Case report

CLEAR CELL AMELOBLASTIC CARCINOMA: A case report and review of the literature

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ABSTRACT

OBJECTIVE: This is a report of clear cell ameloblastic carcinoma with a dual histomorphologic feature of clear cell odontogenic carcinoma (CCOC) and ameloblastic carcinoma (AC) coexisting in a single lesion. To the best of our knowledge, this is the first reported case of clear ameloblastic carcinoma (CCAC) among Nigerians.

CASE REPORT: A 53-year old Nigerian woman presented with an anterior jaw swelling of 7 months duration. The swelling was associated with toothache and tooth mobility. Cervicofacial Computed Tomography (CT) done revealed an expansile, non-corticated unilocular radiolucency with scalloped margins. A pre-operative incisional biopsy of the lesion gave a diagnosis of clear cell odontogenic carcinoma, which showed proliferation of sheets of clear cells and a covering hyperplastic para-keratinized squamous epithelium. The patient had a total surgical excision of the tumour under general endotracheal anaesthesia. A definitive diagnosis of clear cell ameloblastic carcinoma was made from histologic examination of the post-surgical specimen which showed a biphasic lesion consisting of odontogenic epithelium with foci of crowded outer ameloblast-like cells and inner stellate cells with foci of hyperchromatic, vacuolated nuclei, spindle cells, clear cell change, squamous metaplasia, keratin peals, necrosis and mitoses. The stroma consists of loose fibrovascular connective tissue and there was a covering hyperplastic para-keratinized squamous epithelium. No radiotherapy or chemotherapy was performed. The patient was followed up for 18 months without evidence of recurrence or metastasis to distant sites.

CONCLUSION: This study reports a rare case of odontogenic carcinoma in a Nigerian female diagnosed as CCAC, which presented histologically with biphasic component that mimics AC and COCC but a biologically less aggressive lesion. The findings of this study agree with previous reports which describe CCAC as a unique entity.

KEY WORDS: Clear cell tumour, Ameloblastic carcinoma, Odontogenic carcinoma.

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INTRODUCTION

The term "clear cell ameloblastic carcinoma" (CCAC) was loosely used to describe clear cell ameloblastoma (CCAM) due to its metastatic potential in 2003,[1] but it is unclear if CCAC is accepted universally. Also, CCAC was used to describe the ameloblastomatous pattern of clear cell odontogenic carcinoma (CCOC) in 1985[2]. CCOC is a rare malignant odontogenic tumour [3]. Other reported malignant odontogenic tumours are ameloblastic carcinoma (AC) and ameloblastic sarcoma (AS) [3]. Malignant odontogenic tumours are rare and represent up to 6.1% of all odontogenic tumours [4]. The incidence of malignant odontogenic tumours which vary worldwide, have been reported with a higher frequencies in Africans and Asians than in Americans and Europeans [4]

Clear cell odontogenic tumour (CCOT) and clear cell ameloblastoma (CCAM) were first reported by Hansen et al[2] and Waldron et al[5] respectively in 1984. Due to both lesions having similar biologic behaviour (local aggressiveness, recurrent and metastatic potential), these lesions were synonymously termed clear cell odontogenic carcinoma (CCOC). The precise relationship between both lesions however remains controversial. Some investigators[1,7] support Waldron's assertion which suggests that CCOC and CCAM may represent entities along a single histopathologic spectrum (rather than separate entities) making both low-grade carcinomas. Other researchers disagree with Waldron's hypothesis and suggest that CCOC should be separated from CCAM[8,9].

Ameloblastic carcinoma is a tumour that histologically presents with malignant transformation of ameloblastomatous cells with or without metastasis.[10] It was initially reported as a rare malignant odontogenic neoplasm that can arise either as a de novo lesion or from pre-existing ameloblastoma[11]. However, a recent report in a Nigerian population[12] suggests that it is the commonest malignant odontogenic tumours. It is a locally aggressive and destructive tumour that presents with rapid growth (with or without pain), paraesthesia, and tooth mobility. It has been reported with local recurrences and metastasis to distant sites such as lung, liver, and brain[18]. Rarely, ameloblastic carcinoma presents with clear cell changes, which some author preferably designate as clear cell ameloblastic carcinoma or clear variant of ameloblastic carcinoma. [19] Whereas, CCOC is characterised histologically predominantly of clear cells with or without polygonal or ameloblast-like cells with eosinophilic cytoplasm [2].

