Case report

Giant KeratoacanthomaCentrifugumMarginatum: A rare case report with note on literature review

Abstract

Introduction; Keratoacanthoma Centrifugum Marginatum (KCM) is a rare variant of keratoacanthoma that closely mimics squamous cell carcinoma (SCC), posing significant diagnostic challenges.

Case Report: A 45-year-old male presented with a progressively enlarging hyperkeratotic lesion on the right cheek. Histopathological examination revealed pseudocarcinomatous hyperplasia with a central keratin plug, and MRI confirmed the lesion was confined to subcutaneous tissues without deeper invasion. Surgical excision was advised.

Conclusion: This case highlights the importance of distinguishing KCM from SCC to prevent overtreatment. Surgical excision remains the preferred treatment, complemented by regular postoperative follow-ups for recurrence monitoring.

Keywords: Keratoacanthoma Centrifugum Marginatum, pseudocarcinomatous hyperplasia, squamous cell carcinoma mimic, surgical excision.

Introduction:

Keratoacanthoma Marginatum Centrifugum (KMC) is an uncommon variant of keratoacanthoma characterized by a progressively enlarging lesion that maintains a distinct rolled border and central healing [12]. The lesion's clinical and histopathological resemblance to squamous cell carcinoma presents significant diagnostic challenges. This report aims to describe a typical presentation of KMC, underscore its distinctive features, and discuss the therapeutic approaches.

Case description

A 45-year-old male, with no significant medical history, presented with a notable cutaneous lesion on his right cheek, extending to the ear lobe and post-auricular area. The patient reported that the lesion had appeared several months prior and had gradually increased in size. The lesion was hyperpigmented, hyperkeratotic, and papillomatous, forming a cone-shaped verrucous plaque with an erythematous, indurated, crateriform base (Fig.1, 2). It was hard on palpation, measuring 5-6 cm in height and 6-7 cm in width, with sporadic hair growth within the lesion. on dermatoscopic examination a central yellowish, whitish, or brownish structure indicating hyperkeratosis with linear irregular and arborizing vessels at the lesion's edge.Areas of hemorrhage or crust within the lesion. White circles or structures reflecting adnexal orifices or keratinization processes.Pinkish background is showing inflammation or tumor stroma.The lipping of margins, especially in combination with central keratinization, is a hallmark of keratoacanthoma (fig.3).

Fig.1, 2: Showing front and lateral view of Keratocanthoma centrifugum marginatum with multiple cutaneous horn like growth with epidermal lipping at base.

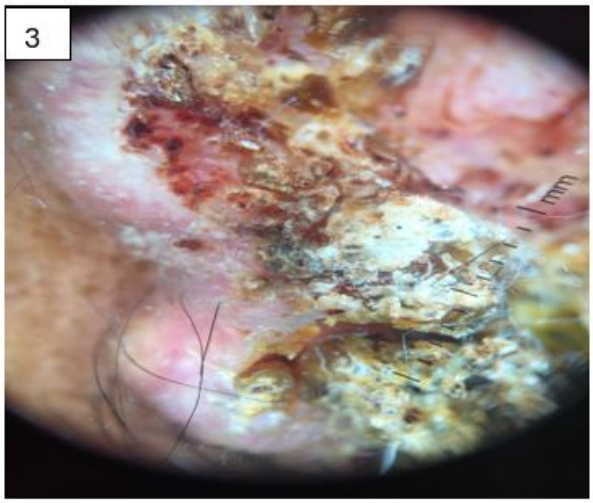
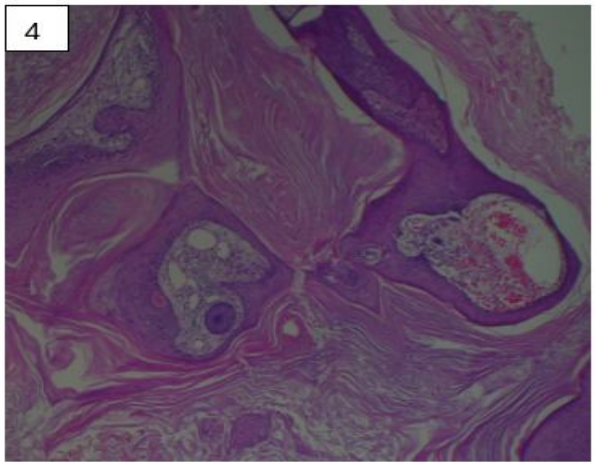


