Case Report

"Migratory Kerato osteomyelitis" – A refractory lesion of the mandible: A pathologist's and surgeon's dilemma!!

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Abstract

A 62 year old female patient presented with a chief complaint of non healing extraction socket in the lower left back teeth region. She underwent extraction of 37 at a private clinic following which an ulceroinfiltrative lesion developed at operated side. Multiple biopsies from the lesion were inconclusive. Computed tomography revealed an osteolytic lesion radiologically simulating carcinoma or a chondrosarcoma. Because of persistent debilitating symptoms the patient underwent Wide local excision (WLE) with left segmental mandibulectomy. Frozen sections were negative for malignancy. All margins were free from malignancy. Lymph nodes dissected showed reactive morphology. Ziehl–Neelsen, Periodic acid-Schiff and Gram stain were all negative. The lesion continued to spread even after successful surgical intervention with adequate surgical margin. The patient was eventually lost because of severe cardiac arrest during her last surgical intervention for mandibular arch reconstruction. As the lesion migrated from one side of the mandible to the other, kept showing clinical features of inflammation of the bone and bone marrow simulating features of osteomyelitis and the continued presence of keratin histologically, we contemplated whether we could give a nomenclature to the lesion as that of "Migratory Kerato osteomyelitis of the oral cavity." This could be one of case of a lifetime where multiple consultations with oral and general pathologists failed to reach a conclusive diagnosis!

Keywords: Osteolytic lesion, malignant ulcer, migratory kerato osteomyelitis

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INTRODUCTION

From the time since, the specialty of pathology sets its roots in the field of dentistry a number of cases has been documented as elusive lesions ranging from proliferative verrucous leukoplakia of the oral mucosa, oral plasma cell granuloma, presence of cholesterol granuloma in odontogenic cysts, benign migratory glossitis; the list is just endless. The treatment protocols in all such cases vary from mere wait and observe policy to radical surgery involving curettage to resection of the oral tissues. Our case was an extremely aggressive osteolytic expansile lesion which originated in the angle of the mandible region crossed the mid line to reach the body of the mandible on the other side. Such was the clinical presentation and behavior of the lesion, that we found it extremely difficult to trace the histological origin of the lesion. Varied possibility of epithelial pathology, soft tissue or bony pathology, hematologic or lymphoid origin was postulated. It presented a continuous spectrum of varied histopathologic expression, though the entire picture throughout the sections gave a very innocuous appearance with an absolute contradiction to the clinical behavior of the lesion.

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CASE REPORT

A 62 year old postmenopausal female patient, a reformed tobacco chewer (Paan) for the past 25 years and had discontinued the same since the past 10 years [Figure 1]. She presented in our outpatient department with a chief complaint of nonhealing extraction socket in the lower left back teeth region with no other known comorbidities.

She gave a history of progressive loosening of teeth with associated pain over left lower premolars. Pain was continuous nonradiating in nature and responded moderately to analgesics. She underwent extraction of tooth 37 at a private clinic about 10 days back following which an ulcero-infiltrative lesion developed at the operated side [Figure 2].

Axial computed tomography (CT) image and reconstructed orthopantomography (OPG) of mandible showing osteolytic destructive lesion involving left body of mandible [Figures 3 and 4].

She underwent multiple biopsies from the ulcero-infiltrative lesion. The histopathological features depicted defragmented epithelial lining and stromal connective tissue infiltrated with inflammatory cell infiltrate. A marked amount of keratinous flakes were noticed within the section. Focal areas of epithelial islands showing mild nuclear pleomorphism were noticed. A diagnosis of residual/radicular cyst was rendered. As the lesion failed to heal after necessary surgical intervention a biopsy was repeated after 2 months which again showed prominent keratinous flakes, marked chronic inflammatory cell infiltrate and epithelium with spongiosis and acanthosis. However, no evidence of dysplasia or malignancy was noticed. A diagnosis of inflammatory induced epithelial hyperplasia was given [Figures 5 and 6].

As multiple biopsies resulted in inconclusive findings and the lesion failing to heal, the patient was referred to the Malignant Diseases Treatment Centre (MDTC). The findings at the MDTC noted a 2 cm × 2 cm ulceroinfilterative growth in the left lower alveolus with no palpable cervical lymph nodes.

