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REVIEW

Clear Cell Odontogenic Carcinoma a Systematic Review

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Abstract

Clear cell Odontogenic Carcinoma (CCOC) is an uncommon malignant odontogenic tumor (MOT). It is the fifth most common MOT. A systematic review is presented of reported cases, case series and retrospective studies of CCOC, to determine trends in presentation, diagnostic features, treatment, and patient outcome. Searches of detailed databases were carried out to identify papers reporting CCOC. The variables were demographics, patient symptoms, tumor location, histopathological findings, immunohistochemical studies, treatment, follow-up, and recurrence. 117 cases were identified; CCOC was most frequently seen in mature females 65% (n = 76). The total average age was 55.4 with a range from 17 to 89 years, for females 56.4 and males 53.6 years. The mean size was 3.41 cm. The most common location was in the mandibular body 36.2% (n = 42), followed by the anterior mandible 23.3% (n = 27). The most common clinical presentation was a swelling 80.4% (n = 74), and the main symptom was pain 41.3% (n = 31), followed by painless lesion 24% (n = 18). The most common Immunohistochemistry positive expression was CK19, EMA, and CEA, and for special staining periodic acid Shiff (PAS); 97% of cases were treated surgically. The average follow-up was 30.3 months, and recurrence was reported in 52.4% of the cases. Conclusion: CCOC shows a strong predilection for the body and anterior mandible, and females are more frequently affected. CCOCs can be painful and the principle clinical sign is swelling, CCOCs can metastasize, and the prognosis is fair.

Keywords Clear cell odontogenic carcinoma · Malignant odontogenic tumor · Jaws · Immunohistochemistry

Introduction

Clear Cell Odontogenic Carcinoma (CCOC) is an infrequent malignant odontogenic tumor, possibly originating from the dental lamina [1]. CCOC was first described by Hansen in 1985, as a clear-cell odontogenic tumor [2]. Later the WHO classification in 2005, designated the CCOC as a malignant tumor of odontogenic origin [3]. MOTs represents 6.1% of all odontogenic tumors [4]. CCOC is characterized by pain or asymptomatic slow growth and it has

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a notable predilection for the mandibular bone followed by maxillary bone [5]. There is predilection for females [1, 4]. Histologically CCOC is composed of sheets, cords, or nests of monomorphic, plump, polygonal-to-round clear cells with eccentric nuclei, often separated by hyalinized fibrous septa [4, 5]. Pleomorphism can be seen, but mitoses are uncommon, CCOCs are PAS positive, diastase-sensitive [6]. The treatment is block resection, hemimandibulectomy or hemimaxillectomy, however where only resections have been performed, CCOCs have a nearly 34% local/regional recurrence rate, and have the ability to metastasize (14%) to distant sites, most commonly to the lungs [5, 7, 8]. Tumors with a visible clear cell component can promote difficulties for differential diagnoses, because other tumors can be partially or totally clear cell, including some odontogenic tumors, primary salivary tumors, melanoma and metastatic tumors, particularly renal cell carcinoma [9, 10]. The literature contains various case reports, case series, and retrospective studies, and one systematic review in 2015 [4]. In order to update our understanding of this tumor this is the most actualized systematic review of CCOC, with 117 cases, to determine trends in presentation, demographics, diagnosis, treatment, and outcome.

Materials and Methods

A systematic review of the literature on cases of CCOC was performed. IRB approval was not necessary because only a literature search was done and non-human subject research was conducted. The protocol of this review was registered in the National Institute for Health Research PROSPERO, International Prospective Register of Systematic Reviews (Registration Number CRD-239136).

Search Strategy

A systematic review was carried out according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses). A PubMed/Embase/Scopus/Science-direct search was carried out using the search term 'clear cell odontogenic carcinoma' "malignant odontogenic tumor", after 1985. The Embase search included a combination of relevant terms such as 'odontogenic malignant tumor, clear cell odontogenic carcinoma, mandible CCOC, metastasing CCOC, maxillary CCOC. The results were limited to human subjects, the language was English only, and publications were analyzed.

Selection Criteria

Data from studies of individuals with CCOC were included. Criteria for exclusion were: not English language, animal studies, cadaveric studies, and studies deemed non-diagnostic by the authors. Two investigators (A.P.L. and L.M.) independently performed the search review to determine that all appropriate articles were included in the analysis. Any disagreements were resolved through discussion with all authors.

Data Extraction

The variables were for author, year, study type, sample size, demographics, symptoms, tumor histopathology, immunohistochemistry, treatment, follow-up, recurrences and outcome. Data analysis was carried out using Microsoft Excel 2018 (Microsoft corp., Redmond, Washington, USA).

Data Analysis

The analysis was performed using the Statistical Package for the Social Sciences (SPSS) software, version 20.0 ©Copyright IBM (SPSS Inc., Chicago, IL, USA).

Results

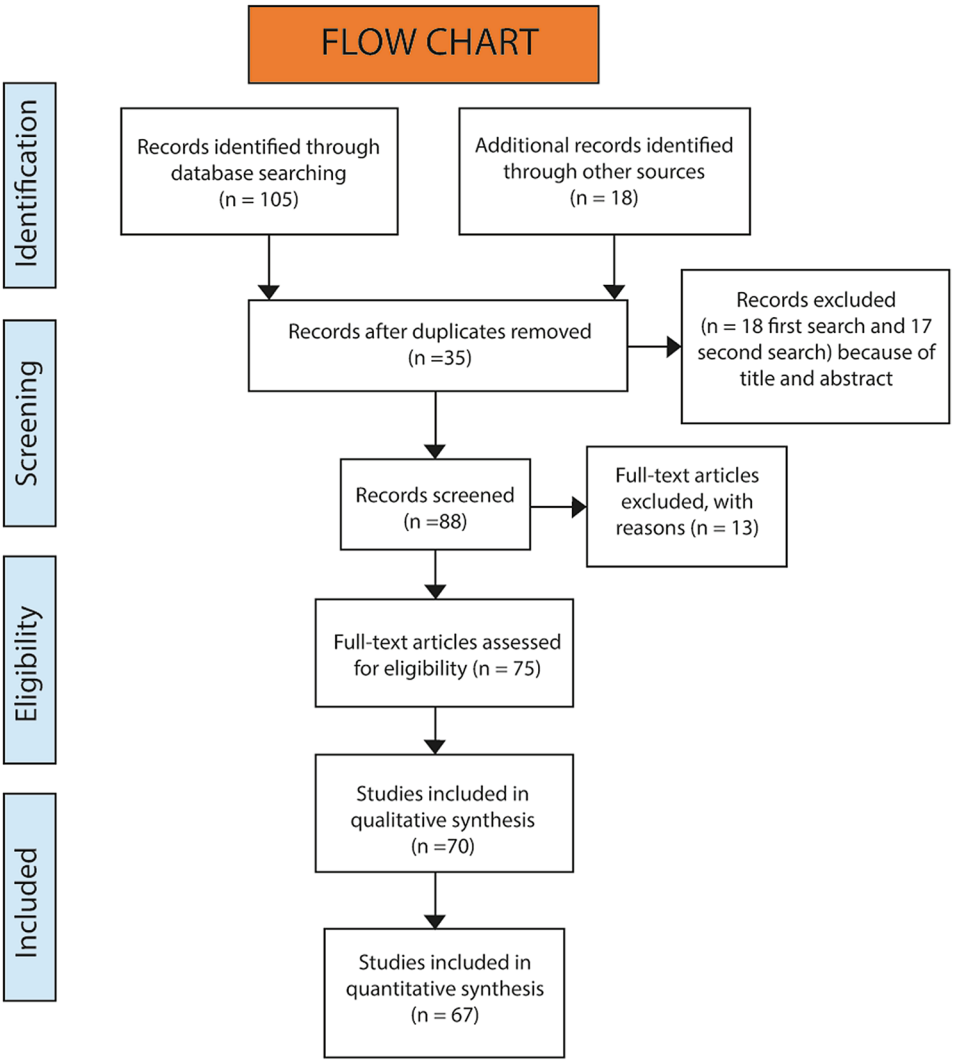
PubMed, Scopus, and Embase searches identified a total 125 papers, and after final analysis according to the inclusion criteria 67 papers were acceptable (Fig. 1), published after the use of the term clear cell odontogenic carcinoma from 1988 to June 2021, were analyzed. There were 53 case reports [1, 7–9, 11–59], 13 were case series [4, 60–71], and 1 retrospective study [72], for a total of 117 cases. Variables included sex, age, tumor localization, clinical presentation, symptoms, diagnosis, treatment, follow-up, recurrence, and the use of immunohistochemistry (IHC), periodic acid Schiff (PAS) and Ewing Sarcoma protein binding 1 (EWSR1) rearrangement. A descriptive analysis was carried out to record the variables and data. Many papers did not report data for all the variables. The strength of evidence of the included articles was assessed with an aggregate level of evidence 3b. (Table 1) Concerning the missing data, for each of the variables studied with the Listwise deletion method, when some cases had missing values of a particular variable; only cases with all or almost all variables in the analyses where used.