Fig. 3. Dermatoscopic view of Keratoacanthoma mimics SCC.



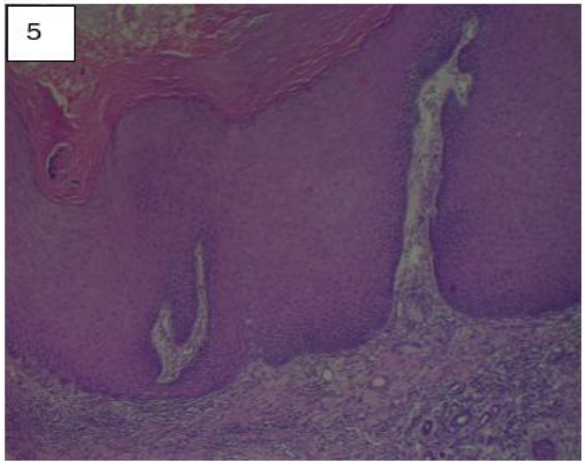


Fig.4,5 :Hyperplasia of follicular infundibula,peripheral overhanging lips,large central plug,papillomatosis, and orthohyperkeratosis,parakeratosis and interface dermatitis.

Biopsy (fig. 4,5) shows hyperplasia of contiguous follicular infundibula resulting in pseudocarcinomatous pattern of hyperplasia. At the periphery the hyperplastic epidermis forms overhanging lips. The crater thus formed by hyperplastic epithelium contains a large plug. Plugs show parakeratotic and dyskeratotic cells in lamellated pattern. Surface shows marked papillomatosis, hypergranulosis and orthohyperkeratosis with foci of parakeratosis. The dermoepidermal junction is encroached by an infiltrate of lymphocytes and shows several necrotic

keratinocytes/colloid bodies. In view of clinical features these findings are suggestive of keratoacanthoma centrifugum marginatum.