This is report of a rare malignant odontogenic tumour diagnosed as clear cell ameloblastic carcinoma with a dual histomorphologic feature of clear cell odontogenic carcinoma (CCOC) and ameloblastic carcinoma. To the best of our knowledge, this is the first reported case of clear ameloblastic carcinoma (CCAC) among Nigerians.

CASE REPORT

A 53-year-old female presented at the Oral and Maxillofacial Surgery Clinic, University of Benin Teaching Hospital (UBTH), Benin City, for evaluation of a painless fast growing swelling of the anterior mandible of 7 months duration. There was associated history of toothache and tooth mobility prior to presentation. Her medical condition at time of dental examination was regarded as noncontributory to her dental condition.

Intraoral examination revealed a cauliflower-like sessile exophytic growth that involved both lower alveolus and floor of her mouth, extending from the mandibular left central incisors (41) to the right first molar (36). The surface of the lesion appeared both irregular and proliferative. On palpation, the swelling was non-tender, with indurated base. Superiorly, the exophytic growth was soft to firm in consistency and there was an obvious lingual expansion of the mandible (Figure 1). The right lateral incisor was missing (31) and the right central incisor (41), canine (43), first (44) and second premolars (45) were mobile. The right canine (43), first (44) and second premolars (45) were displaced labially. Regional lymph nodes were not palpable, and

neuronal sensation was intact. General physical examination, posterio-anterior (PA) chest radiograph and abdominal ultrasonography (USG) showed no metastasis. Cervicofacial Computed Tomography (CT) however revealed an expansile, non-corticated unilocular radiolucency with scalloped margins (Figure 2).

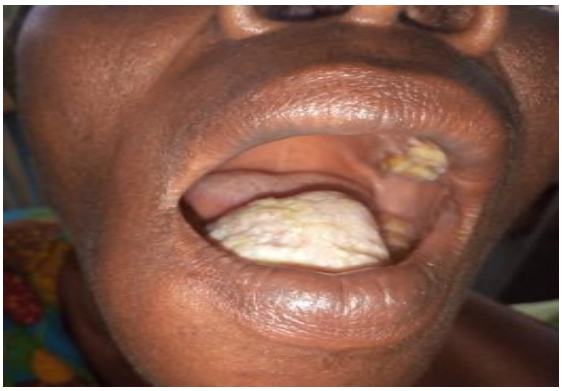


Figure 1. Preoperative photograph showing a lingual papiliferous swelling

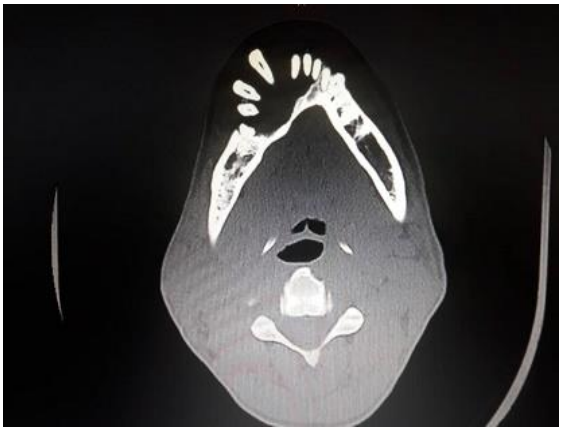


Figure 2. CT scan showing irregular margins, marked bone destruction of the mandible

Incisional biopsy revealed hyperplastic stratified squamous epithelium overlying a fibrous connective tissue containing proliferating islands and trabeculae of odontogenic epithelial cells. The odontogenic epithelial cells consist of peripheral columnar/ cuboidal hyperchromatic cells (which show reverse nuclear polarity) and central loose stellate cells with foci of clear cell change. There were few mitotic figures observed within the central cells. Also present were few blood vessels and foci of chronic inflammatory cell infiltrations within the stroma (Figure 3a and b). A pre-operative diagnosis of clear cell odontogenic carcinoma was made.

