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Case Report

Keratoacanthoma Centrifugum Marginatum with Spontaneous Regression and Its Possible Differential Diagnosis

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Keywords
Keratoacanthoma centrifugum marginatum · Spontaneous regression · Cutaneous T-cell lymphoma · Tumor-infiltrating lymphocytes

Abstract
Keratoacanthoma centrifugum marignatum (KCM) is a rare variant of keratoacanthoma, which is characterized by the dense infiltration of inflammatory cells throughout the dermis, especially around the keratinocytic islands. Therefore, it is sometimes difficult to differentiate between KCM and cutaneous T-cell lymphomas. In this report, we describe a case of KCM with spontaneous regression that showed dense infiltration of CD3+CD8+ T cells. Our present case suggested the importance of investigating tumor-infiltrating lymphocytes to avoid the misdiagnosis of KCM as cutaneous T-cell lymphoma.

Introduction

Keratoacanthoma centrifugum marignatum (KCM) is a rare variant of keratoacanthoma (KA) first described by Miedzinski and Kozakiewicz [1]. Unlike conventional KA, cases of KCM are rarely reported [1–4]. Since KCM shows dense infiltration of inflammatory cells [2–4], it is

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sometimes difficult to differentiate KCM into cutaneous T-cell lymphomas. In this report, we describe a case of KCM with spontaneous regression that showed dense infiltration of CD3+CD8+ T cells.

Case Presentation

A 26-year-old Japanese female visited our outpatient clinic with a 1-month history of an asymptomatic nodule on the upper arm. At her initial visit, physical examination revealed a red nodule with a central ulceration, 50 × 50 mm in size, on the upper arm (Fig. 1a). A biopsy specimen showed islands of keratinocytes with squamous pearls, pseudoepitheliomatous hyperplasia, and dense infiltration of inflammatory cells throughout the dermis (Fig. 1b). These keratinocytic islands were composed of well-differentiated squamous epithelium with a mild degree of pleomorphism, individual cell keratinization, and keratin pearls (Fig. 1c). In addition, immunohistochemical staining revealed that these infiltrating cells were mainly composed of CD3+ T cells (Fig. 1d), which were also positive for CD8 (Fig. 1e) and were mixed with CD4+ cells, CD20+ cells, and CD79a+ cells. CD30+ cells (Fig. 1f) were merely detected at the T-cell area. Keratinocytic tumor cells were positive for PD-L1 (Fig. 2a), which were surrounded by granulysin-bearing cells (Fig. 2b) and TIA1-bearing cells (Fig. 2c). From the above findings, our first diagnosis was KCM, well-differentiated cutaneous squamous cell carcinoma, or cutaneous T-cell lymphoma.

Surprisingly, during our screening period, her nodule rapidly regressed with hyperkeratosis, central depression and prominent erythema around the tumor (Fig. 3a). We excised the tumor with a 5-mm margin. Histological findings of the resected tumor showed well-differentiated squamous epithelium surrounded by dense infiltration of neutrophils, plasma cells, and lymphocytes (Fig. 3b, c). Moreover, assessment of T-cell receptor (TCR) gene rearrangement by southern blot analysis confirmed the lack of monoclonality in the TCR chain. From the above findings, our final diagnosis was KCM with spontaneous regression. One year after resection, there was no evidence of tumor recurrence.

Discussion

Unlike conventional KA, KCM is not characterized by spontaneous regression [2–4]. Although only 1 case of KCM has been reported as KCM with spontaneous regression [2], dense infiltration of inflammatory cells was observed in the lesional areas in all reported cases [2–4]. Since Kambayashi et al. [5] reported the characteristic profiles of tumor-infiltrating lymphocytes (TILs) that could be correlated with the spontaneous regression of conventional KA, we hypothesized that the profiles of TILs might explain, at least in part, the pathogenesis of KCM.

In our present case, immunohistochemical staining revealed TILs that were mainly composed of CD3+CD8+ T cells bearing cytotoxic molecules such as granulysin and TIA1, suggesting the preparation for an antitumor immune response in KCM. Unlike conventional KA, KCM might express the immune checkpoints to suppress the antitumor immune responses at the tumor site, and immune suppression might be abrogated by other immunological events (e.g., infection, tumor progression). Indeed, in our present case, about 30% of the keratinocytic tumor cells express PD-L1, suggesting that antitumor immune response was suppressed at the tumor site. To test this hypothesis, further cases are needed.

Since a dense infiltration of TILs around the islands of keratinocytes is characteristic in KCM [1–4], ruling out cutaneous T-cell lymphoma, especially cutaneous CD30+ lymphoproliferative disorders, is important for the diagnosis of KCM. Indeed, in our case the tumor mass spontaneously regressed just as cutaneous CD30+ lymphoproliferative disorders [6, 7]. Therefore, we assessed the TCR gene rearrangement by southern blot analysis, which showed the lack of monoclonality in the TCR chain. In addition, immunohistochemical staining for CD30 revealed that most TILs did not express CD30. Our present case suggests the importance of investigating TILs to avoid a misdiagnosis of KCM as cutaneous T-cell lymphoma.

Statement of Ethics

The patient gave written informed consent.

Disclosure Statement

The authors have no conflicting interests to declare.

