Multiple Keratoacanthoma Centrifugum Marginatum in a Patient with Primary Myelofibrosis: A Case Report with Dermoscopic Findings

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Keratoacanthoma centrifugum marginatum (KCM) is a rare variant of keratoacanthoma (KA), with fewer than 60 cases reported in the English literature to date. Unlike classical KA, KCM is characterized by a chronic, locally destructive course, progressive peripheral growth with central atrophy and no tendency for spontaneous involution. Lesions may reach up to 20–30 cm in diameter (1–10). KCM usually develops on sun-exposed skin, mainly in white males in the 5th or 6th decade of life. The aetiology remains unknown, although environmental factors, including ultraviolet light, mineral oils and chemical carcinogens as well as trauma, infectious factors and immunosuppression, are suggested to contribute to the development of the lesions (2, 3). Due to its rarity, KCM often poses a diagnostic challenge, with squamous cell carcinoma (SCC), mycobacterial and fungal infections, hypertrophic lupus erythematosus and halogenoderma constituting main differential diagnoses (4, 5).

We report here a patient with multiple KCMs who was diagnosed with advanced primary myelofibrosis (PMF). We also discuss the dermoscopic findings in this entity and review the cases of multiple KCMs reported to date.

CASE REPORT

A 65-year-old man presented to the Department of Dermatology with a 6-month history of multiple asymptomatic nodules and tumours with a tendency for centrifugal growth, involving the face, neck and upper extremities. The first nodules that developed in the occipital area were initially misdiagnosed as viral warts and treated with monochloroacetic acid and cryosurgery. This treatment led to rapid deterioration and peripheral spreading of the lesions. The patient associated development of tumours on the face with minor injuries during shaving. However, nodules on the upper extremities developed with no apparent trigger factor. The patient denied having any constitutional symptoms and his family history was negative for similar lesions, other dermatological conditions and malignancies.

On admission, the patient presented with multiple nodules and tumours on the face, neck, occipital area and upper extremities. On the face, there were 3 exophytic tumours with a crateriform depression in the centre filled with keratin masses located above the upper lip, under the lower lip and on the left cheek (Fig. 1a). In addition, several smaller pink nodules were observed on the forehead and cheeks. Lesions on the neck and in the occipital area had annular morphology, hyperkeratotic borders, and displayed central yellowish scales, multiple white circles surrounding keratotic plugs, several ill-defined blue-grey round or oval areas and blood spots (Fig. 1e). As the diagnosis of skin lesions remained unclear, several incisional and excisional biopsies were taken from lesions on the face and upper extremities. Histopathology showed pseudoepitheliomatous hyperplasia, preserved maturation with minimal atypia, single mitotic figures and irregular craters filled with keratin. Pronounced reactive fibrosis and dense chronic lymphohistiocytic infiltrations were present in the dermis (Fig. 1f). Based on the histological findings and clinical presentation, the diagnosis of multiple KCMs was made.

Laboratory investigations revealed macrocytic anaemia (haemoglobin (Hgb) 10.1 g/dl and mean corpuscular volume 103.4 fl) with the presence of blasts (16%) on manual blood smear, elevated lactate dehydrogenase in the serum (645 U/l; reference: 120–246 U/l) and an accelerated erythrocyte sedimentation rate 38 mm/h. HIV serology was negative. Abdominal ultrasound revealed splenomegaly. Whole-body computed tomography displayed no evidence of internal malignancy. As myeloproliferative neoplasm (MPN) was suspected, further haematological work-up was performed: JAK2 V617F mutation was detected, while BCR-ABL testing was negative. Biopsy of the bone marrow showed megakaryocyte atypia with dense clustering and grade 3 reticulin and collagen fibrosis, which, combined with other test results, was consistent with the diagnosis of PMF of intermediate-2 risk category according to Dynamic International Prognostic Scoring System.

A pronounced progression with development of multiple new nodules and peripheral spreading of existing lesions was observed when the patient showed for reassessment after 4 weeks (Fig. 1g–i). Peripheral blood count also deteriorated at that time and revealed anaemia (red blood cell count 2.83×10¹²/µl and Hgb 8.9 g/dl), leukocytosis (white blood cell count 13.98×10³/µl), thrombocytosis (platelet count 510×10³/µl) and presence of blasts (23%) including erythroblasts (4%) on manual blood smear. Treatment with acitretin at a dose of 25 mg/day (0.3 mg/kg) was initiated to control skin lesions. This treatment resulted in improvement of central atrophy and no tendency for spontaneous invo-

DISCUSSION

Multiple KAs may develop sporadically or in the course of genetic syndromes including xeroderma pigmentosum, Ferguson-Smith, Muir-Torre and Witten and Zak syndromes. Multiple KCMs are extremely rare. Reviewing the literature, we have identified 10 case reports, including 7 available in full text (2–11). Characteristics of these cases are summarized in Table S1.

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Discussion

Multiple KAs may develop sporadically or in the course of genetic syndromes including xeroderma pigmentosum, Ferguson-Smith, Muir-Torre and Witten and Zak syndromes. Multiple KCMs are extremely rare. Reviewing the literature, we have identified 10 case reports, including 7 available in full text (2–11). Characteristics of these cases are summarized in Table S1.
The development of so many KCMs in a patient with an underlying haematological malignancy (PMF) might not be coincidental. Although no reports of KCM developing in a patient with MPN were found during the literature search, 2 cases of multiple KAs associated with myelodysplastic syndrome have been reported in the English literature (12, 13). The potential link to haematological disorders remains unexplained. Still, multiple KAs may be observed in immunocompromised patients. Impaired immunity might have led to the development of numerous, non-healing and rapidly spreading KCMs in the presented case. Trauma might have been an additional trigger factor, as the development and progression of the lesions on the face were associated with small cuts during shaving.

Although the dermoscopic features of KAs are well-defined and include signs of keratinization (keratin masses/scales, white structureless areas, white circles and white keratin pearls), haemorrhages (blood spots) and vascular structures (glomerular, hairpin and/or linear irregular vessels) (14), we found only 1 report of dermoscopic findings in KCM (15). Polarized dermoscopy of the active part of KCM showed the presence of yellowish-white scales, multiple greyish-white circles surrounding central whitish structures, greyish-white lines, structureless zones on a pinkish background, white and red globules, while dermoscopy of the hyperpigmented regressive part of KCM displayed dark globules, irregular pigment network, milky white areas and fine telangiectatic vessels (15). The current paper describes novel dermoscopic features of KCM, including thick arborizing vessels, comedo-like openings, keratotic plugs and blue-grey round/oval areas. It is worth mentioning that the histology of KCM differs from that of classical KA. KCM frequently poses a diagnostic challenge and may be easily misdiagnosed, both clinically and histopathologically. In the future, dermoscopy might prove to be a valuable additional tool in the differential diagnosis of KCM.

Treatment of KCM remains challenging. Due to large size and anatomical location, surgical excision is not always possible. Other therapeutic modalities include topical application of imiquimod or 5-fluorouracil, radiotherapy or systemic treatment with methotrexate or retinoids (1–11). In the cases of multiple KCMs reported to date, retinoids or methotrexate were most common treatments used (Table SI 1).

In summary, to the best of our knowledge, this is the first report of a patient with multiple KCMs associated with PMF. In addition, we describe new dermoscopic features of KCM, which might pose a valuable diagnostic clue in the differential diagnosis of this challenging entity.

The authors have no conflicts of interest to declare.

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