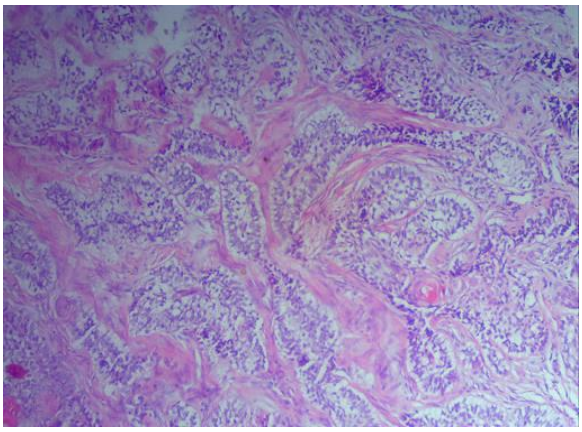


Figure 3a: Pre-operative photomicrograph of CCOC showing lobules of clear cells separated by hyalinized stroma (H&E x 100)

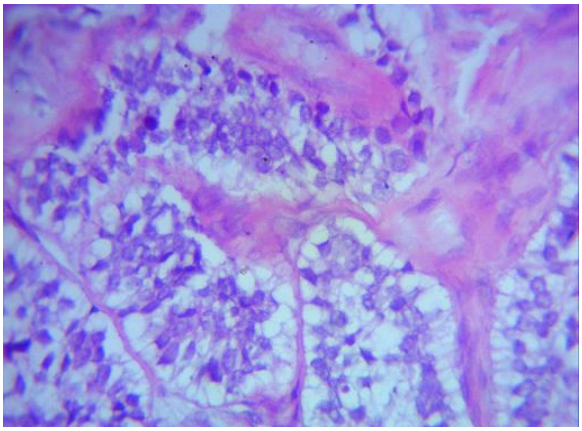


Figure 3b. Pre-operative photomicrograph of CCOC showing lobules of clear cells with distinct cellular outline, hyperchromatic nuclei, mitotic figures and separated by hyalinized stroma (H&E x 400)

Under general endotracheal anaesthesia, the lesion was resected without continuity defect by preserving the basal bone with 1-cm tumour-free margin (Figures 4). The post-operative course was uneventful. There was no evidence of recurrence or metastasis 18 months after surgery (Figure 5).

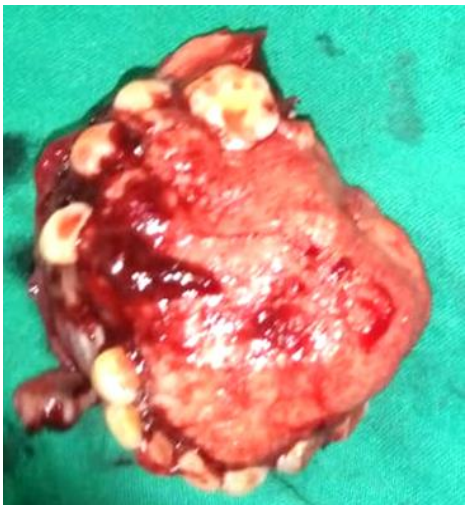


Figure 4. Post-surgical specimen showing resection with preservation of the marginal bone