A punch biopsy from the lesional site revealed only strips of hyperkeratotic and acanthotic superficial squamous epithelium with focus of bacterial colonies. Further investigations with ultrasonography neck revealed multiple lymph nodes noted at Level Ib, II, III and V on the left side of neck, subcentric in size. Fine-needle aspiration cytology and excisional biopsy from lymph nodes revealed features of reactive lymphadenitis. However, contrast-enhanced CT scan depicted a lytic lesion in the left alveolus with an ulcerative growth in gingivobuccal sulcus– radiologically suggestive of carcinoma/chondrosarcoma.

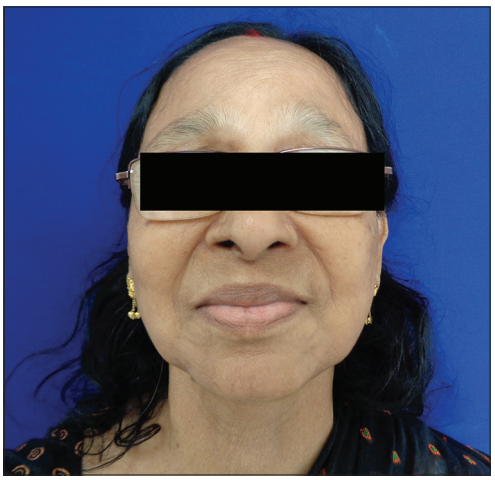

Figure 1: Extraoral image of the patient on her first visit to our outpatient department

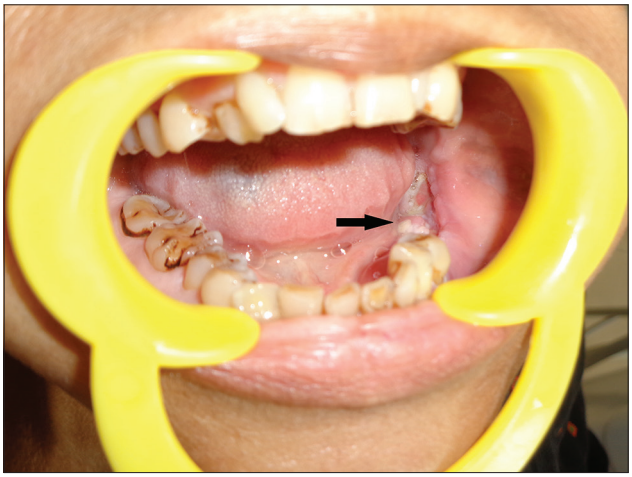

Figure 2: Intraoral image with defect in the left lower posterior quadrant

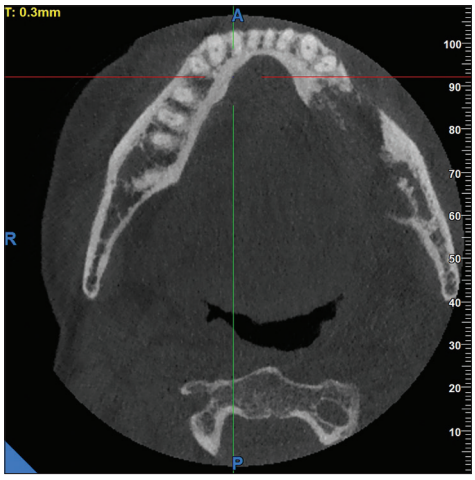

Figure 3: Axial computed tomography of mandible showing osteolytic destructive lesion involving left body of mandible

In view of multiple biopsies from the lesion, submandibular nodes revealing a nonspecific pathology and radiological imaging suggestive of a grave aggressive lesion, which did not respond to conservative management with antibiotic and analgesics, the case was taken up for resection of the lesion with left side supraomohyoid neck dissection under General Anaesthesia (GA). Postoperative recovery of the patient was uneventful. The postoperative OPG image revealed safe resection margins [Figure 7].

Peroperative finding exhibited a 4 cm × 4 cm lytic lesion noted over Lt RMT. This lesion was extending from left lower premolars to retromolar trigone. Medially reaching up to the floor of mouth and laterally to the lower gingivobuccal sulcus. Thick whitish discharge was noted from the center of the lesion. The frozen section margins during the peroperative surgery were found to be negative for malignancy.