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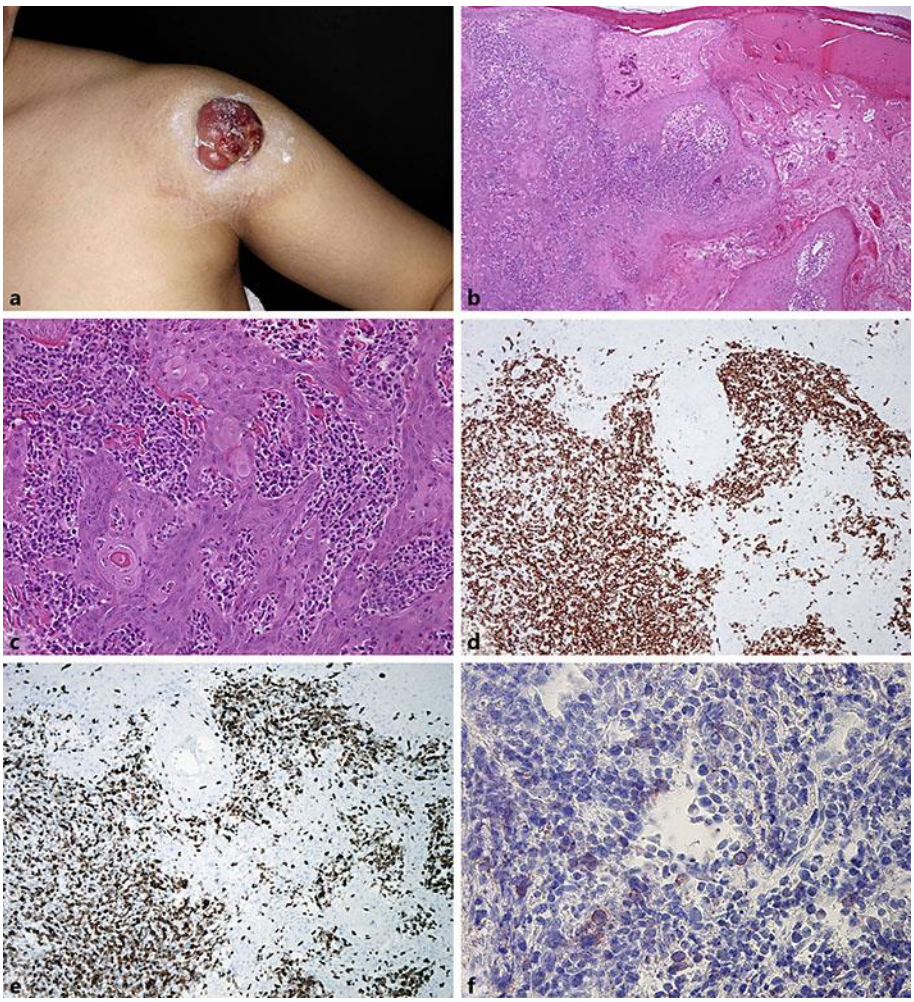

Fig. 1. A red nodule with central ulceration on the upper arm (**a**). Islands of keratinocytes with squamous pearls, pseudoepitheliomatous hyperplasia, and dense infiltration of inflammatory cells throughout the dermis (**b**). Keratinocytic islands composed of well-differentiated squamous epithelium with a mild degree of pleomorphism, individual cell keratinization, and keratin pearls (**c**). Paraffin-embedded samples were deparaffinized and stained with anti-CD3Abs (**d**), anti-CD8 Abs (**e**), and anti-CD30 Abs (**f**). The sections were developed with Liquid Permanent Red.

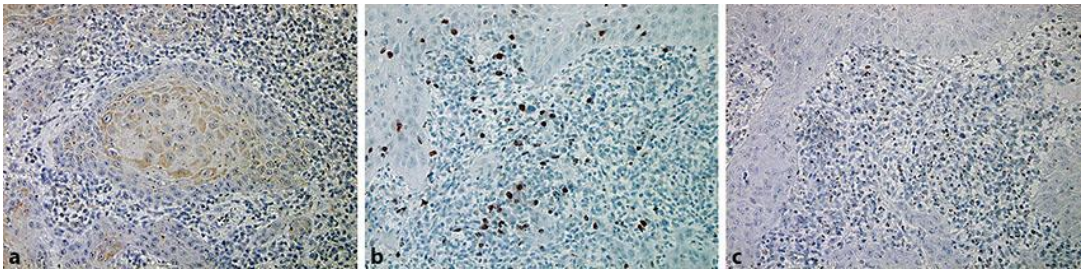

Fig. 2. Paraffin-embedded samples were deparaffinized and stained with anti-PD-L1 Abs (**a**), anti-granulysin Abs (**b**), and anti-TIA-1 Abs (**c**). The sections were developed with Liquid Permanent Red.

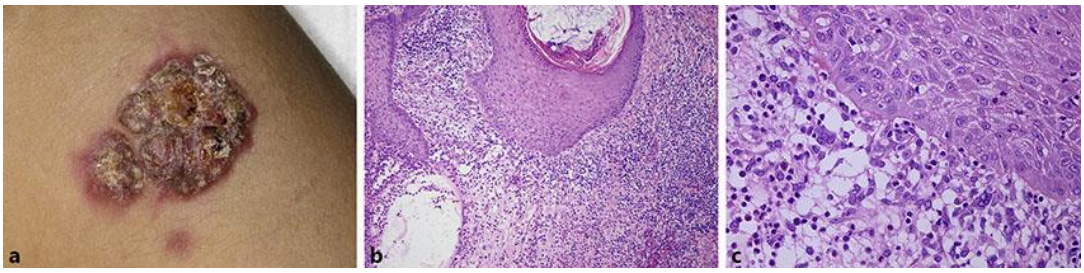

Fig. 3. A nodule with hyperkeratosis, central depression, and prominent erythema around the tumor (**a**). A well-differentiated squamous epithelium surrounded by dense infiltration of neutrophils, plasma cells, and lymphocytes (**b** low magnification; **c** high magnification).