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Review

Odontogenic carcinosarcoma: A systematic review

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ABSTRACT

The aim of this study was to integrate the available data published on odontogenic carcinosarcoma into a comprehensive analysis of their features, treatment and recurrence. An electronic search with no publication date or language restriction was undertaken in March 2018 in the following databases: Medline Ovid, PubMed, Web of Science, Scopus and LILACS. Eligibility criteria included publications having enough clinical, imaginological and histopathological information to confirm a definite diagnosis of the neoplasm. Data were evaluated descriptively and statistically using the MedCalc software. The Kaplan-Meier method was used for survival analysis. The systematic review detected nine articles from eight countries. Six cases with no age predilection occurred in male individuals complaining of painful swelling in the posterior mandible. Radiographically, the lesions were large, with expansive radiolucency and with ill-defined borders and seven cases were associated with preexisting odontogenic lesions. Radical surgery was the treatment of choice in the majority of cases. Recurrences (n = 6), metastasis (n = 4) and death (n = 4) were frequently observed in many cases. Odontogenic carcinosarcoma is a very aggressive neoplasm with a poor prognosis. This study provides knowledge that could help surgeons, oncologists, otorhinolaryngologists and oral maxillofacial pathologists with the diagnosis and management of these lesions.

Introduction

Odontogenic carcinosarcoma (OCS), an extremely rare malignant lesion of the jaws, was first included in the classification of the World Health Organization (WHO) in 1992 [1]. The overall architecture of this malignancy resembles ameloblastic fibroma (AF), of which both the epithelial and the mesenchymal components show morphological parameters of a malignant neoplasm [2]. The histopathological findings portray a distinct biphasic neoplasm with well-demarcated islands and cords of invasive malignant epithelial cells embedded in pleomorphic, hyperchromatic and hypercellular mesenchymal cells [3].

The terms ameloblastic carcinosarcoma and malignant odontogenic mixed tumor are synonyms of OCS. This malignancy can occur as a *de novo* lesion, arising from remnants originated from the embryologic process of odontogenesis or can develop from a preexisting odontogenic lesion [2,4]. Clinically, OCS has an aggressive behavior with high rates of recurrence [3,5–9] and frequent metastasis [5–7,9]. Some cases of OCS can be easily misdiagnosed as ameloblastic carcinoma due to failure to identify the malignant mesenchymal component [3].

To the best of our knowledge, no systematic review summarizing the information about the clinicoradiological appearance and adequate treatment for OCS has been conducted in the literature thus far. In this context, the objective of the present study was to integrate the available data published in the literature on OCS into a systematic review of the clinical, imaginological and histopathological features, treatment, recurrence frequency and survival of this condition.

Material and methods

Protocol and registration

This systematic review of case reports of OCS was conducted according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Statement [10]. A protocol was drafted and registration was carried out at the International Prospective Register of Systematic Reviews (PROSPERO) under the number CRD42018090515.

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Information sources and search strategies

Electronic searches without publication date or language restriction were undertaken in March 2018 in the following databases: Medline Ovid (Wolters Kluwer), PubMed (National Library of Medicine), Web of Science (Thomson Reuters), Scopus (Elsevier) and LILACS (Latin American and Caribbean Center on Health Sciences Information). The following search strategy was used for the databases: (odontogenic carcinosarcoma) OR (ameloblastic carcinosarcoma) OR (malignant odontogenic mixed tumor).

Hand searches were also conducted by cross-checking the reference lists of the included articles in order to identify publications that might have been missed during the searches in the electronic databases. Finally, a partial gray literature search was conducted using Google Scholar, limiting the search to the first 100 listed hits. The retrieved references were exported to the EndNote software (Thompson Reuters, New York, NY, USA). Duplicates were removed upon identification.

Eligibility criteria

Articles describing case reports or case series of OCS with enough clinical, radiological and histopathological information to confirm the diagnosis were included.

Exclusion criteria were experimental and *in vitro* studies, letters to the editor, and review articles, unless any of these publication categories had reported cases of OCS with enough clinical, radiological and histopathological information.

Study selection

Titles/abstracts of all references retrieved through the electronic searches were read independently by two review authors (L.F.S. and J.A.A.A.). If the title/abstract met the eligibility criteria, the article was included. The full text of the articles with titles/abstracts providing insufficient information for a clear decision was obtained. Following the full text assessment, the references that met the eligibility criteria were also included. Disagreements between L.F.S. and J.A.A.A. were solved upon discussion between two oral and maxillofacial pathologists with 20 years of experience (R.A.M. and T.A.S.).