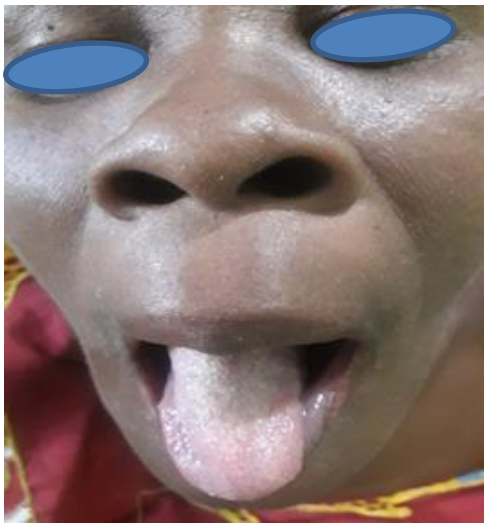
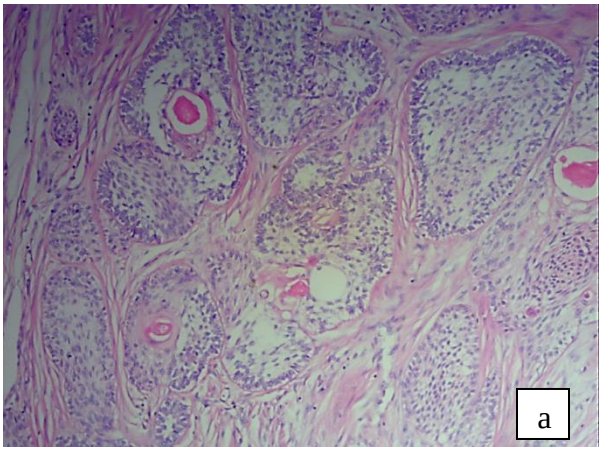


Figure 5. Postoperative photograph at 18 months follow up visit.

Histological examination of excisional biopsy specimen revealed features which were inconsistent with those of incisional biopsy. Excisional biopsy histological examination revealed islands, sheets and strands of odontogenic epithelium with outer palisaded ameloblast-like cells and inner stellate cells. There were foci showing crowding of the outer cells, and central hyperchromatic and vacuolated cells, spindle cells, clear cells, squamous metaplasia, keratin peals, necrosis and mitoses. The intervening stroma consisted of loose fibrous connective tissue, with a few blood vessels. There was a covering hyperplastic para-keratinized squamous epithelium. A definite diagnosis consistent with clear cell ameloblastic carcinoma (ameloblastic carcinoma with clear cell change). Confirmatory diagnoses with special staining or immunohistochemical staining were not done (Figure 6a and b).



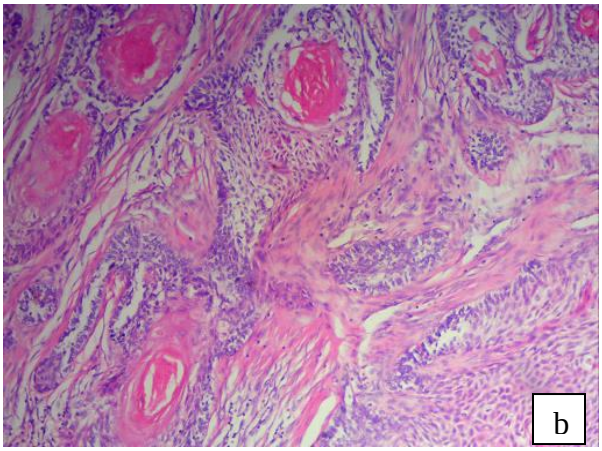


Figure 6a and b. Post-operative photomicrograph showing islands of clear cells (a) [x 40], with central area of squamous metaplasia and keratin pearls, and peripheral ameloblast-like cells (b)[x100] and intervening fibrous connective tissue stroma. (H & E)

DISCUSSION

The rarity and varied clinical course of odontogenic carcinomas has resulted in considerable confusion as evidenced by several

changes in terminologies and nosology over the years[20]. AC is reported to be more common among the Caucasians unlike COCC which has been reported to occur more among Africans.[21] AC is predominant in males while COCC shows female predilection. [22]. The present case of CCAC was reported in a Nigerian female patient. The reported peak ages for AC[23] and COCC[24] are 33.3 and 60 years respectively, which were in contrast with the 53 years observed in this present case of CCAC. However, Braunshtein et al, [1] reported a mean age of 44 years and male predilection for CCAC (a term used to describe clear cell ameloblastoma/CCAM).

