}\) \(\text{case No. 2}\) | 20/F         | Poikiloderma          | Topical steroid            | Good response   | Negative |
| Present case             | 40/M         | Erythroderma          | nUVB                      | Limited response | Negative |

F, female; nUVB, narrowband ultraviolet B; PUVA, psoralen plus ultraviolet A; M, male.
Mycosis Fungoides CD8+ CD56+

5. Wain EM, Orchard GE, Mayou S, Atherton DJ, Misch KJ, Russell-Jones R. Mycosis fungoides with a CD56+ immunophenotype. J Am Acad Dermatol 2005; 53: 158-63.

6. Santucci M, Pimpinelli N, Massi D, et al. Cytotoxic/natural killer cell cutaneous lymphomas. Report of EORTC Cutaneous Lymphoma Task Force Workshop. Cancer 2003; 97: 610-27.

7. Horst BA, Kasper R, LeBoit PE. CD4+, CD56+ mycosis fungoides: case report and review of the literature. Am J Dermatopathol 2009; 31: 74-6.

8. Klekotka PA, Faulkner-Jones B, Heffernan MP. A case of CD56+ mycosis fungoides. Arch Dermatol 2006; 142: 1370-2.

9. Massone C, Crisman G, Kerl H, Cerroni L. The prognosis of early mycosis fungoides is not influenced by phenotype and T-cell clonality. Br J Dermatol 2008; 159: 881-6.

10. Um SH, Oh CW. CD8 expression in mycosis fungoides. Korean J Dermatol 2004; 42: 1525-30.