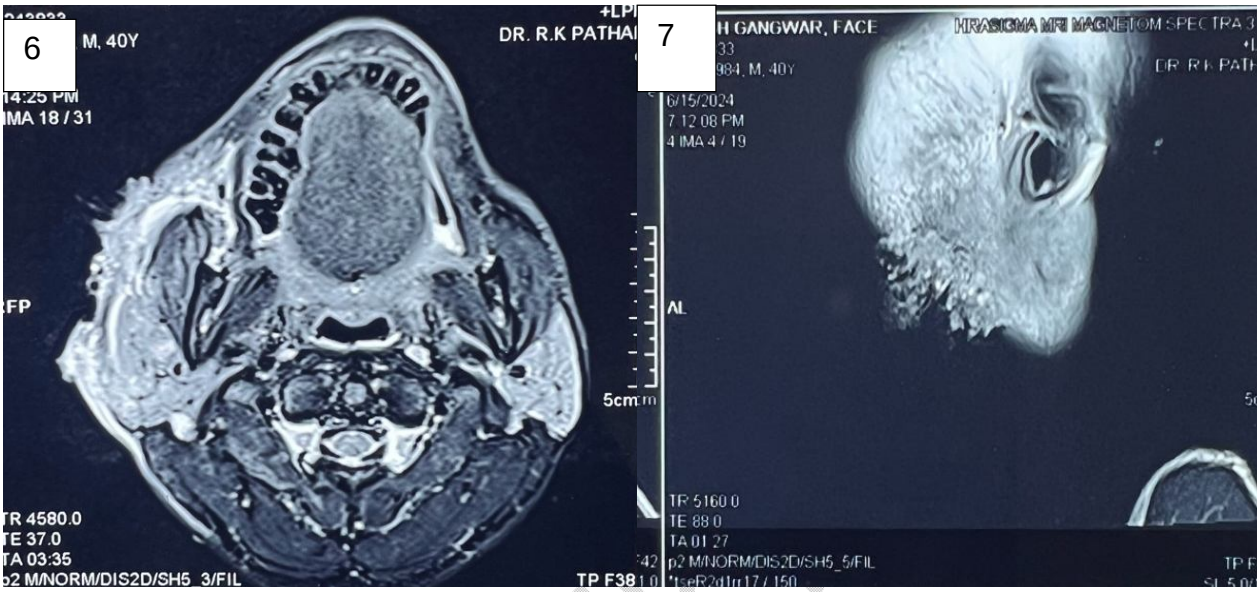


Fig.6,7: Multiplanar multiecho MR of the face was performed from neck to the base of brain which shows growth up to subcutaneous plane.

In MRI (fig.6,7) Well defined irregular thickening is seen in the skin and subcutaneous tissues anterior to the right pinna and in the masseteric region, of size 6.1 x 3.9 x 1.6 cm. It is seen in the subcutaneous tissues. It is effacing the right masseter muscle, superficial lobe of right parotid gland and right zygomatic arch, no involvement of the underlying structures seen. The lesion is hyperintense on T1W and 2W images. No invasion of adjacent structures seen.Enlarged lymph nodes are seen around right parotid gland and at level 2 and 3 on right side of neck, largest measuring about 12 x 11 mm.Rest of the facial soft tissues is normal.

Management and outcome

Given the benign yet potentially disfiguring nature of the lesion, surgical excision was considered the best approach. The patient was advised complete excision of the lesion with face reconstruction by flap by surgery (ENT and plastic surgery) side, ensuring clear margins to prevent recurrence. Postoperative recovery was uneventful, and follow-up over six months showed no signs of recurrence.

Histological examination post-excision reiterated the non-invasive nature of KMC, confirming the initial diagnosis.

Discussion:

Keratoacanthoma Centrifugum Marginatum (KCM) is an extremely rare variant of keratoacanthoma, predominantly reported in middle-aged adults. It is characterized by an enlarging plaque with a central keratin-filled crater and peripheral hyperkeratotic rolled edges. The pseudo carcinomatous hyperplasia seen in KCM often mimics squamous cell carcinoma (SCC), both clinically and histologically. However, KCM lacks the invasive nature of SCC, often confined to the epidermis and superficial dermis [1,2].Differential diagnosis primarily includes SCC, verrucous carcinoma, and other pseudoepitheliomatous hyperplasia.

Table1: Comparative analysis of KMC, SCC and Verrucous carcinoma [3,4]

Feature	KCM	Squamous Cell Carcinoma (SCC)	Verrucous Carcinoma
Clinical Appearance	Central keratin plug, rolled borders	Rapid growth, ulceration, invasive edges	Papillomatous, slow growing, locally invasive
Histopathology	Pseudo carcinomatous hyperplasia	Atypical keratinocytes invading dermis	Verrucous growth with minimal atypia
Growth Behavior	Non-invasive, peripheral expansion	Invasive	Locally invasive
Preferred Treatment	Wide local excision	Surgery, radiotherapy, chemotherapy	Surgery

Genetic basis of keratoacanthoma centrifugum marginatum

The genetic understanding of KCM remains limited due to its rarity. However, insights from related keratoacanthomas and SCC provide valuable clues about the potential molecular mechanisms involved:

TP53 mutations: The tumor suppressor gene TP53, frequently mutated in SCC and keratoacanthomas, may contribute to the abnormal proliferation of keratinocytes in KCM. UV-induced DNA damage is a likely mechanism triggering these mutations [5].