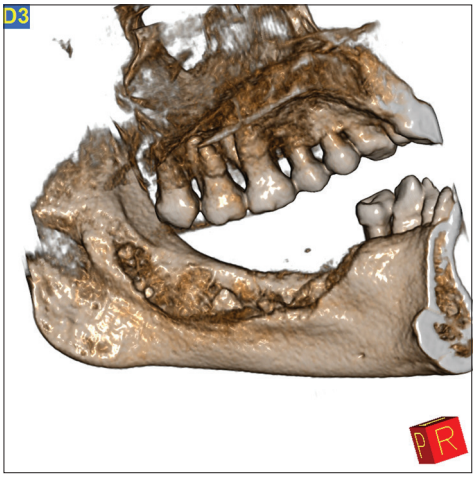

Figure 4: Three-dimensional reconstruction of osteolytic destructive lesion involving the left body of mandible

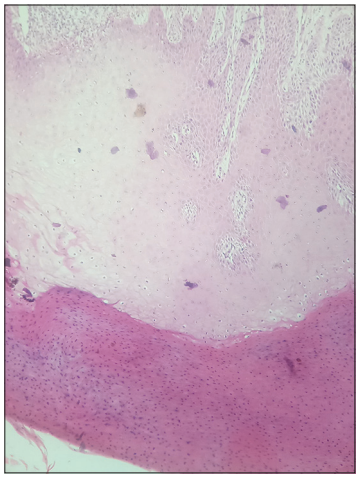

Figure 6: A repeat biopsy showed prominent keratinous flakes, marked chronic inflammatory cell infiltrate and epithelium with spongiosis and acanthosis. However, no evidence of dysplasia or malignancy was noticed (H&E, ×200)

In the postoperative period, she had minor orocutaneous fistula which responded for conservative management. However, unfortunately, the patient continued to be symptomatic as her pain persisted.

Final biopsy report carried out at the general pathology department exhibited a hyperkeratotic squamous lining epithelium with dense inflammatory infiltrate comprising of sheets of plasma cells, lymphocytes, eosinophils and histiocytes with numerous congested and dilated blood vessels with foreign body giant cells was noted. No breach of epithelial basement membrane was noted. All margins were free from malignancy. Twenty-nine lymph nodes were dissected, all showed reactive morphology.

Special stain with Ziehl–Neelsen, Periodic acid–Schiff, and Gram stain were all negative. A final histopathological diagnosis of chronic nonspecific inflammation was rendered [Figures 8 and 9].

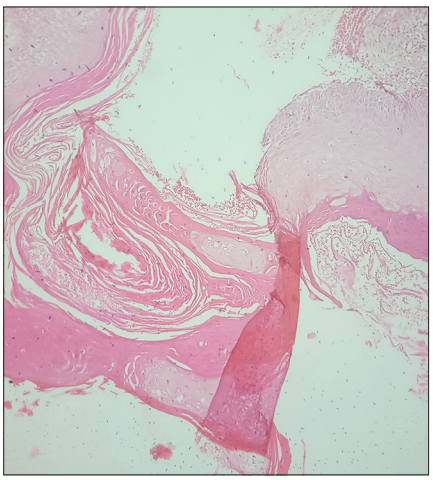

Figure 5: Marked amount of keratinous flakes were noticed within the section (H&E, ×100)

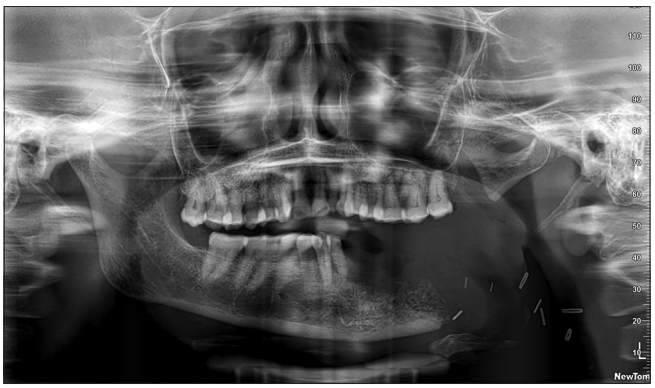

Figure 7: Postoperative orthopantography image after 6 months showing a osteolytic changes in the parasymphysis region on the left quadrant of the mandible

Later, after about 6 months from the postoperative period, a 5 cm × 2 cm ulceroinfiltrative lesion redeveloped in 32–42 region slowly progressing towards 45. She still had pain at the operated site which had aggravated over the period of time. An ulcer which had involved the lower central incisors 31, 41, 42 was noted which eventually led to the exfoliation of the involved teeth. The pain was continuous debilitating in nature and was radiating to the left ear.

