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AMELOBLASTIC CARCINOMA: A CASE REPORT AND UPDATE ON CLASSIFICATION SYSTEM OF ODONTOGENIC MALIGNANCIES

Pathology

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ABSTRACT

Ameloblastic carcinoma is a rare malignant lesion with characteristic behaviour that dictates a more aggressive surgical approach than that of a simple ameloblastoma. However, due to less number of cases reported till now in the literature and scarcity of documentations, reliable evidence of its biologic activity is currently unavailable. Because the lesion is usually found unexpectedly after an incisional biopsy of diagnosed case of Ameloblastoma or after the removal of a cyst, a guide to differential diagnosis is not usually useful. Most ameloblastic carcinomas are presumed to have arisen de novo with a few cases of malignant transformation of ameloblastomas. Although rare, these lesions have been known to metastasize, mostly to the regional lymph nodes or lungs. Here we reported a case of 62year old male and his clinical, radiographical and histological features has been discussed with an insight on the classification systems of odontogenic malignancies.

KEYWORDS

Ameloblastic Carcinoma, Malignant Ameloblastoma, Proliferative index

Case Report

A 62-year-old male patient reported to the Department of Oral and maxillofacial pathology with a chief complaint of recurrent swelling in the right lower jaw from 6 months. The swelling was slow growing in nature and other symptoms like pain, or paresthesia was not seen. The patient was present with no significant medical history. Patient gave history of curettage of the same swelling 2 years ago for which the diagnosis of follicular ameloblastoma was given.

Extraorally, while palpating the lesion the swelling was oval in shape, non-tender and soft in consistency. There was no local rise of temperature. Right submandibular lymph nodes were enlarged but non-tender on palpation and unattached to the overlying skin or underlying structures. Intraorally, large oval shape swelling present lingually on the right side of mandible extending from 46 till mid-ramus region sparing the condyle & coronoid process. Swelling was well defined in margins. On palpation the swelling was soft and non tender.

Radiographic findings revealed a well-defined multilocular radiolucency with scalloped borders extending from the distal aspect of the root of 46 till mid ramus region sparing condylar and coronoid process. The lower border of mandible is intact showed expansion with thinning of inferior cortex. Missing 47 and 45, resorption of distal root of 46 and retained 85 were also evident. (Figure 1).

Based on above clinical and Radiographic findings, a diagnosis of Ameloblastoma Carcinoma was considered.

Differential diagnosis

Odontogenic myxoma, Ameloblastic Fibroma, Malignant Ameloblastoma, Primary intraosseous carcinoma and metastatic malignancy were considered.

Hemimandibulectomy of right side of the mandible was done. Resected specimen along with level I lymph nodes was sent for histopathologic examination.

Macroscopic analysis showed a hemi mandibular specimen which is creamish brown in color having a cauliflower like exophytic growth on the anterosuperior surface along with small bits of soft tissue specimen. The gross specimen measured 6 × 6 × 5 cm and was hard in consistency.

Cortical perforation was seen on the lingual aspect of the left body of mandible.

Microscopic Analysis

For histopathologic examination, multiple tissue were taken from different areas of the resected specimen including all the surfaces, area of perforation, solid and the cystic areas. The surgical margins were obtained for marginal clearance. Level I lymph nodes were harvested from the specimen including both sub-mental and right and left submandibular lymph nodes that were soft to firm in consistency.

Microscopic examination showed odontogenic tumour islands were arranged in follicular, plexiform, growth patterns in a mature fibrous connective tissue stroma. At Focal areas, tumor cells were arranged in solid nest, long anatomizing cords and in islands.(Figure 2 a). Predominantly follicular growth pattern was seen in multiple sections. The peripheral cells in tumor islands were cuboidal to columnar in shape and arranged in a palisaded manner and shows reverse polarization. Tumor cells exhibited high mitotic rate of abnormal and atypical mitotic figures (2-3 mitotic figures per high-power field). (Figure 2 d). The tumor islands were showing other evident features of malignancy such as basilar hyperplasia, vesiculated and hyperchromatic nuclei, nuclear enlargement with granular, stippled nucleoplasm, cellular and nuclear pleomorphism, increased nucleo-cytoplasmic ratio.(figure 2 b, e). Central cells of follicles shows hypercellular angular cells which were loosely arranged resembling stellate reticulum like cells present in a less orderly pattern. Focal areas also show squamous metaplasia in the center of the follicles replacing stellate reticulum like cells and vascular invasion(figure 2 c, f) The connective tissue stroma is composed of mature collagen fibers with mild chronic inflammatory cells chiefly lymphocytes.

On the basis of previous diagnosis of Follicular ameloblastoma, final diagnosis of Ameloblastic Carcinoma was given. The anterior and posterior surgical margins were negative for tumor infiltration and all the harvested lymph nodes received were negative for tumor metastasis and showed only reactive hyperplasia.

