

Proliferative endophytic lesion of the maxilla: A diagnostic challenge

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Abstract

Carcinoma cuniculatum (CC) is an extremely rare neoplasm of the oral cavity. It is essentially a well-differentiated variety of squamous cell carcinoma and shows lower metastasis risk. The histological features of CC can mimic that of papillary squamous cell carcinoma or verrucous carcinoma. CC commonly affects the plantar region of the foot, and very few cases have been described in the oral cavity. The classical histological characteristics noted are infiltration of underlying connective tissue by squamous epithelium with keratin cores and keratin-filled crypts. Herewith, we present a case of CC of the right maxilla in a young Dravidian male patient who works in a battery factory. The case presented a diagnostic challenge both clinically and histopathologically before it was completely resected using a total maxillectomy technique. The case delineates the diagnostic challenge and management of the disease.

Keywords: Carcinoma cuniculatum, inverted verrucous carcinoma, keratocystic odontogenic tumor, squamous cell carcinoma

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INTRODUCTION

Carcinoma cuniculatum (CC) is a very rare type of tumor that occurs in the head and neck region. It is often plagued by the delay in diagnosis, especially due to its protracted growth, benign appearance and lack of suspicion due to its rarity.^[1,2] It is a discrete variant of verrucous carcinoma.^[3] It is difficult to diagnose, and a combination of critical clinical examination and deep surgical biopsy is needed.^[4] The name refers to the tendency of the lesion to “burrow” into the underlying connective tissue.^[5] The lesion frequently occurred in the lower extremities of foot.^[6] A few cases were observed in the oral cavity, where the lesion usually shows preference to alveolar mucosa or hard palate.^[7]

In the present case study, we report a CC case of a young man aged 40 years who had a significant history of working in a battery factory for a decade. The case presented a diagnosis challenge to the clinician and was finally treated by total maxillectomy.

CASE REPORT

A 40-year-old Dravidian male patient presented to the Department of Oral Medicine and Radiology, The Oxford Dental College and Hospital, Bengaluru, India, with a chief complaint of swelling in the right maxilla associated with severe pain. The patient was healthy and did not have any significant medical or surgical history. His family history was also noncontributory. He did not smoke or consume

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alcohol. His social history was significant for working in a battery factory for the last 10 years with the possibility of exposure to toxic chemicals such as lead, lithium and cadmium.

The patient reported that he underwent a tooth extraction of the right maxillary canine due to mobility and pain at a private clinic exactly a month ago. Following it, he observed a pebbly white material in and around the extracted socket [Figure 1]. The pain was gradual in onset, intermittent in nature, moderate in intensity and radiating into the infraorbital region and the adjacent teeth.

The extraoral examination did not show any significant changes. However, the intraoral examination revealed a whitish, pebbly material that appeared to be arising out of a partially healed socket in the right maxillary canine region. There were tiny white finger-like projections. On palpation, the swelling was soft and anterior teeth were mobile in the right maxillary segment. Based on the clinical examination, an initial diagnosis of a deep fungal infection was considered.

Investigations included intraoral periapical radiograph (IOPA) in relation to the right maxillary canine and first premolar region [Figure 2], orthopantomogram (OPG) [Figure 3] and histopathological examination (HPE). IOPA showed an osteolytic lesion in relation to the right maxillary canine. OPG showed a radiolucent lesion extending from the unhealed socket and the lesion raised the sinus floor to a higher level in relation to the extraction socket. The white finger-like lesions were biopsied, the unhealed socket was curetted and tissues were sent for HPE. HPE was inconclusive as only epithelial tissue was seen in tangential sections without any connective tissue. The patient was lost to follow-up before any intervention could be initiated.