On maxillofacial examination, an interincisal opening of only 2 fingers width, a well healed scar from the previous surgery and induration was noted over the scar on the neck measuring 3 cm × 2 cm in size. Intraoral examination revealed a 5 cm × 2 cm ulceroinfilterative lesion involving the arch of the mandible. Slough was noted over the base of the lesion involving the gingivolabial sulcus. Lesion bled to touch. No surrounding induration was present [Figure 10].

On WB PET CT, a 29 mm × 15 mm heterogeneously enhancing mass in the left anterior mandibular alveolus with likely neoplastic or infective etiology was noted [Figure 11]. Low-grade FDG was noted at left internal mammary lymph node and at left IX, X, and XI ribs anterolaterally. Otherwise, no significant active disease was noted in the rest of the visualized segment of the body.

A possibility of IG-4-related disease was even thought of and serum analysis was carried out. The results showed a finding of 0.76 g/L which was well within the permissible range of 0.03 and 2.01 g/L. The relative absence of marked and increased number of plasma cells from the tissue sections which could have prompted us to carry out IG-4 test on tissue sections also did not arise, thus the same was negated.

Because of increased suspicion of malignancy, again WLE up to 47 was carried out by a team of oral surgeons and the Oncosurgery Department of Medical Hospital. Excised specimen was received and taken up for

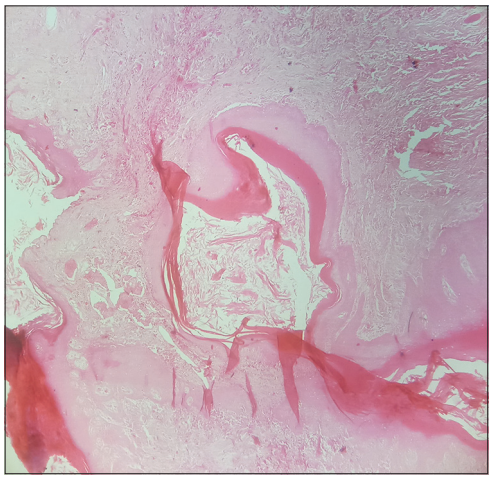

Figure 8: Hyperkeratotic squamous lining epithelium with dense inflammatory infiltrate comprising of sheets of plasma cells, lymphocytes, eosinophils and histiocytes (H&E, ×100)

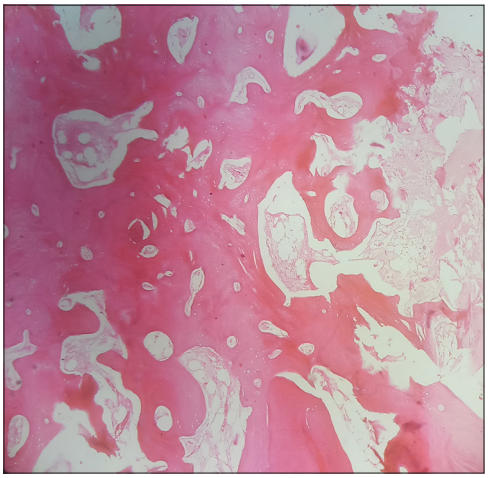

Figure 9: Bony trabeculae showing compact nature of bone, osteoblasts with no evidence of dysplaia or malignancy (H&E, ×200)

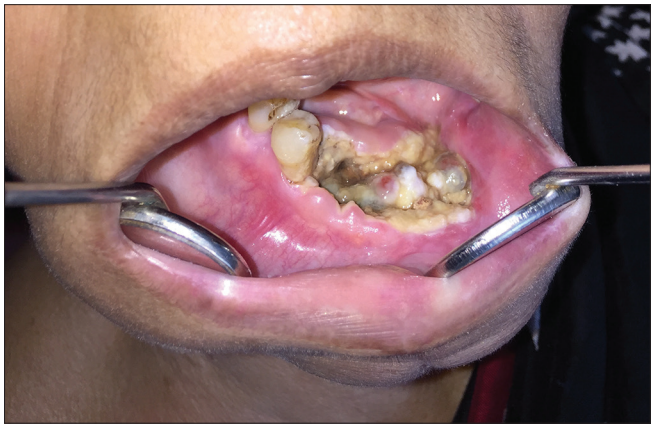

Figure 10: Intraoral image showing nonhealing large burrowing soft tissue lesion with everted margins post-WLE