Data extraction

For each study included, the following data, when available, were extracted on a standard form: authors' name, publication year, continent and country where the case(s) was(were) reported, number of case(s) reported, patients' age and sex, duration of the lesion before diagnosis, and anatomical location (maxilla/mandible). For anatomical location, data were detailed according to the following parameters: site (anterior: lesions in the incisor and canine region; posterior: lesions in the premolar/molar/retromolar/ramus/condyle region; anterior and posterior: lesions at both sites; and maxillary sinus). Clinical presentation and symptoms, radiological features (radiolucent/radiopaque/mixed), locularity (unilocular/multilocular) and image definition (well-defined/ill-defined), histopathological features, immunohistochemistry (IHC) test, lesion size (determined according to the largest diameter in centimeters), origin of lesion (preexisting lesion or *de novo*), treatment performed, recurrence (yes/no), metastasis (yes/no and location), follow-up period (months), and individual's status.

Quality assessment

Critical appraisal of the included articles was carried out by means of the Joanna Briggs Institute – University of Adelaide tool for case reports or case series [11]. The included articles were evaluated according to the following parameters: clear description of patient's demographic characteristics, medical history, current clinical condition, clear description of the propaedeutic, treatment, post-intervention clinical condition, adverse events, and lessons provided by the case report, i.e., histopathological analysis with representative images. For each parameter, the included article was rated as "yes", "no", "unclear" or "not applicable".

Data analysis

Statistical analysis of the data provided by the included articles was performed using the MedCalc software (MedCalc software bvba, Ostend, Flanders, Belgium). Overall survival was determined by survival analysis with the Kaplan-Meier method.

Results

Study selection

The electronic searches yielded 136 references. Following the removal of 40 duplicates, inclusion and exclusion criteria were applied to 96 references. Ten articles reporting ten cases of OCS were selected. However, since two articles described the same case report [7,12], we considered the one that featured the microscopic aspects and excluded the one that contained only cytological findings [12]. Therefore, nine articles were included in this systematic review [2–9,13]. No reference that met the eligibility criteria was identified in the hand searches or in the gray literature search. The flowchart in Fig. 1 depicts the search and the selection process.

Clinical features of individual studies

Two cases were reported in Japan [7,8]. Studies from Saudi Arabia [13], South Korea [2], France [9], Germany [5], United States [4], Venezuela [6] and Brazil [3] reported one case each. Patient age ranged from nine to 79 years and the mean age at diagnosis was 43.8 (± 25.3) years. Six (66.7%) patients were males and three (33.3%) were females. The mean age of affected males was 56.7 years and that of female patients was 18 years. The patients were affected in the first (n = 1), second (n = 1), third (n = 1), fourth (n = 1), sixth (n = 2), seventh (n = 2) and eighth (n = 1) decades of life. The posterior mandible was involved in seven (77.8%) reports. One (11.1%) case was in the maxilla, and one affected the posterior mandible and maxilla concomitantly. Duration of the tumor before diagnosis was provided in only one case (6 months) [4]. All individuals showed swelling as the clinical presentation. As regards symptoms, pain (six cases), numbness of the lip (two cases), discomfort (one case) and intermittent paresthesia (one case) were reported; in two cases, no information was available.

Radiolucency was the most common imaginological characteristic, appearing in 75% of the reports. Information on locularity was poorly provided. One case showed a bilocular image [3]. Regarding image definition, six cases (75%) were ill-defined lesions. Five articles [2,4,6,9,13] provided information about lesion size, which ranged from 4.1 to 8.0 cm. The mean size was 6.0 (± 1.4) cm. Histopathological features included malignant epithelial and mesenchymal components. IHC was performed in six studies. The markers used were AE1/AE3, CAM5.2, CKs (5, 6, 8, 14, 19, 17), Ki-67, p53, and vimentin (Table 1).

With respect to origin, two (22.2%) cases were reported as *de novo*, whereas seven (77.8%) involved preexisting odontogenic lesions such as ameloblastoma (n = 3), AF (n = 3) and cementomatous lesion/benign osteoblastoma (n = 1). Most cases were treated with radical excision. Recurrence was reported in six (75%) patients and metastasis in four (50%). Lung, lymph node, ribs and pelvis were the anatomical locations where recurrence and metastasis took place.

Seven reports provided information about the follow-up period. The mean duration of surveillance ranged from 15 to 65 months, with a mean of 33.4 (± 15.9) months. Four (57.1%) patients died. The complete information about the characteristics and results of individual