HRAS mutations: Alterations in the HRAS gene, which regulates cellular growth and differentiation, have been associated with hyperproliferative lesions and could play a similar role in KCM [6]

Epigenetic alterations: Hypermethylation of tumor suppressor genes and dysregulation of histone modifications might influence keratinocyte behavior, promoting hyperplasia characteristic of KCM [7].

Wnt signaling pathway: Aberrant activation of the Wnt/β-catenin pathway, implicated in keratoacanthomas, could also underlie the unique growth dynamics of KCM [8].

Chronic inflammation-associated genes: Genes such as COX-2 and NF-κB, activated by chronic inflammation, might contribute to the lesion's hyperproliferative and inflammatory environment [9].

These genetic and molecular insights not only enhance our understanding of KCM's pathogenesis but also open avenues for potential molecular diagnostics and targeted therapies.

Histopathological features of KCM [3,4]

Histopathological examination plays a pivotal role in differentiating KCM from malignant conditions like SCC. Key histopathological characteristics of KCM include:

Pseudo carcinomatoushyperplasia: Hyperplasia of contiguous follicular infundibula, resulting in a pattern resembling invasive carcinoma.

Crateriform architecture: Hyperplastic epidermis forms overhanging lips at the periphery, creating a crater-like structure.

Keratin plug: The crater is filled with parakeratotic and dyskeratotic cells arranged in a lamellated pattern.

Epidermal changes: Surface epithelium often exhibits marked papillomatosis, hyper granulosis, Ortho hyperkeratosis, and focal parakeratosis.

Dermo epidermaljunction: Lymphocytic infiltration is commonly observed, accompanied by necrotic keratinocytes (colloid bodies) at the junction.

Absence ofinvasion: Despite its alarming appearance, KCM typically lacks invasive features, which distinguishes it from SCC.

These features, combined with clinical presentation, confirm the diagnosis and help avoid overtreatment.

Clinical implications

Accurate differentiation of KCM from SCC is critical to avoid overtreatment. While SCC may require aggressive therapies, KCM is best managed with surgical excision. Incorporating genetic studies into diagnostic workflows could aid in distinguishing KCM from its malignant mimics. For example, identifying specific TP53 or HRAS mutations could reinforce the diagnosis of KCM.

Therapeutic and prognostic considerations

The non-invasive nature of KCM makes surgical excision the preferred treatment. Ensuring clear margins prevents recurrence while minimizing the risk of overtreatment. A margin of 6-10 mm is recommended for Squamous Cell Carcinoma (SCC), especially for high-risk lesions, while a margin of 4-6 mm is generally sufficient for Keratoacanthoma (KA) due to its low-grade behavior and limited invasiveness. This difference reflects the more aggressive nature of SCC compared to KCM. Post-operative histological confirmation is essential, particularly for atypical lesions. Regular follow-up at 1, 3, and 6 months ensures early detection of potential recurrence.

Future directions

Further research using next-generation sequencing and gene expression profiling is necessary to uncover specific genetic mutations and molecular pathways unique to KCM. Such studies could pave the way for novel diagnostics and targeted therapies, offering alternatives for patients unsuitable for surgical intervention [10].

Most cases emphasize surgical excision with clear margins as the preferred treatment. Alternative treatments like cryotherapy, intralesional methotrexate, or systemic retinoids have been attempted in limited case studies, mainly in patients unable to undergo surgery [11].

Treatment plan

The treatment plan for KCM begins with a thorough diagnostic workflow (flow chart: figure 7). Initial clinical examination identifies key lesion features such as hyperkeratotic borders, crateriform structure, and slow progression. Histopathological examination confirms the pseudo carcinomatous growth pattern, ruling out malignancy, while imaging helps assess soft tissue involvement and exclude deeper invasion.

