Keratoacanthoma centrifugum marginatum

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Abstract

Keratoacanthoma centrifugum marginatum (KCM) is an uncommon variant of keratoacanthoma. Keratoacanthoma centrifugum marginatums are most commonly seen on sun-exposed surfaces and present with progressive peripheral expansion and raised, hyperkeratotic borders. Central clearing with atrophy and lack of spontaneous clearance are other key clinical characteristics. The majority of cases are benign with a low risk of metastasis. The size of such growths is variable with reported cases ranging from 5.0cm×5.0cm to as large as 20.0cm×14.0cm. Treatment options include surgical excision, oral retinoids, and intralesional chemotherapeutics such as methotrexate or bleomycin. We herein present a case of KCM manifesting as an exophytic, crateriform plaque in a 61-year-old man.

Keywords: keratoacanthoma centrifugum marginatum, oncology

Introduction

Keratoacanthomas (KAs) are low-grade neoplasms that originate from the pilosebaceous unit with low risk of metastasis [1]. Risk factors for its development include immunosuppression, radiation, and trauma. These eruptive tumors are typically solitary in nature and range from one-to-two cm in diameter [2]. However, variants of KAs, such as keratoacanthoma centrifugum marginatum (KCM) and giant KAs, can become much larger spanning up to 20cm [3]. These lesions have similar risk factors as their less expansive KA counterparts. Because of their rapid proliferation and size, KCMs are often locally destructive and disfiguring. However, like their smaller KA counterparts, KCMs have low risk for metastasis [4]. Key clinical characteristics include progressive peripheral expansion and raised, hyperkeratotic borders with central clearing and atrophy. Spontaneous regression in these neoplasms is rarely seen. In addition, KCMs are typically larger than another KA variant, the giant KA [4]. Once diagnosed, surgical excision is the treatment of choice. We report herein a patient with a large KCM along with a review of the literature.

Case Synopsis

A 61-year-old man presented with a rapidly enlarging plaque on his left forearm. He reported that it began as a "quarter-sized" lesion 1.5 years prior. It had remained stable in size for one year before rapidly expanding over the subsequent six months. Prior to being evaluated in our clinic, the patient was seen by another clinician and a skin biopsy showed pseudoepitheliomatous hyperplasia concerning for a fungal infection. However, the ensuing fungal culture was negative and empiric therapy with itraconazole showed minimal improvement. Skin examination revealed an exophytic, crateriform plaque with prominent, elevated borders measuring 14.0cm×9.5cm on the left forearm (**Figure 1**).

Biopsies revealed an endophytic, focally crateriform squamous proliferation comprised of keratinocytes with glassy, eosinophilic cytoplasm with underlying lymphoplasmacytic inflammation (**Figure 2**). Repeat bacterial, fungal, and atypical mycobacterial cultures were negative. After discussion of treatment options,

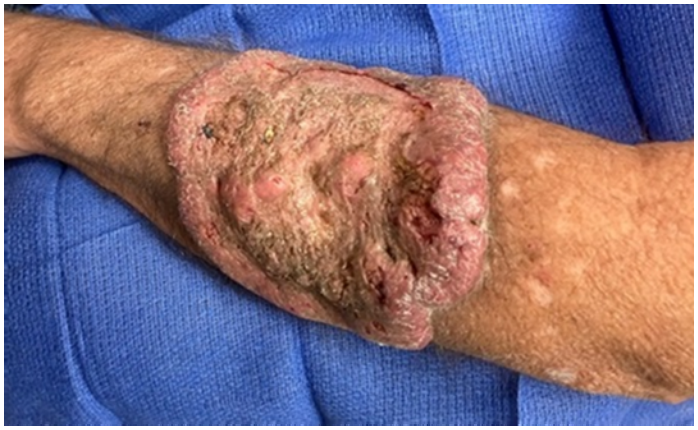

Figure 1. *Keratoacanthoma centrifugum marginatum of the left forearm measuring 14.0cm×9.5 cm with characteristic raised, hyperkeratotic borders and central atrophy.*

surgical excision was performed with clear margins and the defect was repaired with skin grafting. The combination of histopathologic findings and distinctive clinical appearance confirmed the diagnosis of keratoacanthoma centrifugum marginatum.

Case Discussion

Keratoacanthoma centrifugum marginatum was first reported in the literature in 1962 by Miedzinski and Kozakiewsz [5]. However, Belisario is credited for describing KCM as a separate entity in 1965. In the cases described by Belisario, the largest lesion measured up to 7cm in diameter with most resolving spontaneously within 12 months [6]. However, more recent case reports have described lesions that enlarge progressively over years without involution [3,4]. Risk factors for its development mirror those of typical KAs and squamous cell carcinomas (SCC) which include UV irradiation, smoking, other chemical carcinogens, and trauma [3]. Clinically, KCM is known for its progressive peripheral growth with raised, keratotic papules and central clearing with atrophy. In addition to its tendency to rapidly expand, a key differentiating characteristic between KA and KCM is that the latter rarely undergoes spontaneous regression [3,4]. Histologically, these neoplasms commonly display pseudoepitheliomatous hyperplasia with elongation of the rete ridges and a nonspecific inflammatory infiltrate containing lymphocytes, eosinophils, and neutrophils [7].