The patient reappeared after 2 months. The right maxilla swelling and pain was still ongoing at that time. The extraoral examination did not reveal any facial asymmetry. On examining the neck, two right submandibular lymph nodes were found to be palpable, measuring 1 cm × 1 cm, nontender and not fixed to the underlying structures. Intraoral examination revealed a white proliferative lesion in relation to the first premolar and second premolar region in the right maxilla. The lesion was 3 cm × 4 cm in size, with the proliferative surface extending from the right maxillary canine region to the second premolar region. The swelling appeared as soft white finger-like projections around the unhealed socket. On palpation, the lesion was tender, scrapable and soft but had a firm base and was fixed to the underlying tissue. Grade II mobility of the teeth



Figure 1: Clinical appearance of lesion

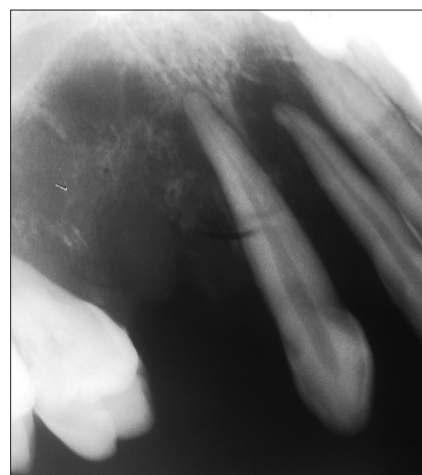


Figure 2: Periapical radiograph of the right maxillary canine region



Figure 3: Panoramic radiograph exhibiting radiolucent lesion

(maxillary central incisor, lateral incisor and first molar) in the same segment was also noted.

When the patient came in for the second consultation, further investigations were done. The cone-beam computed tomography (CBCT) [Figure 4] of the maxillary arch and 3D image of the skull showed an osteolytic lesion that

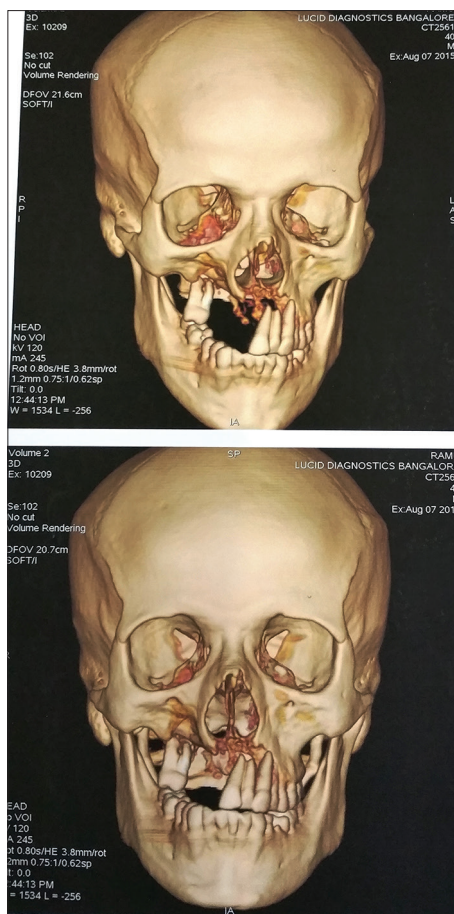


Figure 4: Cone-beam computed tomography image demonstrating osteolytic lesion

appeared to be extending from the right anterior segment of maxilla up to the last molar; the severe bone loss was seen in relation to teeth right maxillary lateral incisor and canine. The medial nasal wall was also perforated. The cheesy material was sent for culture test and it was negative for virus, bacteria and fungus.

A surgical opening of the unhealed socket in the right maxillary canine region was performed to obtain sufficient tissue for histopathological review. The HPE of the biopsy indicated an aggressive keratocystic odontogenic tumor (KCOT). Since the HPE diagnosis did not match the clinical presentation, a second opinion was sought. The lesion showed features of the verrucous lesion with parakeratin plugging with numerous long rete ridges. However, there was no invasion of epithelium into deeper connective tissue stroma, indicating verrucous carcinoma arising from an odontogenic cyst. Segmental maxillectomy was performed as a treatment. HPE of the excised maxilla showed a picture of either an aggressive KCOT or an early invasive squamous cell carcinoma arising from an odontogenic cyst. Postoperative healing was uneventful.