Demographics

Sex Data were available for 117 patients, of whom 65% (n = 76) were female, and 35.1% (n = 41) were male.

Age Data for all patients were found, giving a total average age of 55.4 years, with a range from 17 to 89 years, a mean age for females of 56.4 years and for males 53.6 years.

Fig. 1 Flow chart for CCOC



The size of the lesion was mentioned in 109 cases, and the mean for both genders was 3.4 cm, for females 3.3 cm and for males 3.5 cm.

The mean evolution time of 12.3 months was found for 67 cases for both genders. For females 10.2 months, for males 15.3 months. (Table 2).

Localization For all reported cases, the most frequent site for CCOC was the mandible 82.1% (n = 96), followed by the maxillary bone with 18% (n = 21), by sub site the most common location was the mandibular body with 36.1% (n = 42) followed by the anterior mandible 23.9% (n = 28). For the maxillary bone, the posterior area was the most common with 12.1% (n = 14). (Table 2).

For clinical presentation data was available for 92 patients of who presented with swelling or lump 80.4% (n = 74). Symptomatology data was found for 75 cases, where pain was a common finding with 41.3% (n = 31), followed by painless lesion 24% (n = 18). (Table 2).

Radiographic Image

The information was available for 89 cases, with radiolucent ill-defined image the most common 66.3% (n = 59), followed by well-defined radiolucent image 22.5% (n = 20). (Table 2).

Special staining Immunohistochemistry and Molecular tests: The information was available for 95 cases. PAS staining was positive for 64.7% (n = 61) when it was performed. Immunohistochemistry was performed with 95 cases, demonstrating EMA positivity in 47.1% (n = 48) cases, followed by CK19 with 45.1% (n = 43), and CEA 33.3% (n = 17). For molecular tests EWSR1–ATF1 there were only (n = 22) cases published in all the literature, with 95% (n = 21) positive cases.

Table 1 Per the oxford centre for evidence-based medicine classification system

Year	Author	Study type	Cases (n)	Level of evidence
2020	Santana [1]	Case report	1	4
2019	Liu [60]	Case series	5	4
2019	Vogels [61]	Case series	6	3b
2017	Datar [11]	Case report	1	4
2018	Priya [12]	Case report	1	4
2011	Bilodeau [72]	Retrospective	8	3a
2014	Yancoskie [13]	Case report	1	5
2017	Kujiraoka [14]	Case report	1	4
2015	Harbhajanka [15]	Case report	1	5
2011	Prakash [16]	Case report	1	4
2002	Mosqueda-Taylor [17]	Case report	1	3b
2001	Brinck [18]	Case report	1	4
2002	Brandwein [19]	Case report	1	3
2019	Park [20]	Case report	1	4
2015	Walia [21]	Case report	1	4
2001	Li [62]	Case series	5	3b
1992	Fan [22]	Case report	1	3b
2002	Iezzi [23]	Case report	1	4
2003	August [63]	Case series	5	3a
2001	Benton [24]	Case report	1	3b
2015	Kwon [25]	Case report	1	5
2015	Loyola [4]	Case series	7	3a
2013	Servato [26]	Case report	1	5
1994	Piattelli [27]	Case report	1	4
1995	Eversole [64]	Case series	8	3b
1998	Kumamoto [28]	Case report	1	4
1998	Miyauchi [29]	Case report	1	4
1998	Yamamoto [30]	Case report	1	4
2011	Zhang [65]	Case series	6	3a
2002	Adamo [31]	Case report	1	5
2002	Dahiya [9]	Case report	1	4
2003	Braunshtein [32]	Case report	1	4
2003	Kumar [7]	Case report	1	4
2004	Siriwardena [33]	Case report	1	4
2005	Ebert [66]	Case series	2	4
2008	Chera [8]	Case report	1	4
2009	Chaine [34]	Case report	1	4
2009	Werle [35]	Case report	1	3
2012	Dashow [36]	Case report	1	4
2012	Infante-cossio [37]	Case report	1	5
2013	Swain [38]	Case report	1	4
2014	Kalsi [39]	Case report	1	5
2014	Martinez Martinez [67]	Case series	3	4
2003	Carinci [40]	Case report	1	4
2011	Chaisuparat [68]	Case series	2	3b
2014	Krishnamoorthy [69]	Case series	2	4
2001	Maiorano [70]	Case series	2	3a
2017	Ferreira [41]	Case report	1	4
2018	Memtsa [42]	Case report	1	4
2017	Ordioni [43]	Case report	1	5
2014	Ganvir [44]	Case report	1	3b
2015	Ginat [45]	Case report	1	4
2016	Jayapalan [46]	Case report	1	3b
2015	Vineet Narula [47]	Case report	1	4
2014	Kim [48]	Case report	1	4
2014	Krishnamurthy [49]	Case report	1	3b
2019	Upadhyay [50]	Case report	1	4
2011	Yazici [51]	Case report	1	4
2006	Avninder [52]	Case report	1	5
2002	Ariyoshi [53]	Case report	1	3
2000	Nair [54]	Case report	1	3b
2000	Kumamoto [55]	Case report	1	4
1995	Sadeghi [56]	Case report	1	4
2021	Moro [57]	Case report	1	5
1993	Milles [58]	Case report	1	3b
1996	Aguiar [59]	Case report	1	4
1988	Bang [71]	Case series	3	3a

Aggregate: 3b

Metastasis

Data was available for all the cases, and lungs were the principal metastatic region 14.5% (n = 17) followed by the neck with 8.6% (n = 10), 74.4% (n = 87) cases did not report metastasis. (Table 2).