Most cases of AC occur in the mandible with predilection for posterior portion. Swelling and pain are the most common clinical features followed by ulceration, rapid growth and trismus. Other clinical features of AC include teeth mobility, cortical plate perforation, paraesthesia, trismus and dysphonia[25]. Whereas, COCC frequently presents as painless slow growing lesion of several months or years with predilection for the anterior region[8]. Bleeding, paraesthesia of lower lip, trismus, proptosis, and non-healing ulcer are rare [10, 18]. Many clinical features for CCOC were similarly observed both in the present case of CCAC and the cases of CCAC (CCAM) reported by Braunshtein et al. [1] However, this case reported did not present with paraesthesia of lower lip, trismus, proptosis, and ulceration which are the clinical symptoms often observed in patients with AC.

Radiographically, COCC has a varied presentation. It presents as ill-defined unilocular or multilocular radiolucent mass with irregular margins often associated with root resorption and cortical bone perforation. It has also been reported on rare occasions to present as a mixed radiolucent-radiopaque lesion. [1,27] Imaging of AC usually appears as a multilocular radiolucent lesion with ill-defined margins and cortical plate expansion.[19] Imaging of CCAM (CCAC) shows anterior mandibular radiolucent lesion with ill-defined margin and displacement of associated teeth.[28,29] Similarly, the CT examination of the present case revealed an anterior mandibular unilocular radiolucent lesion with displacement of associated teeth, suggesting that CCAC (also referred to as CCAM [1]) may be less biologically aggressive than CCOC and AC.

Histologically, CCOC is characterised by sheets and nests of clear cells (monophasic pattern) with or without eosinophilic polygonal or ameloblast-like cells [1,2]. The preoperative histopathologic features in this case report were predominantly those of clear cells (monophasic pattern). A biphasic pattern which is the most common histologic pattern comprise of clear cells admixed with cells containing eosinophilic cytoplasm. The third variant of CCOC is the ameloblastomatous pattern with ameloblast-like cells and clear cells, which is similar to the pattern observed in the excisional biopsy of the patient in this study. This pattern of CCOC was designated as clear cell ameloblastic carcinoma by Waldron et al. [5] Whereas, AC exhibit malignant histological features such as cellular pleomorphism, mitosis, focal necrosis, perineural invasion and nuclear hyperchromatism[4]. It consists of two subtypes; the primary and secondary. The primary type demonstrates malignancy in the primary tumour with characteristic of ameloblastoma and cytologic atypia. The secondary type consists of malignant changes, which originate in a previously existing ameloblastoma, regardless of the presence or absence of metastasis. [6,30]

Furthermore, some studies [19,30] have reported AC with clear cell changes which some authors have designated as clear cell variant of ameloblastic carcinoma or clear cell ameloblastic carcinoma.[19] Based on histological features CCAC may be used to describe CCAM, [1] ameloblastomatous pattern of CCOC[5] or clear cell variant of AC.[19,28] Clear cells are glycogen-rich cells which can be demonstrated in CCOC, CCAC (CCAM) and AC by positive PAS reaction.[28] However, 40% expression of immunohistochemical staining with Ki-67 has been reported in CCAC.[28] Also, a study by Yoon *et al*.[31] reported a significant expression of cytokeratin 18, parenchymal matrix

metalloproteinases-2 (MMP-2), stromal MMP-9 and Ki-67 in AC, which differentiates AC from ameloblastoma. This present study suggests that CCAC shares similar histological features with CCOC and AC but CCAC may be a distinct entity based on their less biologically aggressive behaviour (clinicoradiological features).