Management involves surgical excision, which provides definitive treatment, prevents disfigurement, and confirms diagnosis postoperatively. The procedure ensures wide excision with clear margins to avoid recurrence. Post-surgical monitoring includes regular follow-ups at 1, 3, and 6 months to ensure no signs of recurrence. Histological evaluation of excised tissue further confirms the diagnosis and margin clarity.

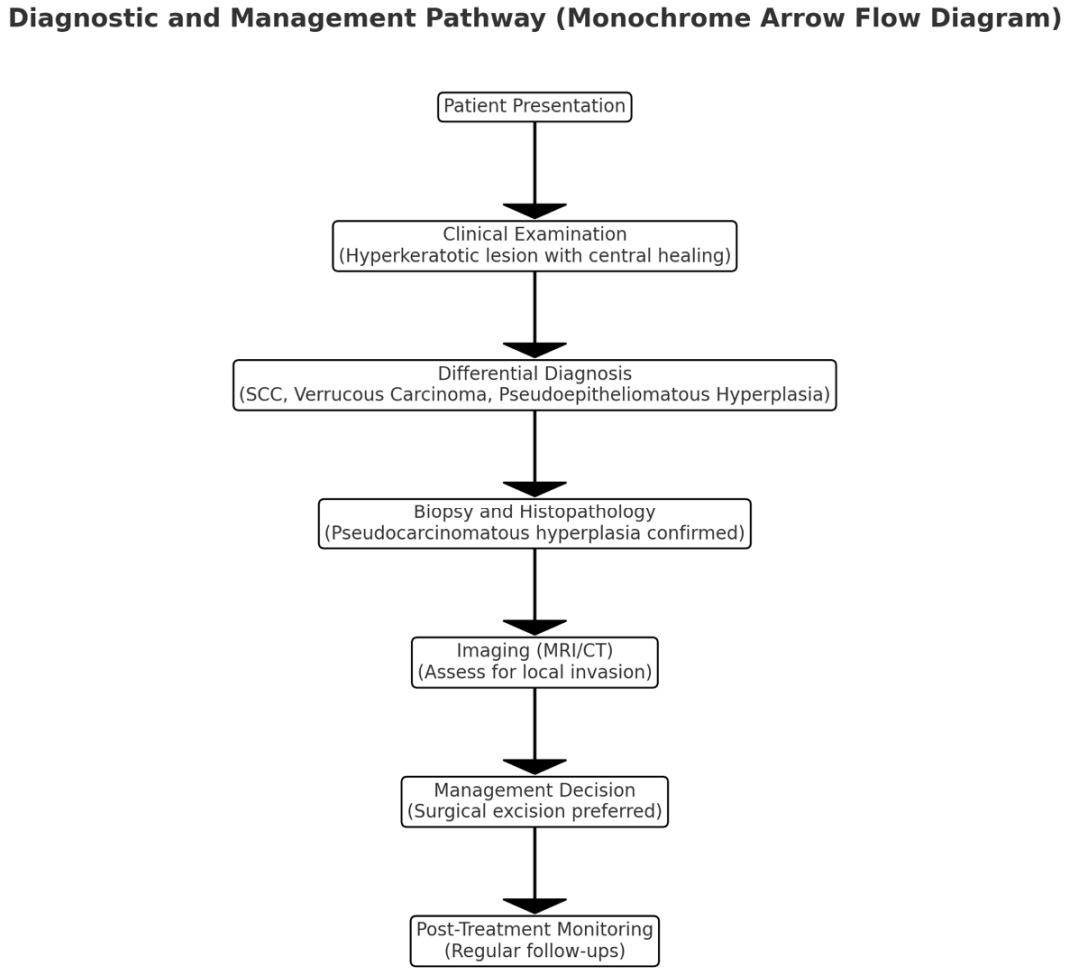


Fig.8: Management pathways of KCM

Conclusion

This case highlights the importance of distinguishing KCM from SCC to prevent overtreatment. Surgical excision remains the preferred treatment, complemented by regular postoperative follow-ups for recurrence monitoring.

Consent

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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