Treatment

Regarding the 117 cases, there was information for 102 cases. The most common type of surgery was resection with 62.7% (n = 64), followed by hemimandibulectomy 22.5% (n = 23). Once the diagnosis was established, approximately 2.5% of patients declined further surgical treatment.

Follow-up Was available for 88 cases, with an average 26.1 months, with a range of 1 months to 152 months (12.6 years).

Recurrence Was available for 84 cases, with an overall recurrent rate of 47%, for females 50% (n = 26) and males 43.8% (n = 14) cases. (Table 2).

Patient's status The information was available for 94 cases, where 12.8% (n = 12) patients died from the disease, and 87.2% (n = 82) were alive at the time of publication. (Table 2).

Table 2 Demographic, interval confidence (CI) standard deviation (SD)

	Female	Male	Total	CI
Total sample size	(n = 76)	(n = 41)	100% (n = 117)	
Age (years)	Mean ± SD (Min/Max)	Mean ± SD (Min/Max)	Mean ± SD (Min/Max)	[CI 95%]
	56.4 ± 17,7 (17/89)	53.6 ± 13.27 (26/81)	55.4 ± 16.3 (17/89)	[52.4–58.4]
Clinical sign	(n = 57)	(n = 35)	100% (n = 92)	
Swelling	82.5% (n = 47)	77.1% (n = 27)	80.4% (n = 74)	[72.3–88.5]
No swelling	17.5% (n = 10)	22.9% (n = 8)	19.6% (n = 18)	[11.5–27.7]
Symptomatology	(n = 47)	(n = 28)	100% (n = 75)	
Pain	53.2% (n = 25)	21.4% (n = 6)	41.3% (n = 31)	[30.2–52.4]
Unhealed post-extraction	4.3% (n = 2)	10.7% (n = 3)	6.7% (n = 5)	[1–12.4]
Bleeding	2.1% (n = 1)	7.1% (n = 2)	4% (n = 3)	[− 0.4–8.4]
Paresthesia/Hypoesthesia	4.3% (n = 2)	17.9% (n = 5)	9.3% (n = 7)	[2.7–15.9]
Pressure	6.4% (n = 3)	14.3% (n = 4)	9.3% (n = 7)	[2.7–15.9]
Discomfort	6.4% (n = 3)	3.6% (n = 1)	5.3% (n = 4)	[0.2–10.4]
Painless lesion	23.4% (n = 11)	25% (n = 7)	24% (n = 18)	[14.3–33.7]
Localization	(n = 76)	(n = 41)	100% (n = 117)	
MandiBLE				
Anterior	22.1% (n = 17)	29.3% (n = 12)	23.9% (n = 28)	[15.6–31]
Body	38.1% (n = 29)	31.7% (n = 13)	36.1% (n = 42)	[27.5–44.9]
Ramus	1.2% (n = 1)	–	0.9% (n = 1)	[− 0.8–2.6]
Posterior	17.1% (n = 13)	22%(n = 9)	19% (n = 22)	[11.9–26.1]
Condyle	1.2% (n = 1)	–	0.9% (n = 1)	[− 0.8–2.6]
Ramus and condyle	2.6% (n = 2)	–	1.7% (n = 2)	[− 0.6–4]
Maxilla				
Anterior	7.8% (n = 6)	2.4% (n = 1)	6% (n = 7)	[1.7–10.3]
Posterior	10.5% (n = 8)	14.6% (n = 6)	12% (n = 14)	[6.2–18]
Radiographic pattern	(n = 62)	(n = 27)	100% (n = 89)	
Radiolucent + ill-defined	66.1% (n = 41)	66.7% (n = 18)	66.3% (n = 59)	[56.5–76.1]
Radiolucent + welldefined	19.4% (n = 11)	29.6% (n = 8)	22.5% (n = 20)	[13.8–31.2]
Radiolucent + unilocular	8.1% (n = 5)		5.6% (n = 5)	[0.8–10.4]
Radiolucent + multilocular	4.8% (n = 3)	3.7% (n = 1)	4.5% (n = 4)	[0.2–8.8]
Radiolucent + Radiopaque	1.6% (n = 1)		1.1% (n = 1)	[− 1.1–3]
Metastases	(n = 76)	(n = 41)	100% (n = 117)	
Lung	14.5% (n = 11)	14.6% (n = 6)	14.5% (n = 17)	[8.1–20.9]
Rib	1.3% (n = 1)	2.4% (n = 1)	1.7% (n = 2)	[− 0.6–4]
Neck	10.7% (n = 8)	4.9% (n = 2)	8.5% (n = 10)	[3.4–13.6]
Optic nerve	–	2.4% (n = 1)	0.9% (n = 1)	[− 0.8–2.6]
No metastases	73.7% (n = 56)	75.6% (n = 31)	74.4% (n = 87)	[66.5–82.3]
Recurrence	(n = 52)	(n = 41)	100% (n = 84)	
No	50% (n = 26)	56.3% (n = 18)	52.4% (n = 44)	[41.7–63.1]
Yes	50% (n = 26)	43.8% (n = 14)	47.6% (n = 40)	[36.9–58.3]
Treatment	(n = 66)	(n = 36)	100% (n = 102)	
Resection	65.2% (n = 43)	58.3% (n = 21)	62.7% (n = 64)	[53.3–72.1]
Enucleation	6.1% (n = 4)	2.8% (n = 1)	4.9% (n = 5)	[0.7–9.1]
Hemimandibulectotomy	19.7% (n = 13)	27.8% (n = 10)	22.5% (n = 23)	[14.4–30.6]
Hemimaxillectomy	9.1% (n = 6)	11.8% (n = 4)	9.8% (n = 10)	[4–15.6]
Patient's status	(n = 58)	(n = 36)	100% (n = 94)	
Dead	8.6% (n = 5)	19.4% (n = 7)	12.8% (n = 12)	[6–19.6]
Alive	91.4% (n = 53)	80.6% (n = 29)	87.2% (n = 82)	[80.4–94]
	Mean ± SD (n)	Mean ± SD (n)	Mean ± SD (n)	[CI 95%]
Size of the lesion (cm)	3.3 ± 1.47(n = 70)	3.5 ± 1.3 (n = 39)	3.41 ± 1.3 (n = 109)	[3.2–3.7]

Table 2 (continued)

	Mean ± SD (n)	Mean ± SD (n)	Mean ± SD (n)	[CI 95%]
Evolution time (months)	10.2 ± 13.1 (n = 40)	15.3 ± 31.1 (n = 27)	12.23 ± 21.9 (n = 67)	[7–17.6]
Follow-up (months)	24.8 ± 20.9 (n = 55)	28.4 ± 22.2 (n = 33)	26.1 ± 21.4 (n = 88)	[21.4–30.4]

Statement of Clinical Relevance

Clear cell odontogenic carcinoma is an infrequent malignant odontogenic tumor with a female predilection. Local recurrences, metastases, and deaths have been reported and documented. Surgery, chemotherapy and radiotherapy have being used, alone or in combination, with an overall reserved prognosis. This study gives an update of the trends in demographics, treatment and outcome for this uncommon malignancy.