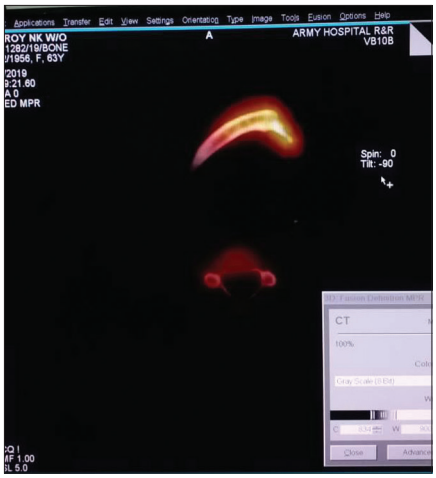

Figure 11: A 29 mm × 15 mm heterogeneously enhancing mass lesion noted in the left anterior mandibular alveolus

grossing [Figure 12]. Excisional biopsy sections revealed hyperkeratosis and acanthosis with chronic inflammation in the subepithelial region. The adjoining bony tissue showed degenerated bony fragments interspersed with flakes of lamellated keratin. No evidence of granulomas was seen. A comprehensive review of all slides was performed with a final opinion of benign cystic lesion of the jaw having squamous epithelial lining with keratin. A differential diagnosis of odontogenic keratocyst (OKC) or orthokeratotic odontogenic cyst was suggested. No evidence of dysplasia or malignancy was noted.

Few sections of the specimen showed signs of uniform compressed epithelium probably cystic epithelium with no rete ridges with the surface having plenty of parakeratin. It is difficult to contemplate whether such an aggressive lesion could be an OKC, as the surgeon's never assumed it to be, as each time they had ensured that adequate chemical cauterization with Carnoy's solution was carried out with sufficient clear surgical margin. However, the lesion persisted each time.

Case was taken up for discussion in tumor board proceedings of medical hospital and in view of high index of suspicion of malignancy both clinically and radiologically repeat biopsy was suggested. Hence, a repeat deep tissue biopsy was done which showed strips of hyperkeratotic and acanthotic superficial squamous epithelium with focus of bacterial colonies but no specific pathology seen. Again, no evidence of dysplasia or malignancy was noted.

Diagnostic dilemma with no definite tissue diagnosis in spite of repeated biopsies was inferred. However, clinically and radiologically, the lesion appeared to be a malignant ulcer. The intractable pain was still a disturbing factor.

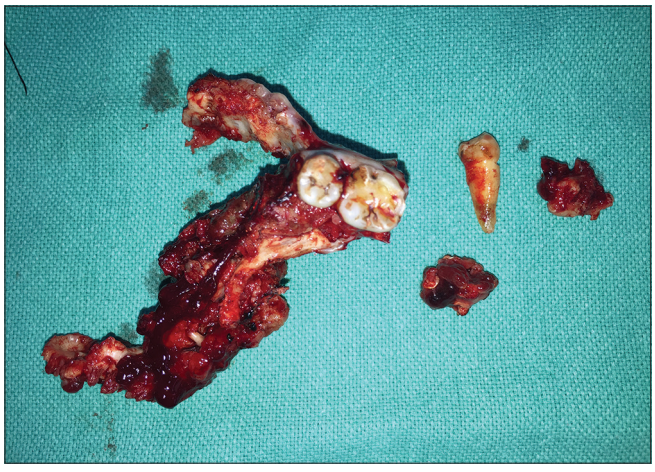

Figure 12: Excised specimen along with teeth and attached soft tissue showing whitish apparent keratinous areas

Postsurgery, the patient finally appeared to have no intraoral defect. The lesion healed well at least up to 48 region confirming the adequacy of clear surgical margin in this surgical intervention, probably the third or fourth intervention [Figure 13]. Only a single extraoral draining sinus persisted in the right lower jaw in the mento labial skin fold region.