Further to determine the aggressive nature of the lesion, molecular analysis was done using proliferative immunohistochemical marker PCNA (Proliferative cell nuclear antigen). Nuclear positivity was seen in tumor cells and Proliferative index was calculated which is more than 10 % indicating a aggressive nature of the lesion. (figure 3)

DISCUSSION

Ameloblastoma is the second most common odontogenic tumor of the jaws arising from dental embryonic remnants from the epithelial lining of an odontogenic cyst; dental lamina or enamel organ, stratified squamous epithelium of the oral cavity; or displaced epithelial remnants. [1]

The question of malignancy in ameloblastoma has been the subject of considerable discussion and controversy for many years and is extremely challenging to study due to their rarity, complexity in their definition, classification and their chance encounter.[2] A little argument or controversy exists in the number of terminologies given to carcinoma derived from ameloblastoma which can be described as malignant ameloblastoma, ameloblastic carcinoma, primary intra alveolar epidermoid carcinoma. Another major controversy is the differentiation made between terms malignant ameloblastomas and ameloblastic carcinomas whether they are the different names given to the same entities or they are two different neoplasms. [3]

Shafer in 1974 first describes the term ameloblastic carcinoma (AC) as a malignant epithelial neoplasm which is aggressive and proliferative in nature even in the absence of metastasis and Ameloblastoma that metastasizes is termed as Malignant Ameloblastoma. It is associated either with an existing ameloblastoma (carcinoma ex ameloblastoma) or arise as de novo ameloblastic carcinoma. Histologically AC resembles a conventional ameloblastoma having greater cytologic atypia, increased mitotic activity and exhibits basilar hyperplasia (expansion of the proliferative compartment of the epithelium) [4,5]. On contrary these findings are sufficient enough to designate it as "atypical ameloblastoma" or "proliferative ameloblastoma," instead of giving it as a carcinoma in the absence of other features like nuclear pleomorphism, perineural invasion, other histologic evidence of malignancy or are locally invasive with a evidence of spread to regional lymph nodes or distant sites, such as lung and bones. [6]

After Corio et al' reported eight cases of ACs from the U.S. Armed Forces Institute of Pathology, ameloblastic carcinoma is currently defined as “a malignant epithelial odontogenic tumor that histologically has retained the features of ameloblastic differentiation, yet also exhibits cytologic features of malignancy” [3]

In this article, literature is reviewed and data was extracted from PUBMED, EBSCO and SEER using International Classification of Diseases for Oncology (ICD-O) codes 9310/3 (metastasizing ameloblastomas) and 9270/3(ameloblastic carcinomas). According to the published article in PUBMED in last 10 years, a total of 148 cases of ameloblastic carcinoma has been reported seen predominantly in males with a male to female ratio of 1.4:1.

According to the study done by Rizitelli et al in 2015 where they collected data from 293 malignant ameloblastoma cases reported in the SEER database. They demonstrated that the overall incidence rate of malignant ameloblastoma was 1.79 per 10 million person/year. Both incidence rates and rate ratios increased with age. [7]

Moreover, According to Kar IB et in 2014, they have documented a literature of approximately 92 cases which were reported during the period of 1984 to 2012 in scientific literature predominately between 7 to 91 years. Males are more frequently affected with M:F ratio of 2.3:1. The most common site is mandible with about 56 reported cases, 35 cases in maxilla and in only one case arising from anterior skull base.[8]

The nosology of these tumors has varied over the past years since Various editions of WHO has done the histological typing of odontogenic tumors, jaw cysts and allied lesions. The WHO has published the initial consensus (1st edition 1971) on taxonomy of Odontogenic tumors with little variation in 2nd edition of WHO classification of odontogenic tumors (1992) where they had not included ameloblastic carcinoma as a separate entity in their classification system rather Malignant Ameloblastoma and PIOC were the sub categories.[9] Further in 2005 ameloblastic carcinoma was included as a separate entity and divides into three subtypes types. Corio et al. suggested that primary intraosseous carcinoma (PIOC) (in 1971 and 1992) represent a less differentiated, nonkeratinizing, form of ameloblastic carcinoma therefore distinction between two lesions was quite cumbersome and subjective. Therefore, in 2005, ameloblastic carcinoma was separated from PIOC, and then PIOSCC was used instead of PIOC to avoid taxonomic problems. [10] [11] There seemed little justification to divide such a rare tumor into three subtypes therefore update from the 4th edition of the WHO histological typing of odontogenic tumors in 2017 have continued it as a single entity. [12](Table 1)

Since years additional knowledge about these tumours has accumulated, initiating Elzay,(1982)

Slootweg and Muller (1984), Eversole (2002), to refine the classification, a classification that – by and large – the present authors have adopted (with suggested minor terminological changes).[13] (table 2)

Therefore Histomorphogenitically, two different AC entities may be recoqnized. One is characterized by lesions that initially demonstrate the morphology of a SMA but dedifferentiate over time. The second entity comprises those ACs that have malignant cytologic features de novo.[14,15]

Conclusion

Odontogenic malignancies are uncommon and diagnosing Ameloblastic carcinoma is rarest of rare diagnosis which falls into a completely different category. This lesion earns identity in 2005 when WHO considered it as a separate entity which can either arise as de novo or in existing Ameloblastomas exhibits histologic evidence of malignancy, regardless of whether it has metastasized. Thus, it has been emphasized that Ameloblastoma is a neoplasm of varied spectrum whose biologic behaviour ranges from benign at one end to malignancy at the other end.