Discussion

CCOC is an uncommon malignant epithelial odontogenic tumor, defined in part by its EWS1 gene rearrangement, affecting over 80% of cases [4, 73], EWSR1-ATF1 is the typical translocation although other fusion partners are reported [61]. CCOC was designated as a malignant odontogenic tumor in the WHO classification of 2005 [3].

In this systematic review, we aim to provide a more comprehensive understanding of CCOC. The majority of the cases of CCOC found occurred in the body of the mandible, with 36.1% (n = 42) followed by the anterior mandible 23.9% (n = 28), similar results in location with Avninder et al. who reported most cases in the body of the mandible during the fifth through seventh decades [52, 57]. Li et al. however reported CCOC favored the body and the anterior region between the fourth and fifth decade [62], while Ebert et al. the mandible was the most favored location with (84%) [66].

On the other hand this systematic review found 21 cases in the maxilla; interestingly 14 cases were in the posterior maxillary bone. Concerning the relation between female and males was 2:1 with 75 females and 41 males, different from Ebert et al. [66], who found a 3:1 relation between females and males, however the mean age at presentation was almost similar from his research of 58 years (range 17–89 years). Our study found a mean age of 55.4 years, for females 56.4 with a range from 17 to 89 and males 53.6 years with a range from 26 to 81 years. According to symptomatology Swain et al. found some patients complained of a painless swelling, tooth abnormalities or slow-growing progressive swelling over several months to years [38]. Pain and tooth mobility occurred in approximately one-third of patients, whereas bleeding, paresthesia, and non-healing ulcerations were rare complaints [4, 38]. Our findings for symptomatology in 75 cases [1, 4, 8, 9, 11, 12, 15–17, 19, 21, 22, 26–29, 32–38, 42, 44, 45, 47–53, 55, 56, 58–60, 62–66, 68–70] show that pain was a frequent presentation with 41.3% (n = 31). CCOCs are usually diagnosed as large lesions with mean diameters of 4 cm [4, 5, 66]. However this study found a mean size of 3.4 cm. The mean follow up in our study was 26.1 months (n = 88). According to Ebert et al. the average period of follow-up was 5.5 years (range 0.5–21 years) [66], for Loyola et al. a mean of 59.5 ± 75.8 months, with a range of 3–504 months [4]. Regarding types of treatments this study found 102 cases, 62.7% (n = 64) were treated by resection [3, 7, 12–16, 18–20, 24, 25, 28, 29, 31–35, 38, 43, 44, 46, 47, 49, 54–56, 58, 61–66, 69, 71, 72], followed by hemimandibulectomy [4, 9, 17, 27, 36, 37, 41, 50, 52, 53, 59, 64, 69, 70], with 22.5% (n = 23).

According to Guastaldi et al. the overall recurrence rate for CCOCs was 43% affecting 38 of the 88 cases [5]. Ebert et al. the recurrence rate for these tumors were 55% and local recurrence rates were higher (80%) for curettage alone than for resection alone (43%) [66]. On this topic Loyola et al. in a systematic review with 94 cases, found a recurrence of 40% with a lymph node involvement rate of 10% [4]. Zhang et al. reported a recurrence rate of 34% after resection but only in 6 patients [65]. Our study founds a recurrence rate of 52.4% (n = 44) in 84 cases [4, 7, 9, 14, 18–20, 22, 24, 27, 35, 37, 39, 40, 42, 44, 45, 49, 52, 56, 59, 60, 62, 63, 66, 69, 71, 72], were almost all of those cases were treated with resection alone. Approximately, one half of patients with CCOC experience local recurrence, but this depends on the method of initial therapy and the tumor invasion. Recurrence has been reported as long as 20 years postop [4].

For metastasis, lymph node metastasis on initial presentation is rare (10%) but rapidly increased in those with recurrent disease (33%) [4, 5, 27, 66]. In a large reviews, CCOC can metastasize to regional lymph nodes and lungs [4, 7, 58, 74, 75]. This study found 30 cases of metastasis, most of them 14.5% (n = 17) to the lungs [4, 14, 18, 22, 24, 27, 35, 37, 59, 61–65, 71], followed by lymph node 8.5% (n = 10) [39, 45, 49, 52, 57, 58, 60, 62, 64, 72]. According to some papers, when positive margins were noted on permanent sections, reperforming resection to attain tumor-free margins was recommended because no patient with persistent positive margins has achieved long-term survival [63, 66, 76–78].

Radiographic features are nonspecific, but they are usually radiolucent and poorly defined [4, 5, 63]. We found in

89 cases that radiolucent ill-defined image was the most common 66.3% (n = 59) [1, 7–9, 12, 13, 15, 18–26, 30, 33, 35–37, 40–44, 49, 50, 52, 54, 56, 57, 59, 62–65, 70, 71], followed by well-defined radiolucent image with 22.5% (n = 19) [11, 14, 17, 27–29, 31, 32, 34, 38, 39, 48, 53, 55, 60, 65, 66, 71].

Histology of CCOC

The most common histologic feature is a biphasic tumor characterized by oval and linear nests of clear cells intermixed with smaller islands of polygonal cells with eosinophilic cytoplasm [4]. Occasionally these two cell-types co-exist in a tumor that often yields a "glomeruloid" appearance [6–10]. Typically the clear cells occupy the central areas of the tumor islands and the more eosinophilic cells comprise the peripheral layer of cells. The second variant is represented by islands that show only the clear cell phenotype whereas the third and least common variant is comprised of clear cell nests with a tendency for ameloblastoma-like palisading around the periphery [15]. The clear cells have been reported to result from cytoplasmic accumulation of water, glycogen, mucopolysaccharides, mucin and lipids, fixation artifacts or paucity of cellular organelles, intermediate filaments and immature zymogen granules, or other material that is not stained by Haematoxylin or Eosin [4, 6, 79, 80]. In this regard, the possible clear cell presence in CCOC could be because, at the time of tooth development the primitive oral cavity is lined by ectoderm, which consists of a basal layer of cuboidal to low columnar cells and a surface layer of flattened squamous cells [81]. The cytoplasm of these cells is glycogen rich which gives them an empty appearance (clear cell). Therefore clear cells are considered to be the typical feature of cellular remnants of the primitive stomodaeum, and dental lamina that result from glycogen accumulation [2, 80]. Accordingly Eversole et al. by ultrastructural and histological evaluation considered the odontogenic origin with features similar to the developing enamel organ of presecretory ameloblasts [64]. For this reason CCOC must be distinguished from other odontogenic and nonodontogenic clear cell neoplasms (Table 3). First, metastatic lesions must be ruled out and by far the most common metastatic clear cell carcinoma to the jaws is renal cell carcinoma. The architectural features of renal cell carcinoma are different and consist most often of tightly packed nests of clear cells surrounded by dilated vascular cores of connective tissue. Additionally, metastatic renal cell carcinoma has a significantly different IHC phenotype and PAX 8 is particularly useful [82, 83]. Additionally, some melanomas have a significant clear cell component but these rarely metastasize to jaws [84]. A variety of odontogenic tumors have variable numbers of clear cells, most notably the calcifying epithelial odontogenic tumor. The clear cell CEOT should also have characteristic amyloid production, often showing calcification [6, 79, 81]. Mucoepidermoid carcinomas can contain significant clear cells but this is uncommonly found in the intrabony lesions [85].