The treatment of choice for COCC and AC is surgical resection and neck dissection combined with radiotherapy or chemotherapy. Owing to the different biologic behaviour of the lesions, there has not been consensus on treatment protocol[4,23]. Based on the biologic behaviour, COCC is usually regarded as a low-grade carcinoma, while AC is regarded as a high-grade carcinoma. Both lesions however have the potential to recur and metastasize to local and distant sites[17,21]. The present case of CCAC was treated surgically and followed up for a period of 18 months, and showed no recurrence or metastasis. Although it may be too early to exclude the possibility of recurrence or metastasis, it supports previous report that CCAC should be considered as a low grade carcinoma[1].

Comparison of this report of CCAC with AC [3,4,6,7, 28,30,31] and COCC[1,2,9-27] in the reviewed literature showed that there was difference in their clinicopathologic characteristics and surgical treatment outcome. This supports previous reports[2,5,8] that describe CCAC as a unique entity. Further evaluation of clinicopathologic characteristics and surgical treatment outcome of a large case series of CCAC is recommended.

In conclusion, this study reports a rare case of odontogenic carcinoma in a Nigerian female diagnosed as CCAC, which presented histologically with biphasic component that mimics AC and COCC but a biologically less aggressive lesion. The findings of this study agree with previous reports which describe CCAC as a unique entity.

Conflict of Interest: None declared

REFERENCES

1. Braunshtein E, Vered M, Taicher S, Buchner A. Clear Cell Odontogenic Carcinoma and Clear Cell Ameloblastoma : A Single Clinicopathologic Entity ? A New Case and Comparative Analysis of the Literature. J Oral Maxillofac Surg 2003; 21: 1004-1010
2. Hansen LS, Eversole LR, Green T, Powell NB. Clear cell odontogenic tumor-a new histologic variant with aggressive potential. Head Neck Surg. 1985; 8:115–23.
3. Reichart Pa, Philipsen HP. Odontogenic Tumors and Allied Lesions. Hanover, Germany, 2004.
4. Slootweg PJ. Muller H. Malignant Ameloblastoma or Ameloblastic Carcinoma. Oral Surg Oral Med Oral Pathol 1984;57:168-76
5. Waldron CA, Small IA, Silverman H. Clear Cell Ameloblastoma-An Odontogenic Carcinoma. J Oral Maxillofac Surg 1985;43:707
6. Elzay R P, Primary Intraosseous Carcinoma of the Jaws. Review and Update of Odontogenic Carcinomas. Oral Surg Oral Med Oral Pathol 1982; 54:299-303.
7. Eversole L. Malignant Epithelial Odontogenic Tumors. Semin Diagn Pathol 1999;16:317-24
8. Barnes L, Eveson J, Reichart P, Sidransky D. World Health Organisation Classification Of Tumors; Pathology And Genetics Of Head And Neck Tumors. IARC Press, Lyon, 2005.
9. Yang S, Zhang J, Xinming C, et al. Clear cell carcinoma, not otherwise specified, of salivary glands: a clinicopathologic study of 4 cases and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008; 106:712–720.
10. Bilodeau EA, Hoschar AP, Barnes EL, Hunt JL, Seethala RR. Clear Cell Carcinoma and Clear Cell Odontogenic Carcinoma: a Comparative Clinicopathologic and Immunohistochemical Study. Head Neck Pathol 2011;5: 101-107
11. Li TJ, Yu SF, Gao Y, et al. Clear cell odontogenic carcinoma: a clinicopathologic and immunocytochemical study of 5 cases. Arch Pathol Lab Med. 2001;125:1566–157
12. Omoregie F O, Okoh D S, and Ojo M A. Odontogenic tumours in Benin City, Nigeria: Analysis of 220 Cases and Review of Literature. African Journal of Oral Maxillofacial Pathology and Medicine, 2015; 1(1): 17 – 26.)
13. O'Regan E, Shandilya M, Gnepp DR, et al. Hyalinizing clear cell carcinoma of salivary