Owing to its rarity and shared characteristics with other cutaneous lesions, KCM is a diagnostic challenge. The differential diagnosis often includes deep fungal infections, atypical mycobacterial infections, and botryomycosis, among others. The broad differential diagnosis requires clinicians to have a high index of suspicion for the diagnosis of KCM. In cases of diagnostic uncertainty or recalcitrance to medical therapy, serial biopsies are often needed to establish the diagnosis [8,12]. Classic histologic findings in the correct clinical setting, as mentioned above, help in arri ving at a diagnosis of KCM. In some cases, microbial stains with periodic acid-Schiff (PAS), Gram, acid-fast bacillus (AFB), and Fite stains can assist in the workup and exclude microorganisms as the underlying etiology.

Solitary KCMs most commonly present on sun-exposed surfaces of the head and neck as well as upper and lower extremities [4,7-10]. The sizes of these lesions are variable, with some reports describing marginatum-type lesions as small as 5.0cm×5.0 cm to as large as 20.0cm×14.0cm [9,10]. Given such variability, size alone should not be relied upon as a diagnostic criterion. There have been reports of multiple KCMs in the same patient in which lesions are smaller in size, ranging from 2.0-8.0cm in diameter [11-13]. Moreover, this is typically a disease of adults with only one documented

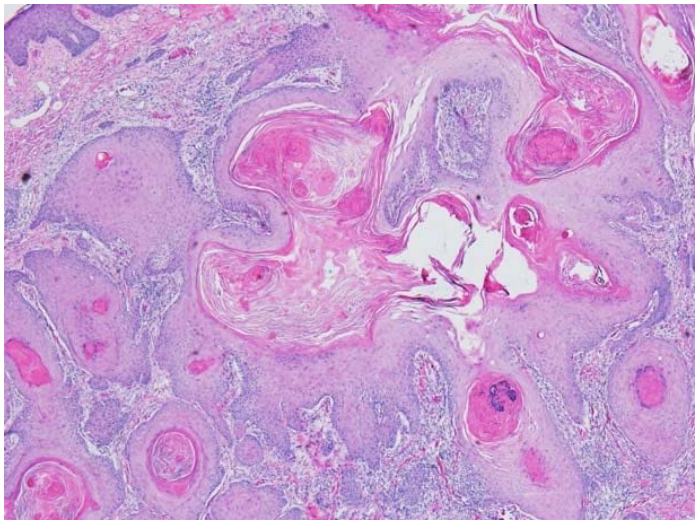

Figure 2. *View of an endophytic, focally crateriform squamous proliferation comprised of keratinocytes with glassy, eosinophilic cytoplasm with underlying lymphoplasmacytic inflammation. H&E, 10×.*

pediatric case describing multiple KCMs on the lower extremities [14].

Clinical presentation of multiple KA-like lesions requires consideration of different KA-related syndromes, including Muir-Torre syndrome (MTS), Grzybowski-type KAs, and Ferguson-Smith type KAs. In MTS, multiple keratoacanthomas and sebaceous adenomas are present, typically appearing as nodular lesions on the head, scalp, and eyelids [15]. However, spontaneous involution of the keratoacanthomas is commonly seen in MTS, often within 6 months. The eruptive keratoacanthomas of Grzybowski are also defined by spontaneous resolution with resultant atrophic scars. These can present with hundreds to thousands of smaller papular lesions [16]. Ferguson-Smith type KAs can also include multiple eruptive KA-like lesions, including KCMs. This keratoacanthoma-related syndrome typically begins in adolescence with keratoacanthomas appearing acutely followed by involution and reappearance of lesions over multiple years [17].

The gold standard of therapy for standard KAs is surgical excision, resulting in the lowest rates of recurrence [1]. However, given the size of most KCMs, surgical intervention may not be feasible. In such situations, medical therapy is often preferred. Oral retinoids have been reported to have variable success in the management of KCMs, ranging from complete to partial clearance [4,12]. Intralesional methotrexate and bleomycin have also shown utility in the management of these lesions [11,18]. Because of the lack of standardized treatment protocols for KCMs, a patient-centered approach with close monitoring of therapeutic response is needed.

Conclusion

Keratoacanthoma centrifugum marginatum is a locally destructive neoplasm with characteristic peripheral growth with central clearing and atrophy. Multiple pharmacologic options can be implemented in situations where tumor burden does not allow for surgical excision. This case demonstrates a striking presentation of a KCM while highlighting the need for serial biopsies in cases with diagnostic uncertainty and unresponsiveness to other therapies.

Potential conflicts of interest

The authors declare no conflicts of interests

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