Concerning immunohistochemistry, CK14, CK19 and EMA immunostaining patterns and cellular distribution may help in the definitive diagnosis of CCOC, and the negativity of CK7, vimentin and EMA helps in the exclusion of other tumors presenting with clear cells [8, 60]. CCOC exhibits prominent diastase-digested PAS-positive granules. PAS-positive granules show intracytoplasmic glycogen deposition [10, 62], our results show a total of 95 cases with a positivity of 64.7% (n = 61) for PAS staining [1, 9, 11, 12, 14, 17, 18, 21–23, 25, 27–30, 32–34, 38, 40, 42, 44, 47, 50, 52, 53, 55, 57, 58, 64, 68–70]. The CCOC is immunoreactive for cytokeratin 8 and cytokeratin 19, carcinoembryonic antigen (CEA), epithelial membrane antigen (EMA) and non-reactive for S-100 protein, glial fibrillary acidic protein, involucrin, vimentin and smooth muscle actin [4, 62]. This study found in 95 reported cases a positivity for EMA

Table 3 IHC: Immunohistochemistry, PAS: Periodic acid shiff, CK: Cytokeratin, EMA: Epithelial membrane antigen, CEA: carcinoembryonic antigen

Similar tumors	Histology	Special studies
Calcifying epithelial odontogenic tumor [6, 79]	Cells arranged as sheets and anastomosing small and large islands, with polyhedral epithelial cells, hyperchromatic mildly pleomorphic nuclei, and amyloid deposits, calcified concentric Liesigang Rings. Clear cell variant	Congo red
Mucoepidermoid carcinoma [85]	Multiple cystic spaces with mucous cells, epidermoid and intermediate cells, and variable clear cells	Mucicarmine MAML2
Metastatic renal cell carcinoma [82, 83]	Solid nests of epithelial cells with clear cytoplasm surrounded by well vascularized cores of connective tissue	RCC, CD10, PAX2, PAX 8, vimentin
Amelanotic melanoma [84]	Nets, sheets of clear cells, with vacuolated cytoplasm	S100, HMB45, Melan A SOX 10

Special staining and immunohistochemistry used. Percentage of cases the IHC was run. (Table 4)

*EWSR1: Ewings sarcoma RNA binding protein 1. For the 22 cases, 21 where positive for this test for a 95%

of 47.1% (n = 48) [9, 11, 12, 15, 18, 19, 21–24, 29, 33, 35, 43, 47, 49, 51, 52, 55, 60, 62, 64, 70, 71], for cytokeratin (CK19) 45.1% (n = 43) [1, 4, 7, 12, 14, 15, 18, 21, 28, 29, 32, 33, 38, 40, 42, 44, 50, 51, 55, 60, 62, 65, 70] and CEA 33.3% (n = 32) [9, 11, 17, 19, 22, 24, 30, 37, 44, 45, 47, 49, 51, 52, 61, 64, 65], showing the percentage of CCOCs cases that were positive. (Table 4).

Combined immunohistochemistry and EWSR1 rearrangement can improve the diagnostic precision for CCOC [60].

Table 4 IHC: Immunohistochemistry, CK: Cytokeratin, EMA: Epithelial membrane antigen, Hmwck: High Molecular Weight Cytokeratin. HMB: Human melanoma black. SOX10 (Sry-related HMg-Box gene 10)

Immunohistochemistry special staining and molecular tests	(n = 95)	%
PAS staining	61	64.7
EMA	48	47.1
CK19	43	45.1
CEA	32	33.3
AE1/AE3	28	29.5
CK8	9	9.5
CK14	18	18.9
CK7	5	5.3
p63	7	7.4
CK5	2	2.1
CK 18	3	3.2
Actin	2	2.1
CK13	2	2.1
CK20	1	1.1
Flaggrin	1	1.1
CREB13	2	2.1
EWSR1–ATF1* for 22 cases only	21	95.0

The rearrangement of EWSR1, was first described in 2013 by Bilodeau et al. [73]. There is evidence that this tumor expresses frequently the fusion of EWSR1 gene [39]. Some studies have reported that frequent fusion of the EWSR1 gene can provide a basis for diagnosis, as 83.3% of CCOCs manifest such genetic expression, commonly with ATF1 [60]. However, clear cell carcinoma of minor salivary glands is also associated with such distinct characteristics, making it difficult to distinguish between CCOC and clear cell carcinoma of minor salivary glands [86]. Our results shows a 95% (n = 21) of 22 cases with the use of EWSR1-ATF1 rearrangement, [1, 13–15, 43, 45, 60, 61, 73], considering that most of the studies did not use this technique in the past. For this reason the EWSR1-ATF1 rearrangement seems to be the key in the diagnosis of CCOC Figs. 2, 3, 4.

Limitation of the Study

The literature reported whose data quality and consistency were the primary limitation. The articles included in this systematic review did not mentioned all the variables, such as tumor size, tumor clinical presentation, symptoms, radiographic image, Immunohistochemistry and molecular tests. Missing values in any category can bias the results in the sample size. Concerning to the Oxford Centre for Evidence-Based Medicine, the majority of the analyzed studies were levels 4 and 5, representing a low evidence, perhaps secondary to the infrequent number of cases evaluated. On the other hand the studies included in this systematic review were from 1988 to December 2020, making a consideration that treatment modalities have evolved over the time, and the cases were not homogenous.

