CASE 21

Patient: A 82-year-old Thai woman from Bangkok

Chief complaint: Expanding lesion on left leg for 2 months

Present illness: The patient noticed asymptomatic faint brownish to erythematous plaque on her left leg. The surface contained multiple keratotic punctum arranged closely set together. The rash gradually expanded over time.

Past history: Diabetes, Hypertension, Dyslipidemia

Family history: nill

Physical examination: unremarkable

Dermatological examination (Figure 21.1-2): Solitary well-defined erythematous annular plaque with indurated border and multiple keratotic punctum

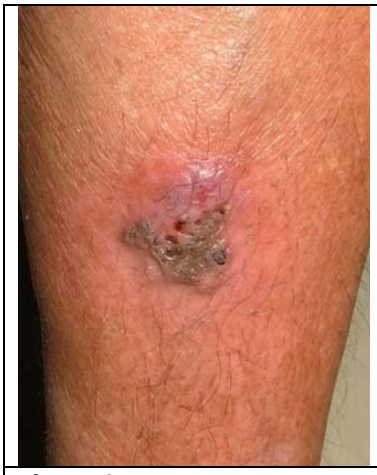

Figure 21.1

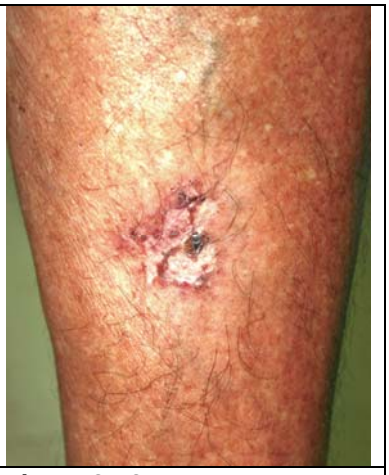

Figure 21.2

Histopathology (S09-19185) (Figure 21.3):

- Deep invasion of flattened epidermis with a hint of keratotic crater
- Scar in the surrounding dermis

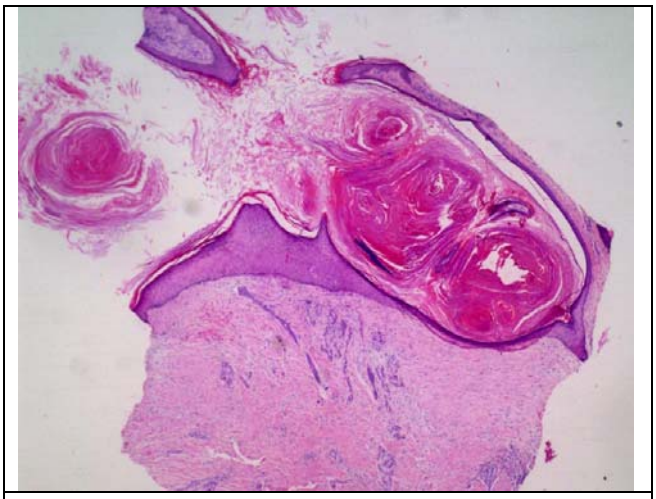

Figure 21.3, H&E 20x

Diagnosis: Keratoacanthoma centrifugum marginatum

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Discussion:

Keratoacanthoma (KA) is a unique epidermal tumor characterized by rapid, abundant growth and a spontaneous resolution, with the classic presentation in middle-aged, light-skinned individuals in hair bearing, sun-exposed area. The KA may present clinically as a solitary lesion or multiple lesions, in a sporadic fashion or in an inherited syndrome, or in association with inflammatory disease. Some KA may metastasize, and there is debate over the relationship

of KA to squamous cell carcinoma and whether to classify KA as benign or malignant. Solitary KA usually develops in sun-exposed areas, primarily on the face (lower lip, cheek, nose, eyelid), neck, and hands, and undergo three distinct stages[1]. The first stage is a rapid proliferative phase, in which the tumor increases in size to reach 10–25 mm in diameter in 6–8 weeks. Histopathological finding demonstrates horned-filled invagination of the epidermis protruding into the dermis. The strands are poorly demarcated from the surrounding stoma in some areas and may contain cell with nuclear atypia. The second stage is the mature KA, where the lesion stops growing, maintains its crater form, and appears as a bud, dome, or berry-shaped structure containing hair, a central keratin plug, and signs of fragmentation. Histology of fully developed lesion shows in its center a large, haphazardly shaped crater filled with keratin. Irregular epidermal proliferation extends both upward into the crater and downward from the base of the crater. Less nuclear atypia is seen than that of the initial stage. Finally, in the involution stage, 50% of KA undergoes spontaneous resolution in 4–6 weeks, with expulsion of the keratin plug and resorption of the tumoral mass, leaving an atrophic and hypopigmented scar. After proliferation has ceased, cells at crater base undergo keratinization. There may be shrunken, eosinophilic cells among the tumor cells located in the stroma, suggesting cell degeneration. Gradually, the crater flattens and disappears.

Keratoacanthoma centrifugum marginatum (KCM) is an extremely rare variant of KA since it was first described in 1962. It is usually seen as a solitary lesion, most frequently appearing on the legs. In contrast with KA, KCM extends horizontally across the surface, reaching a size of 20 cm or more and shows no tendency towards spontaneous resolution [2-3]. Instead, there is persistent peripheral extension

with a raised border, and atrophy in the center of the lesion. Histologic study is the same as in KA. The clinical finding of multiple tiny closely set dome shaped cratered papules with central keratin plug (Figure 21.1) together with histologic finding typical of KA suggested the diagnosis of KCM in this patient (Figure 21.3).