Figure 5: Clinical appearance of lesion after 4 months of initial visit

However, the patient came back after 4 months with a recurrence [Figure 5]. The CBCT as well as chest X-ray was performed and both were nonsignificant. A biopsy of the lesion was taken and sent for HPE.

This time it was observed that the verrucous lesion emanating from the gingival epithelium was noted and it appeared to be like an inverted verrucous carcinoma. This along with the presence of osteolysis pointed to a diagnosis of inverted verrucous carcinoma or CC. A total maxillectomy was performed and an obturator was provided for better healing and prevention of infection. A flow diagram depicting the patient's visit is shown in Figure 6.

In this case, the clinical pictures, as well as the radiological findings, were consistent but not conclusive to arrive at a final diagnosis. The histopathological report was the key to confirm the final diagnosis distinguishing it from verrucous carcinoma and oral squamous cell carcinoma. However, it was only after the third biopsy of the lesion, HPE picture pointed a verrucous lesion with thin rete ridges emanating from the gingival epithelium and extensive osteolysis. The extensive osteolysis resembled a rabbit burrow involving the entire maxilla from the right to the left, confirming the diagnosis of CC was made [Figure 7].^[1,2]

CC is a locally invasive tumor. Metastasis to the regional lymph nodes and distant sites is very rare. Therefore, *en bloc* resection with free margins, without dissecting the lymph nodes, is an ideal treatment. Reconstruction should be done as early as feasible following the resection. In this patient, total maxillectomy on the affected side and partial maxillectomy on the opposite side were done as a treatment. Obturator was given to aid in better healing and to prevent the infection of the site.

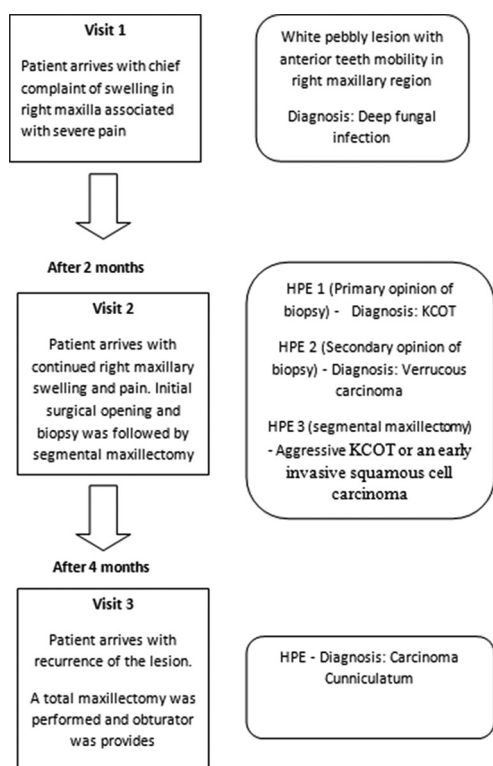


Figure 6: A flow diagram summarizing the patient's visits and outcome

DISCUSSION

CC is more common in males and affects older age group; the average age of occurrence is 52 years. The present case was consistent with gender aspect; however, the patient was significantly younger than the average age of occurrence. CC has been found to be associated with several factors such as human papillomavirus, inflammation, trauma, exposure to radiation, ingestion of arsenic and alcohol, and tobacco consumption. However, the exact etiology for the development of CC is still not defined.^[8] In this case study, the patient gave a history of working at a battery factory for 10 years. It could not be ascertained at this point of time whether he had exposure to arsenic and if it had a definitive role in the etiogenesis.