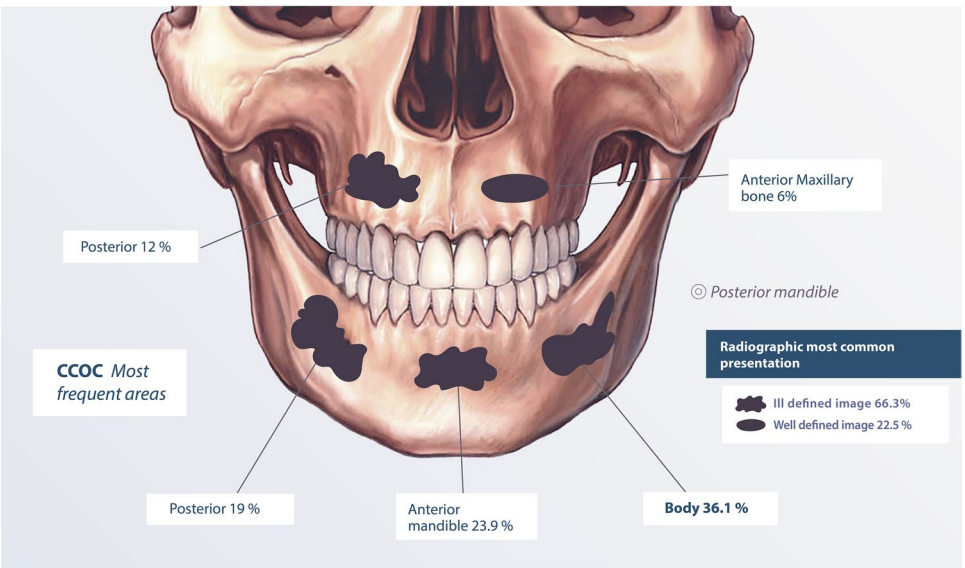


Fig. 2 Most common location and type of image for CCOC in both jaws

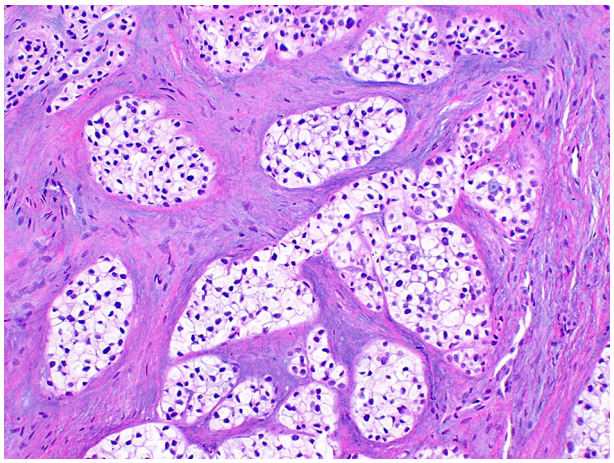


Fig. 3 A significant number of the neoplastic cells show cytoplasmic clearing

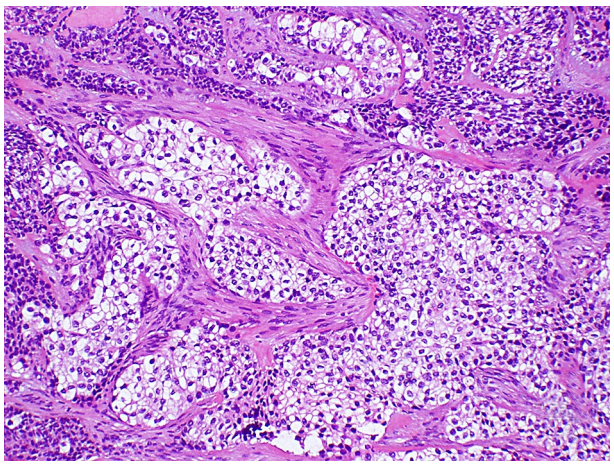


Fig. 4 CCOC. Cytologic detail where the cytologic atypia is minimal and does not necessarily suggest malignancy

Conclusion

CCOC commonly presents as a symptomatic swelling mass most often located in the mandible of elderly females. The histological and immunohistochemical features are not always distinctive and molecular genetic testing helps for diagnosis, which is useful at times to distinguish CCOC from other malignant neoplasms. Wide resection and hemimandibulectomy or hemimaxillectomy are the considered treatment of choice, however recurrences are common. The follow-up of patients is mandatory.

Authors' Contributions AJPL: action performed: search and paper selection, prospero writing, data analyze, oxford codification, excel data, discussion writing. NRGM: action performed: data analyzes, stadistic software analyzes, Table 1. LHMV: action performed: paper selection, oxford codification for papers, writing. MPV. action performed: excel data, Table 1, and oxford codification. KBTS: action performed: excel data, oxford codification, Fig. 2. KARI: action performed: oxford codification, Table 2, prospero writing. BJ: action performed: Fig. 1, Table 3, discussion writing. AVC: action performed: excel data for immunohistochemistry, Fig. 2, Fig. 1. JMW: regents professor, action performed: writing results, oxford codification, Table 4, data analyzes Figs. 3, 4.

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Data Availability Yes, we have all the information that was used to perform the manuscript. Data analyses were performed with Microsoft Excel 2018 (Microsoft Corp, Redmond, Washington).

Code Availability Statistical Package for the Social Sciences (SPSS) software, version 20.0 ©Copyright IBM (SPSS Inc., Chicago, IL, USA).

Declarations

Conflict of interest The author declares that they have no conflict of interest.

Ethical Approval This study met criteria for nonhuman subject research, and as a result board ethics approval was not required. No datasets were generated or analyzed during the current study.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

References

1. Santana T, de Andrade FL, de Sousa Melo MC, da Rocha GBL, Trierveiler M. Clear cell odontogenic carcinoma harboring the EWSR1-ATF1 fusion gene: report of a rare case. Head Neck Pathol. 2020;14(3):847–51.
2. Hansen LS, Eversole LR, Green TL, Powell NB. Clear cell odontogenic tumor—a new histologic variant with aggressive potential. Head Neck Surg. 1985;8:115–23.
3. Bang G, Koppang H. Clear cell odontogenic carcinoma. In: Barnes L, Eveson JW, Reichart P, Sidransky D, eds. World Health Organization classification of tumours. pathology and genetics of head and neck tumours. Lyon, France: IARC Press; 2005:292.
4. Loyola AM, Cardoso SV, de Faria PR, Servato JP, Barbosa de Paulo LF, et al. Clear cell odontogenic carcinoma: report of 7 new cases and systematic review of the current knowledge. Oral Surg Oral Med Oral Pathol Oral Radiol. 2015;120:483–96.
5. Guastaldi FPS, Faquin WC, Gootkind F, Hashemi S, August M, et al. Clear cell odontogenic carcinoma: a rare jaw tumor. A summary of 107 reported cases. Int J Oral Maxillofac Surg. 2019.
6. Jain A, Shetty DC, Juneja S, Narwal N. Molecular characterization of clear cell lesions of head and neck. J Clin Diagn Res. 2016;10:18–23.
7. Kumar M, Fasanmade A, Barrett AW, et al. Metastasizing clear cell odontogenic carcinoma: a case report and review of the literature. Oral Oncol. 2003;39:190–4.
8. Chera BS, Villaret DB, Orlando CA, et al. Clear cell odontogenic carcinoma of the maxilla: a case report and literature review. Am J Otolaryngol. 2008;29:284–90.