The cause of tumor is unknown. Some subtypes of multiple KA are inherited genitically. Some authors have demonstrated human papilloma virus infection in KA[4-6]. Most KAs are found on sun-exposed skin leading to the postulation of reaction from ultraviolet radiation. Tar has been implicated as aggravating KA[7].Trauma may also be a predisposing factor[8]. In additions, there is a subset of KA seen in HIV-positive patients [9-10]. However, no aggravating factor was found in our patient.

Numerous treatment modalities have been described for KA, including surgical excision, Moh's micrographic surgery[11], intralesional methotrexate[12], topical and intraleional bleomycin[13], topical and intralesional 5-fluorourcil[14], topical imiquimod[15], oral isotretinoin[16] and etretinate[17]. A recent literature reported a case of refractory, locally aggressive KCM of scalp having strong epidermal growth factor receptors (EGFRs) expression and demonstrating excellent response to erlotinib[18]. Although KCM typically presents with persistent peripheral growth, the characteristic feature in our patient is gradual tumor growth in 2 months and size stabilization at presentation. Histology was compatible with KA in the involution stage. Hence, there was tendency towards a self-remitted disease. Conservative approach was adopted as a treatment option, the patient was on close followed up. The tumor was photographed every 2-3 weeks. The patient was fully advised about the natural history of the disease and compliance with the follow-up schedule. Finally the tumor

spontaneously regressed and disappeared within 5 months. (Figure 21.2)

This case illustrates an exceptional case of keratoacanthoma centrifugum marginatum with spontaneous remission. The key point in the history is a lesion diminishing in size or at least one that has stopped enlarging. Histology of involuting tumor gave us confident to merely just wait and see with close observation. However in general, therapeutic intervention is preferable because there are no reliable criteria to differentiate with confidence between KA and SCC.

References

1. Karaa A, Khachemoune A. Keratoacanthoma: a tumor in search of a classification. Int J Dermatol 2007;46:671-8.
2. Miedzinski F, Kozakiewicz J. [Keratoacanthoma centrifugum--a special variety of keratoacanthoma.]. Hautarzt 1962;13:348-52.
3. Attili S, Attili VR. Keratoacanthoma centrifugum marginatum arising in vitiligo: a case report. Dermatol Online J 2006;12:18.
4. Forslund O, DeAngelis PM, Beigi M, Schjolberg AR, Clausen OP. Identification of human papillomavirus in keratoacanthomas. J Cutan Pathol 2003;30:423-9.
5. Magee KL, Rapini RP, Duvic M, Adler-Storthz K. Human papillomavirus associated with keratoacanthoma. Arch Dermatol 1989;125:1587-9.
6. Trowell HE, Dyall-Smith ML, Dyall-Smith DJ. Human papillomavirus associated with keratoacanthomas in Australian patients. Arch Dermatol 1990;126:1654.
7. Letzel S, Drexler H. Occupationally related tumors in tar refinery workers. J Am Acad Dermatol 1998;39:712-20.
8. Tamir G, Morgenstern S, Ben-Amitay D, Okon E, Hauben DJ. Synchronous appearance of keratoacanthomas in burn scar and skin graft donor site shortly after injury. J Am Acad Dermatol 1999;40:870-1.
9. Payne D, Newman C, Tyring S. Human papillomavirus DNA in nonanogenital keratoacanthoma and squamous cell carcinoma of patients with HIV infection. J Am Acad Dermatol 1995;33:1047-9.
10. Warschaw KE, Eble JN, Hood AF, Wolverton SE, Halling KC. The Muir-Torre syndrome in a black patient with AIDS: histopathology and molecular genetic studies. J Cutan Pathol 1997;24:511-8.

11. Benest L, Kaplan RP, Salit R, Moy R. Keratoacanthoma centrifugum marginatum of the lower extremity treated with Mohs micrographic surgery. J Am Acad Dermatol 1994;31:501-2.
12. Cohen PR, Schulze KE, Teller CF, Nelson BR. Intralesional methotrexate for keratoacanthoma of the nose. Skinmed 2005;4:393-5.
13. de la Torre C, Losada A, Cruces MJ. Keratoacanthoma centrifugum marginatum: treatment with intralesional bleomycin. J Am Acad Dermatol 1997;37:1010-1.
14. Gray RJ, Meland NB. Topical 5-fluorouracil as primary therapy for keratoacanthoma. Ann Plast Surg 2000;44:82-5.
15. Aroni K, Mastoraki A, Agrogiannis G, Ioannidis E, Patsouris E. Successful treatment of keratoacanthoma centrifugum marginatum with local application of imiquimod cream. Int J Dermatol 2007;46:1321-2.
16. Schaller M, Korting HC, Wolff H, Schirren CG, Burgdorf W. Multiple keratoacanthomas, giant keratoacanthoma and keratoacanthoma centrifugum marginatum: development in a single patient and treatment with oral isotretinoin. Acta Derm Venereol 1996;76:40-2.
17. Ogasawara Y, Kinoshita E, Ishida T, Hamamoto Y, Fujiyama J, Muto M. A case of multiple keratoacanthoma centrifugum marginatum: response to oral etretinate. J Am Acad Dermatol 2003;48:282-5.
18. Bulj TK, Krunic AL, Cetner AS, Villano JL. Refractory aggressive keratoacanthoma centrifugum marginatum of the scalp controlled with the epidermal growth factor receptor inhibitor erlotinib. Br J Dermatol 2010.