The patient was referred to the plastic surgery department for the facial reconstruction of the entire facial surgical defect. On evaluation, the cosmetic surgeon was quite optimistic on the success of the surgery and all necessary planning, work up, preanesthetic checkup was carried out.

The patient was taken up for the reconstruction surgery but unfortunately an unprecedented cardiac event and emergency developed. All necessary steps to resuscitate the patient were instituted within the operation theatre complex. However, all efforts went in vain as our patient finally succumbed to the cardiac eventuality.

This could be one odd case where even after multiple biopsies and end number of referrals to several pathologists, we could not reach a conclusive diagnosis.

DISCUSSION

The case mandated a multidisciplinary approach, accordingly multiple consultations with senior oral and general pathologists was undertaken. On examination of histopathological slides, it was inferred on one of the rare case being designated as a "creeping gingival keratosis.[1]" Creeping gingival keratosis is reported to be a benign and locally extremely aggressive entity characterized by an unusual pattern of tissue destruction, loss of supporting

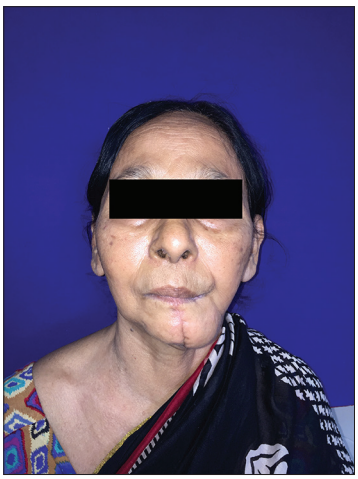

Figure 13: Postsurgery images of the patient after third/fourth intervention showing the external scar marks finally appearing to have no intraoral defect

tissues, and progressive exfoliation of associated teeth. This condition is unreported in the literature. In the two reported cases, the white lesion appeared first on the buccal and lingual gingival margin starting on the external surface before moving inside down into the bony component and destructing the same leading to progressive exfoliation of the involved teeth and loss of supporting bony structure. Our case appeared to have a little different clinical course as the defect initially presented with a ulcero-infiltrative lesion and slowly the defect migrated from inside to outside destructing bone and teeth on its course. There was no clear white lesion in our case. Histopathologically, the reported case of creeping gingival keratosis revealed keratosis without dysplasia. In our case also, microscopically, lots of keratin flakes were noted along with bland pale features with no evidence of any dysplasia or malignancy. No evidence of any cystic epithelium or any abnormal hyper chromatic or pleomorphic cells was identified.

In an E-mail consultation with the group of same authors of the above reported case, another lesion came up in mind was oral carcinoma cuniculatum (OCC). Carcinoma cuniculatum was first described in the foot by Arid *et al*., in 1954.[2] However, OCC was first described in the oral cavity by Fliegar and Owanski in 1977.[3] The diagnostic feature of OCC is well differentiated epithelial cells which lack cytological atypia, exhibiting blunt papillary or pebbly surface and keratin filled crypts extending deep in the connective tissue[4,5]

A wide age range of 7–92 years has been reported in the literature of cases diagnosed with OCC with slight male preponderance.[6] But, also in two recent case series of OCC slight female predominance was observed.[7]

A remarkable similarity between OCC and verrucous carcinoma (VC) exists which demonstrated a peculiar overlap in their histological and clinical presentation, but demonstrated a different biological course. Hence, the differentiation of the two lesions is essential. Both the lesions could present with exophytic and endophytic components. They exhibit minimal cytological atypia, well-differentiated tumor cells, and excessive keratin production. These features where quite similar to that of our reported case as similar features of excessive keratin production with minimal to no evidence of cytological atypia or dysplasia was evident. Our case however did not exhibit pathognomonic feature of OCC of invasive epithelial component arranged in the form of keratin filled channels and cores. OCC is locally aggressive with minimal evidence of distant metastasis burrowing deep into underlying muscles and bone, features evident in our present case also. The burrowing pattern has been acknowledged as a hallmark of OCC consistent with our case, exhibiting a similar burrowing pattern with mouse eaten prototype affecting the mandible.