9. Dahiya S, Kumar R, Sarkar C, Ralte M, Sharma MC. Clear cell odontogenic carcinoma: a diagnostic dilemma. Pathol Oncol Res. 2002;8(4):283–5.
10. Muramatsu T, Hashimoto S, Inoue T, Shimono M, et al. Clear cell odontogenic carcinoma in the mandible: histochemical and immunohistochemical observations with a review of the literature. J Oral Pathol Med. 1996;25:516–21.
11. Datar UV, Kamat MS, Kanitkar SS, Byakodi SS. Clear cell odontogenic carcinoma: a rare case report with emphasis on differential diagnosis. J Cancer Res Ther. 2017;13(2):374–7.
12. Priya NS, Annaji AG, Keerthi R, Umadevi HS. Clear cell odontogenic carcinoma of mandible: an unclarified entity. J Oral Maxillofac Pathol. 2018;22(3):392–5.
13. Yancoskie AE, Sreekantaiah C, Jacob J, Rosenberg A, Edelman M, et al. EWSR1 and ATF1 rearrangements in clear cell odontogenic carcinoma: presentation of a case. Oral Surg Oral Med Oral Pathol Oral Radiol. 2014;118(4):e115–8.
14. Kujiraoka S, Tsunematsu T, Sato Y, Yoshida M, Ishikawa A, Tohyama R, et al. Establishment and characterization of a clear cell odontogenic carcinoma cell line with EWSR1-ATF1 fusion gene. Oral Oncol. 2017;69:46–55.
15. Harbhajanka A, Lamzabi I, Jain R, Gattuso P, Kluskens L. Cytomorphology and immunohistochemistry of a recurrent clear cell odontogenic carcinoma with molecular analysis: a case report with review of literature. Diagn Cytopathol. 2015;43(9):743–6.
16. Prakash AR, Sairam V, Srinivas RP. Clear cell odontogenic carcinoma-a rare case report. J Maxillofac Oral Surg. 2015;14:60–3.
17. Mosqueda-Taylor A, Meneses-García A, Ruíz-Godoy Rivera LM, de Lourdes S-R. Clear cell odontogenic carcinoma of the mandible. J Oral Pathol Med. 2002;31(7):439–41.
18. Brinck U, Gunawan B, Schulten HJ, Pinzon W, Fischer U, Füzesi L. Clear-cell odontogenic carcinoma with pulmonary metastases resembling pulmonary meningothelial-like nodules. Virchows Arch. 2001;438(4):412–7.
19. Brandwein M, Said-Al-Naief N, Gordon R, Urken M. Clear cell odontogenic carcinoma: report of a case and analysis of the literature. Arch Otolaryngol Head Neck Surg. 2002;128(9):1089–95.
20. Park JC, Kim SW, Baek YJ, Lee HG, Ryu MH, et al. Misdiagnosis of ameloblastoma in a patient with clear cell odontogenic carcinoma: a case report. J Korean Assoc Oral Maxillofac Surg. 2019;45(2):116–20.
21. Walia C, Chatterjee RP, Kundu S, Roy S. Clinical enigma: a rare case of clear cell odontogenic carcinoma. Contemp Clin Dent. 2015;6(4):559–63.
22. Fan J, Kubota E, Imamura H, Shimokama T, Tokunaga O, et al. Clear cell odontogenic carcinoma. A case report with massive invasion of neighboring organs and lymph node metastasis. Oral Surg Oral Med Oral Pathol. 1992;74(6):768–75.
23. Iezzi G, Rubini C, Fioroni M, Piattelli A. Clear cell odontogenic carcinoma. Oral Oncol. 2002;38(2):209–13.
24. Benton DC, Eisenberg E. Clear cell odontogenic carcinoma: report of a case. J Oral Maxillofac Surg. 2001;59(1):83–8.
25. Kwon IJ, Kim SM, Amponsah EK, Myoung H, Lee JH, Lee SK. Mandibular clear cell odontogenic carcinoma. World J Surg Oncol. 2015;24(13):284.
26. Servato JP, Prieto-Oliveira P, de Faria PR, Loyola AM, Cardoso SV. Odontogenic tumours: 240 cases diagnosed over 31 years at a Brazilian university and a review of international literature. Int J Oral Maxillofac Surg. 2013;42(2):288–93.
27. Piattelli A, Sesenna E, Trisi P. Clear cell odontogenic carcinoma. Report of a case with lymph node and pulmonary metastases. Eur J Cancer B Oral Oncol. 1994;30B(4):278–80.
28. Kumamoto H, Kawamura H, Ooya K. Clear cell odontogenic tumor in the mandible: report of a case with an immunohistochemical study of epithelial cell markers. Pathol Int. 1998;48:618–22.
29. Miyauchi M, Ogawa I, Takata T, Ito H, Nikai H, et al. Clear cell odontogenic tumour: a case with induction of dentin-like structures? J Oral Pathol Med. 1998;27(5):220–4.
30. Yamamoto H, Inui M, Mori A, Tagawa T. Clear cell odontogenic carcinoma: a case report and literature review of odontogenic tumors with clear cells. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1998;86(1):86–9.
31. Adamo AK, Boguslaw B, Coomaraswarmy MA, Simos C. Clear cell odontogenic carcinoma of the mandible: case report. J Oral Maxillofac Surg. 2002;60(1):121–6.
32. 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;61(9):1004–10.
33. Siriwardena BS, Tilakaratne WM, Rajapaksha RM. Clear cell odontogenic carcinoma-a case report and review of literature. Int J Oral Maxillofac Surg. 2004;33(5):512–4.
34. Chaine A, Pitak-Arnnop P, Dhanuthai K, Bertrand JC, Bertolus C. An asymptomatic radiolucent lesion of the maxilla Clear cell odontogenic carcinoma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;107(4):452–7.
35. Werle H, Blake FA, Reichelt U, Schmelzle R, Heiland M. Clear-cell odontogenic carcinoma: a new case and long-term follow-up of an old case, and review of the literature. J Oral Maxillofac Surg. 2009;67(6):1342–8.
36. Dashow JE, McHugh JB, Edwards SP. Swelling of the anterior mandible. J Oral Maxillofac Surg. 2012;70(3):e204–9.
37. Infante-Cossio P, Torres-Carranza E, Gonzalez-Perez LM, Gonzalez-Cardero E, Sanchez-Gallego F. Atypical presentation of clear cell odontogenic carcinoma. J Craniofac Surg. 2012;23:e466–8.
38. Swain N, Dhariwal R, Ray JG. Clear cell odontogenic carcinoma of maxilla: a case report and mini review. J Oral Maxillofac Pathol. 2013;17(1):89–94.
39. 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(5):935–8.
40. Carinci F, Volinia S, Rubini C, Fioroni M, Francioso F, Arcelli D, et al. Genetic profile of clear cell odontogenic carcinoma. J Craniofac Surg. 2003;14(3):356–62.
41. Ferreira S, Faverani LP, Santos GMD, Martins EP, Garcia Júnior IR. Clear cell odontogenic carcinoma of the mandible: a treatment strategy. J Appl Oral Sci. 2018;26:e20160645.
42. Memtsa, P., Papadopoulou, A., Vachtsevanos, K., Tzitzikas, I.. Management of Clear Cell Odontogenic Carcinoma: A Case Report. J Med Cases, North America, 2018.
43. 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(5):302–5.
44. Ganvir SM, Gajbhiye NY. An unusual presentation of clear cell odontogenic carcinoma in mandibular anterior region. J Oral Maxillofac Pathol. 2014;18(3):442–8.
45. Ginat DT, Villaflor V, Cipriani NA. Oral cavity clear cell odontogenic carcinoma. Head Neck Pathol. 2016;10(2):217–20.
46. C. S. Jayapalan, A. George, A. Noufal, M. Pynadath, Ummar Mangalath. Clear Cell Odontogenic Carcinoma (CCOC): mini-review of literature and case report of mandibular radiolucency in 17-year girl. Diagn Pathol Open. 2016; 1:3.
47. Narulaa V, Divya Sharma B, Bhargavaa EK, Ravi Meher A, et al. Clear cell odontogenic carcinoma of maxilla: a rare case in a rarer presentation. J Oral Maxillofac Surg Med Pathol. 2016;28:95–9.
48. Kim M, Cho E, Kim JY, Kim HS, Nam W. Clear cell odontogenic carcinoma mimicking a cystic lesion: a case of misdiagnosis. J Korean Assoc Oral Maxillofac Surg. 2014;40(4):199–203.
49. Krishnamurthy A, Ramshankar V, Majhi U. Clear cell odontogenic carcinoma of the mandible and temporomandibular joint