Clinically, when there is a nonhealing ulcer or a long-standing verrucous growth, CC should be one of the conditions that should be considered.^[9] Clinically, on examination, it gives an appearance of erythroleukoplakia, cobblestone-like surface and is hard on palpation, which was consistent in this case.^[10,11] CC has an exophytic and endophytic growth component. The exophytic growth is modest while the endophytic growth penetrates deep into the underlying tissue. The endophytic growth in the form of crypt-like structures resembles that of a rabbit burrow. The crypts are filled with keratin and discharge a whitish-yellow secretion as they reach the oral mucosa.^[8,10] The tumor cells show minimal atypia.

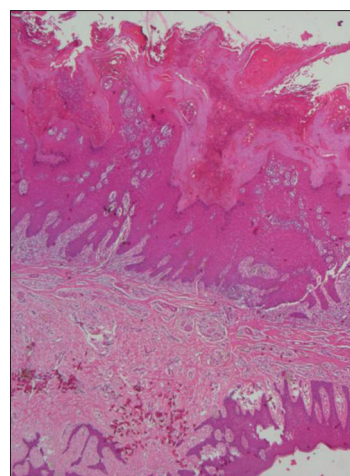


Figure 7: Hyperkeratotic and hyperplastic epithelium showing both endophytic and exophytic growth patterns. Rete ridges are narrow whereas superficial epithelial surface is broad. On the other side, normal gingival epithelium is appreciated

The endophytic component is believed to be responsible for inducing bone loss.^[8,10,11] All the above features were observed in the third HPE done in this case. The locally aggressive, invasive nature and local recurrence indicate its carcinogenic potential. However, it shows minimal dysplasia, which makes it less aggressive when compared with verrucous carcinoma and oral squamous cell carcinoma.^[12]

The keratin-filled crypts resembling a rabbit burrow, minimal atypia and extensive bone loss are very typical of CC.^[8,10,11] In fact, it is the hallmark of its diagnosis. The diagnosis of Carcinoma cuniculatum based on only HPE is challenging; it can be made easy by correlating it with the clinical and radiographic evidences.^[1,10]

A high degree of suspicion along with a close working relationship between the treating physician, pathologist and radiologist is required to arrive at the diagnosis.^[2]

Immunohistochemistry panel also aids in the diagnosis of CC.^[12,13] E-cadherin is responsible for branching crypt and integrin $\alpha 6$ and laminin 5 $\gamma 2$ is responsible for burrowing. CC shows a higher expression of E-cadherin, integrin $\alpha 6$ and laminin 5 $\gamma 2$ when compared with oral squamous cell carcinoma and verrucous carcinoma. Furthermore, the expression of immunohistochemical markers of Ki-67, p53 and p63 was lesser in oral carcinoma cuniculatum (OCC) when compared with oral squamous cell carcinoma and verrucous carcinoma. High levels of Ki-67, p53 and p63 indicate proliferation and p63 may regulate epithelial cell differentiation.^[12,14]

In the current case, immunohistochemistry was not used; the diagnosis was arrived at through a thorough evaluation

of the medical records, oral examination, radiological images, histopathology examination and surgical findings. This was further aided by a close working relationship between the clinician and the pathologist.

In the patient described in this case study, there was a nonhealing post extraction wound with the presence of whitish pebbly material, along with long-standing verrucous projection, which is part of the presentation of CC. However, the biopsy report did not very conclusive in the first instance, and in the second instance, it indicated an odontogenic cyst. Only during the third biopsy following recurrence, due to the suspicion of the possibility of CC, the close association between the clinician and pathologist and review of the case in its entirety led to the diagnosis of CC.

CC is a unique and rare clinical entity. Oral CC is even rarer. As HPE plays a vital role, for an early diagnosis, it should be supported by a large deep biopsy with normal skin on one side. More than one deep sample should be provided if required. Equally important is the close cooperation between the clinician and the pathologist. The clinician should provide the pathologist the clinical details and a clinical photograph of the lesion. The association between the pathologist and the clinician will help in earlier diagnosis and treatment of the patient, leading to a better outcome.

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 initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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