gland: an aggressive variant. Oral Oncol. 2004; 40: 348–352.
14. Ginat DT, Villaflor V, Cipriani NA. Oral Cavity Clear Cell Odontogenic Carcinoma. Head Neck Pathol. 2016; 10: 217-20. .
15. Kalsi AS, Williams SP, Shah KA, Fasanmade A. Clear cell odontogenic carcinoma: a rare neoplasm of the maxillary bone. J Oral Maxillofac Surg. 2014; 72: 935-8.
16. Walia C, Chatterjee RP, Kundu S, Roy S. Clinical enigma; A rare case of Clear Cell Odontogenic Carcinoma. Contemp Clin Dent. 2015; 6:559-63.
17. Avninder S, Rakheja D, Bhatnagar A. Clear cell odontogenic carcinoma: a diagnostic and therapeutic dilemma. World J Surg Oncol. 2006; 4:91-96.
18. Adebiyi KE, UgbokoVI, Ndukwe KC, Emeka C I. Hybrid clear cell odontogenic carcinoma and ameloblastic carcinoma-report of a case. Nig Dent J 2009; 17(2): 77-79
19. Srikanth MD, Radhika B, Metta K, Renuka NV. Ameloblastic carcinoma: Report of a rare case *World J Clin Cases* 2014; 2(2): 48-51
20. Ferriera S, Faverani LP, dos Santos GM, Martins EP, Garcia Júnior IR. Clear Cell Odontogenic Carcinoma; a treatment strategy. J Appl Oral Sci. 2018;26:
21. Datar UV, Kamat MS, Kanitkar SS, Byakodi SS. Clear cell odontogenic carcinoma: A rare case report with emphasis on differential diagnosis. J Can Res Ther 2017;13:374-7
22. Priya NS, Annaji AG, Keerthi R, Umadevi HS. Clear cell odontogenic carcinoma of the mandible: An unclassified entity. J Oral Maxillofac Pathol 2018;22:392-395
23. Vogel R, Baumhoer D, van Gorp J, Eijkelenboom A, et al.,. Clear cell odontogenic carcinoma. Occurrence of EWSRI-CREB1 as alternative fusion gene to EWSR1-ATF1. Head and Neck Pathology 2018;
24. Ordioni U, Benat G, Hadj Saïd M, Gomez-Brouchet A, Chossegros C, Catherine JH. Clear cell odontogenic carcinoma, diagnostic difficulties. A case report. J Stomatol Oral Maxillofac Surg. 2017; 118:302-305.
25. Bang G, Koppang HS, Hansen LS et al., Clear cell odontogenic carcinoma: report of three cases with pulmonary and lymph node metastasis J Oral Pathol Med 1989; 18: 113-118
26. Narula V, Sharma D, Bhargava EK, Rana K. Clear cell odontogenic carcinoma of the Maxilla: A rare case in a rarer presentation. Oral Maxillofac Surg Med Pathol 2016; 28 (1):95-99
27. Jayapalan CS, George A, Noufal A, Pynadath MK, Mangalath U. Clear Cell Odontogenic Carcinoma (CCOC): Mini-Review of Literature and Case Report of Mandibular Radiolucency in 17-year Girl. Diagn Pathol Open 2016; 1:1-5.
28. García-Ramos C, Tapia R O, Portilla-Robertson J. Clear Cell Ameloblastic Carcinoma. A Case Report. July 2019volume 128, Issue 1, Page E34
29. Gamoh1 S, Wato M, Akiyama1 H, Tsuji K, Ishikawa H, Naruse K, Et Al. The role of computed tomography and magnetic resonance imaging in diagnosing clear cell ameloblastoma: A case report. Oncology Letters 2017; 14: 7257-7261.
30. Soyele OO, Adebiyi KE, Adesina OM, Ladeji AM, Aborisade A, Olatunji A, Adeola HA Ameloblastic carcinoma: a clinicopathologic analysis of cases seen in a Nigerian Teaching Hospital and review of literature. Pan Afr Med J. 2019;31:208.doi:10.11604/pamj.2019.31.208.14660
31. Yoon HJ, Hong SP, Lee JI, Lee SS, Hong SD. Ameloblastic carcinoma: an analysis of 6 cases with review of the literature. Oral surg, Oral Med, Oral path, Oral rad, andendod. 2009; 108(6): 904-913.