with cervical lymph nodal metastasis. Natl J Maxillofac Surg. 2014;5(2):221–3.
50. Upadhyay S, Bhavthankar JD, Mandale MS, Barewad B. Clear cell odontogenic carcinoma: case report of a deceptive pathology. J Oral Maxillofac Pathol. 2019;23(1):140–3.
51. Yazici ZM, Mete O, Elmali Z, Sayin I, Yilmazer R, Kayhan FT. Clear cell odontogenic carcinoma of the maxilla. Acta Medica (Hradec Kralove). 2011;54(3):122–4.
52. Avninder S, Rakheja D, Bhatnagar A. Clear cell odontogenic carcinoma: a diagnostic and therapeutic dilemma. World J Surg Oncol. 2006;12(4):91.
53. Ariyoshi Y, Shimahara M, Miyauchi M, Nikai H. Clear cell odontogenic carcinoma with ghost cells and inductive dentin formation - report of a case in the mandible. J Oral Pathol Med. 2002;31(3):181–3.
54. Nair MK, Burkes EJ, Chai-U-Dom O. Radiographic manifestation of clear cell odontogenic tumor. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2000;89(2):250–4.
55. Kumamoto H, Yamazaki S, Sato A, Yamaguchi T, Tezuka F, Ooya K. Clear cell odontogenic tumor in the mandible: report of a case with duct-like appearances and dentinoid induction. J Oral Pathol Med. 2000;29(1):43–7.
56. Sadeghi EM, Levin S. Clear cell odontogenic carcinoma of the mandible: report of a case. J Oral Maxillofac Surg. 1995;53(5):613–6.
57. Moro A, Gasparinia G, Saponaro G, Barberaa G, Doneddu P, et al. Clear cell odontogenic carcinoma: a case report and literature review. Oral and Maxillofac Surg Cases. 2021;7(2):1–8.
58. Milles M, Doyle JL, Mesa M, Raz S. Clear cell odontogenic carcinoma with lymph node metastasis. Oral Surg Oral Med Oral Pathol. 1993;76(1):82–9.
59. de Aguiar MC, Gomez RS, Silva EC, de Araújo VC. Clear-cell ameloblastoma (clear-cell odontogenic carcinoma): report of a case. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1996;81(1):79–83.
60. Liu L, Zhang JW, Zhu NS, Zhu Y, Guo B, Yang XH. Clear cell odontogenic carcinoma: a clinicopathological and immunocytochemical analysis. Pathol Oncol Res. 2020;26:1559–64.
61. Vogels R, Baumhoer D, van Gorp J, Eijkelenboom A, Verdijk M, van Cleef P, et al. Clear cell odontogenic carcinoma: occurrence of EWSR1-CREB1 as alternative fusion gene to EWSR1-ATF1. Head Neck Pathol. 2019;13(2):225–30.
62. Li TJ, Yu SF, Gao Y, Wang EB. Clear cell odontogenic carcinoma: a clinicopathologic and immunocytochemical study of 5 cases. Arch Pathol Lab Med. 2001;125(12):1566–71.
63. August M, Faquin W, Troulis M, Kaban L. Clear cell odontogenic carcinoma: evaluation of reported cases. J Oral Maxillofac Surg. 2003;61:580–6.
64. Eversole LR, Duffey DC, Powell NB. Clear cell odontogenic carcinoma. A clinicopathologic analysis. Arch Otolaryngol Head Neck Surg. 1995;121(6):685–9.
65. Zhang J, Liu L, Pan J, Tian X, Tan J, et al. Clear cell odontogenic carcinoma: report of 6 cases and review of the literature. Med Oncol. 2011;28(Suppl 1):S626–33.
66. Ebert CS, Dubin MG, Hart CF, Chalian AA, Shockley WW. Clear cell odontogenic carcinoma: a comprehensive analysis of treatment strategies. Head Neck. 2005;27:536–42.
67. Martínez Martínez M, Mosqueda-Taylor A, Carlos R, Delgado-Azañero W, de Almeida OP. Malignant odontogenic tumors: a multicentric Latin American study of 25 cases. Oral Dis. 2014;20(4):380–5.
68. Chaisuparat R, Sawangarun W, Scheper MA. A clinicopathological study of malignant odontogenic tumours. Histopathology. 2012;61(1):107–12.
69. Krishnamoorthy R, Ravi Kumar AS, Batstone M. FDG-PET/CT in staging of clear cell odontogenic carcinoma. Int J Oral Maxillofac Surg. 2014;43(11):1326–9.
70. Maiorano E, Altini M, Viale G, Piattelli A, Favia G. Clear cell odontogenic carcinoma. Report of two cases and review of the literature. Am J Clin Pathol. 2001;116(1):107–14.
71. Bang G, Koppang HS, Hansen LS, Gilhuus-Moe O, Aksdal E, Persson PG, Lundgren J. Clear cell odontogenic carcinoma: report of three cases with pulmonary and lymph node metastases. J Oral Pathol Med. 1989;18(2):113–8.
72. 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(2):101–7.
73. Bilodeau EA, Weinreb I, Antonescu CR, Zhang L, Dacic S, et al. Clear cell odontogenic carcinomas show EWSR1 rearrangements: a novel finding and a biological link to salivary clear cell carcinomas. Am J Surg Pathol. 2013;37(7):1001–5.
74. Kubota E, Imamura H, et al. Clear cell odontogenic carcinoma: a case report with massive invasion of neighbouring organs and lymph node metastasis. Oral Surg Oral Med Oral Pathol. 1992;74:768–75.
75. Sesenna E, Trisi P. Clear cell odontogenic carcinoma: report of a case with lymph node and pulmonary metastases. EurJ Canc Oral Oncol. 1994;30B:278–80.
76. Waldron CA, Small IA, Silverman H. Clear cell ameloblastoma an odontogenic carcinoma. J Oral Maxillofac Surg. 1985;43:707–17.
77. Duffey DC, Bailet JW, Newman A. Ameloblastoma of the mandible with cervical lymph node metastasis. Am J Otolaryngol. 1995;16:66–73.
78. Marí A, Escutia E, Carrera M, Pericot J. Clear cell ameloblastoma or odontogenic carcinoma. A case report. J Craniomaxillofac Surg. 1995;23:387–90.
79. Said-Al-Naief N, Klein MJ. Clear cell entities of the head and neck: a selective review of clear cell tumors of the salivary glands. Head Neck Pathol. 2008;2:111–5.
80. Reichart A, Phillipsen O. Odontogenic Tumours and Allied Lesions Quintessence Publishing Co Ltd; 2004. pp. 25–27.
81. Maiorano E, Altini M, Favia G. Clear cell tumours of the Salivary Gland, Jaws and Oral Mucosa. Semin Diagn Pathol. 1997;14:203–12.
82. Ozcan A, Shen SS, Hamilton C, Anjana K, Coffey D, et al. PAX 8 expression in non-neoplastic tissues, primary tumors, and metastatic tumors: a comprehensive immunohistochemical study. Mod Pathol. 2011;24(6):751–64.
83. Truong LD, Shen SS. Immunohistochemical diagnosis of renal neoplasms. Arch Pathol Lab Med. 2011;135(1):92–109.
84. Soares RR, Carlos CD, Andrade BAB R, Cunha JLS, Agostini M, et al. Oral amelanotic melanomas: clinicopathologic features of 8 cases and review of the literature. Int J Surg Pathol. 2021;29(3):263–72.
85. Peraza A, Gómez R, Beltran J, Amarista FJ. Mucoepidermoid carcinoma. An update and review of the literature. J Stomatol Oral Maxillofac Surg. 2020;121(6):713–20.
86. Hadj Saïd M, Ordioni U, Benat G, Gomez-Brouchet A, Chossegros C, Catherine JH. Clear cell odontogenic carcinoma. A review. J Stomatol Oral Maxillofac Surg. 2017;118:363–70.