Furthermore, VC which has predominantly exophytic component and has pushing margins along with broad bulbous rete ridges[8] into the lamina propria which was not evident in our case. There was minimal exophytic component and normal looking surface epithelia with no evidence of dysplasia and intact basement membrane. The rete ridges were also mostly uniform in shape and appearance.

However, to say with affirmation that our reported case is one of a case of OCC or VC was the dilemma. An attention was also given to another rare entity off immunoglobulin 4 (Ig4)-related disease. The patient's serum was evaluated for Ig4 levels which came out to be 0.76 g/dl well within the normal range of 0.03–2.01 g/dl. IgG4-related disease (IgG4-RD) is a systemic autoimmune fibroinflammatory disease that produces sclerotic, tumefactive masses containing dense lymphoplasmacytic infiltrates rich in immunoglobulin (Ig) $G4^+$ plasma cells.[9] Histopathologically, dense lymphoplasmacytic inflammatory infiltrate along with storiform fibrosis defined by dense, wire like strands of fibrotic collagen deposition radiating outward from a central point is pathognomonic. Our reported case however did not have a classical lymphoplasmacytic response and though we had a little evidence of scarring but the same was not prominent enough. Furthermore, Ig4 immunohistochemical assay on the tissue blocks was not carried out.

With the findings of flakes of lamellated keratin and squamous epithelium lined by parakeratin a possibility of OKC was postulated in our case. OKCs are known to have an aggressive nature with high chances of recurrence.[10] Nevertheless, a clear uniform cystic lining with basal cell palisading was never appreciated in any of the sections.

After multiple surgical interventions with resection of the mandible extending angle to angle, the patient was eventually lost because of severe cardiac arrest during her last surgical intervention for mandibular arch reconstruction using fibula.

As the lesion migrated from one side of the mandible to the other side, kept showing clinical features of inflammation of the bone and bone marrow simulating features of osteomyelitis and the continued presence of keratin histologically in all the biopsy specimens with no

evidence of dysplasia or malignancy, we contemplated whether we could give a nomenclature to the lesion as that of "Migratory Kerato osteomyelitis of the oral cavity." No such lesion has been documented in the literature till date, to the best available knowledge of the authors.

This could be one of case of a lifetime where multiple consultations with oral and general pathologists failed to reach an irrefutable diagnosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial s will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Shah N, Graham J, Morgan P, McGurk M. Creeping gingival keratosis: A diagnostic and clinical dilemma .British Journal of Oral and Maxillofacial Surgery. P 145| Volume 53, ISSUE 10, e89, December 01, 2015.
2. Aird I, Johnson HD, Lennox B, Stansfeld AG. Epithelioma cuniculatum: A variety of squamous carcinoma peculiar to the foot. Br J Surg 1954;42:245-50.
3. Flieger S, Owiński T. Epithelioma cuniculatum an unusual form of mouth and jaw neoplasm. Czas Stomatol 1977;30:395-401.
4. Thavaraj S, Cobb A, Kalavrezos N, Beale T, Walker DM, Jay A. Carcinoma cuniculatum arising in the tongue. Head Neck Pathol 2012;6:130-4.
5. Padilla RJ, Murrah VA. Carcinoma cuniculatum of the oral mucosa: A potentially underdiagnosed entity in the absence of clinical correlation. Oral Surg Oral Med Oral Pathol Oral Radiol 2014;118:684-93.
6. Datar UV, Kale A, Mane D. Oral carcinoma cuniculatum: A new entity in the clinicopathological spectrum of oral squamous cell carcinoma. J Clin Diagn Res 2017;11:ZD37-9.
7. Sun Y, Kuyama K, Burkhardt A, Yamamoto H. Clinicopathological evaluation of carcinoma cuniculatum: A variant of oral squamous cell carcinoma. J Oral Pathol Med 2012;41:303-8.
8. Alkan A, Bulut E, Gunhan O, Ozden B. Oral verrucous carcinoma: A study of 12 cases. Eur J Dent 2010;4:202-7.
9. Weindorf SC, Frederiksen JK. IgG4-related disease: A reminder for practicing pathologists. Arch Pathol Lab Med 2017;141:1476-83.
10. Shear M. The aggressive nature of the odontogenic keratocyst: Is it a benign cystic neoplasm? Part 3. Immunocytochemistry of cytokeratin and other epithelial cell markers. Oral Oncol 2002;38:407-15.