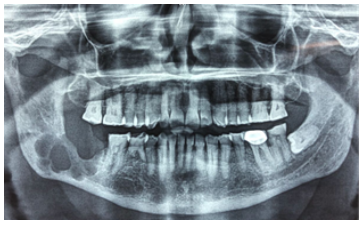

Figure 1: Orthopantomogram showing multilocular radiolucency in right lower jaw

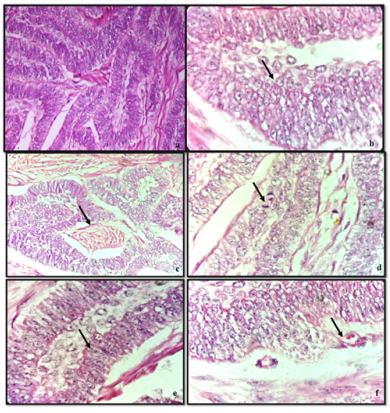

Fig 2(a)H and E showing the epithelial tumour islands arranged in the form strands and cords in a fibrous connective tissue stroma.(10x) (b) Tumor cells showing Basilar Hyperplasia (100x), (c) Tumor islands showing Squamous metyaplasia (100x), (d) Tumor islands demonstrates the presence of Mitotic figures (100x), (e) Tumors cells in odontogenic island showing granular stippled nucleoplasm (100x), (f) tumor islands showing Vascular invasion (100x).

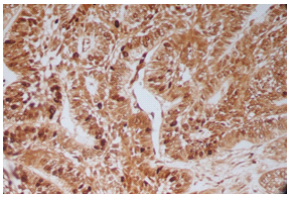

Fig 3 Nuclear Immunopositivity of PCNA depicting aggressive nature of Ameloblastic carcinoma

Table 1 : WHO Histological Typing of Odontogenic Malignancies [4,9,11]

1971 (1st edition)	1992 (2nd edition)	2005 (3rd edition)	2017 (4th edition)
a.Malignant ameloblastoma	1.2.1.1 Malignant ameloblastoma	1.Metastasizing, malignant ameloblastoma	1.Ameloblastic carcinoma
b.Primarv intra-osseous carcinoma	1.2.1.2 Primary intraosseous carcinoma	2. Ameloblastic carcinoma (a) Primary (b)Secondary(dedifferentiated), intraosseous (c)Secondary(dedifferentiated), extraosseous	2.Primary intraosseous carcinoma
c.Other carcinomas arising from odontogenic epithelium, including those arising from odontogenic cysts	1.2.1.3 Malignant variants of other odontogenic epithelial tumours	3.Primary intraosseous squamous cell carcinoma (PIOSCC) (a) PIOSCC solid type (b)PIOSCC derived from odontogenic cysts (c) PIOSCC derived from kerationizing cystic odontogenic tumor	3.Sclerosing odontogenic carcinoma
	1.2.1.4 Malignant changes in odontogenic cysts	4. Clear cell odontogenic carcinoma 5. Ghost cell odontogenic carcinoma	4. Clear cell odontogenic carcinoma 5. Ghost cell odontogenic carcinoma 6.Odontogenic carcinosarcoma

Table 2: Refined classification of Odontogenic malignancies [3,4]

Elzay (1982)	Slootweg and Muller (1984)	Eversole (2002)
Type 1: Arising from an odontogenic cyst	Type 1: PIOC ex odontogenic cyst	Type 1: PIOC ex odontogenic cyst
Type 2: Arising from an ameloblastoma	Type 2:	Type 2:
a. well differentiated (malignant ameloblastoma)	a. malignant ameloblastoma	a. malignant ameloblastoma (metastasizing malignant ameloblastoma)
b. poorly differentiated (ameloblastic carcinoma)	b. ameloblastic carcinoma, arising de novo, ex ameloblastoma or ex odontogenic cyst	b. ameloblastic carcinoma as primary AC, Dedifferentiated AC, peripheral AC
Type 3: Arising de novo	Type 3: PIOC arising de novo	Type 3: PIOC arising de novo
a. nonkeratinizing	a. nonkeratinizing	a. Nonkeratinizing
b. keratinizing.	b. keratinizing.	b. keratinizing.

Table 3: Practice points for diagnosis of Ameloblastic Carcinoma[1]

1. Associated with an ameloblastoma (carcinoma ex ameloblastoma) or histologically resembles an ameloblastoma (de novo ameloblastic carcinoma).
2. Greater cytologic atypia and mitotic activity than ameloblastoma
3. Basilar hyperplasia and an increased proliferative index
4. Nuclear pleomorphism, perineural invasion, or other histologic evidence of malignancy.
5. High proliferative index of proliferative markers in comparison to Ameloblastoma

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