AMELOBLASTIC CARCINOMA – REVIEW AND HISTOPATHOLOGY OF 5 CASES

Maya Ramesh [1] B. Sekar [2] S. Murali [3] Saramma Mathew [4] James Chacko [5] George Paul [6]

[1]Senior Lecturer [2]Reader [3]Professor and Head, [4]Ex Professor Emeritus,
Department Of Oral Pathology, Vinayaka Missions Sankarachariyar Dental College,
Vinayaka Missions University, Ariyanoor, Salem, Tamil Nadu
[5]Oral Surgeon, Penang International college, Malaysia, 6 Consultant Oral Surgeon, Sharon hospital, Salem)

Corresponding Author: Maya Ramesh,144, Andal Street, Thirumal Nagar, Alagapuram, Salem-636004.
0091 427 2444886 ®, 0091 9600918804(Mob), Email: mayaramesh96@gmail.com

Abstract

Ameloblastic carcinoma is a rare malignant lesion that occurs primarily in the mandible in a wide range of age groups. No sex or race predilection has been noted. Ameloblastic carcinomas have characteristic histopathologic features and dictate more aggressive surgical approach than that of ameloblastoma. It is difficult to differentiate between a benign and malignant odontogenic lesion. Only less than 60 cases have been published in the English literature between the years 1984-2007. We are presenting the review and histopathologic features of 5 ameloblastic carcinoma cases here which were reported to our institution in a short span of 5 years in order to throw more light on the clinical features, histopathology, treatment and prognosis of the rare lesion.

Keywords : Ameloblastic carcinoma, Ameloblastoma

Introduction:

Odontogenic carcinomas[1] are malignant odontogenic epithelial tumours that are of odontogenic origin and that bear little or no resemblance to odontogenic apparatus. The term ameloblastic carcinoma[2] was first used by Shafer in 1974. The term ameloblastic carcinoma is currently defined as 'a malignant epithelial odontogenic tumour that has retained the features of ameloblastic differentiation, yet also exhibits cytologic features of malignancy.'

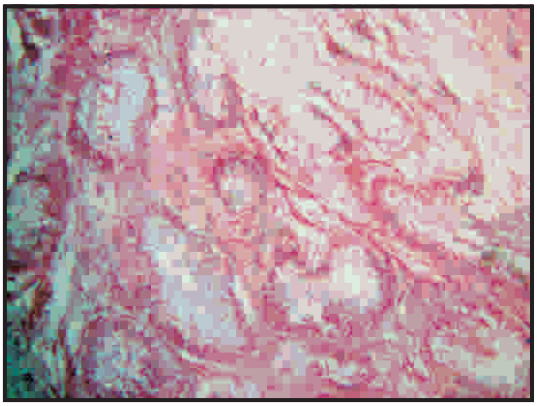
Ameloblastic carcinomas[3] seem to be more common compared to malignant ameloblastoma in the ratio 2:1. Ameloblastic carcinomas have been reported to metastasize to the lungs and to distant sites. Male to female ratio is almost 1.4:1. Lesions are located in the mandible and the maxilla in 66% and 34% of the patients, respectively.

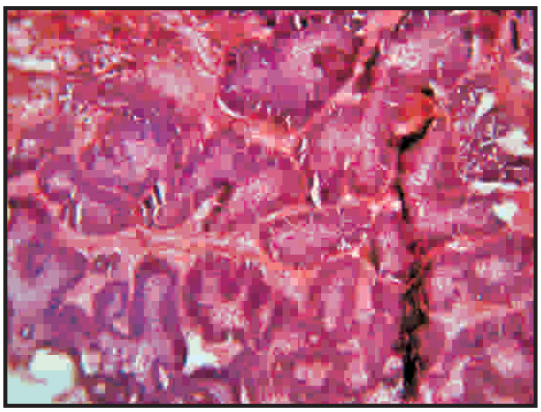
Ameloblastic carcinomas[3] may arise de novo, ex-ameloblastoma, or ex-odontogenic cyst. Most ameloblastic carcinomas are presumed to have arisen de novo, with very few cases of malignant transformation of ameloblastoma being apparent. Dedifferentiation tends to occur in ameloblastoma spontaneously or due to repeated surgical procedures or therapeutic radiation. Peripheral ameloblastic carcinoma arising from gingiva or alveolar mucosal epithelium is very rare.

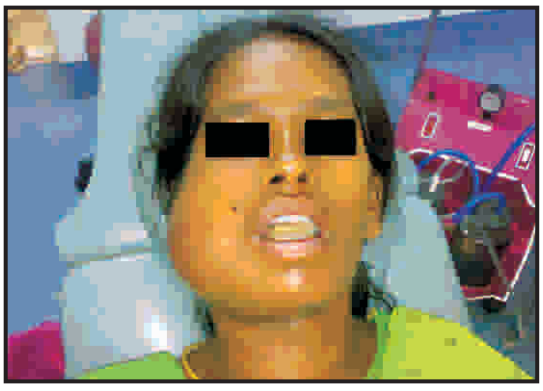
Little information is available on ameloblastic carcinoma, as only less than 65 cases have been published in the English literature between the years 1984-2007. This article reports five additional cases of ameloblastic carcinoma and outlines the clinical features, biological behaviour, histopathology, treatment protocol and the prognosis of this rare tumour.

Case Reports

Our series of patients with ameloblastic carcinoma consisted of three females and two males who visited our institution in the past six years. Two patients sought treatment in 2002, another in 2005 and the other two in 2007. All were in the age group of 25-40 years. All patients reported with swelling and two patients showed intra-oral ulceration. One 40 year old male patient was HIV positive. Three of the cases were provisionally diagnosed as odontogenic tumours, one as sarcoma and the other as a HIV / AIDS related tumour.







The Orthopantomograms revealed solitary large radiolucency in three of the cases, bilocular radiolucency in one case and an ill defined radiolucency in one case. Impacted teeth were present in three of the lesions which were displaced by the growing tumour. All the patients were treated in the Department of Oral and Maxillofacial Surgery of two major hospitals. The case history is given in Table No I. All the five were diagnosed as ameloblastic carcinomas by hematoxylin and eosin sections. The malignancy was confirmed by proliferation marker PCNA which showed almost 5-6 times the value of ameloblastomas.

Discussion

Some of the reported cases of ameloblastic carcinoma in the literature are shown in Table II. The review by various authors showed more number of cases in the mandible (60-80 %) especially in the posterior region. Four of my cases were also in the mandibular posterior area. Only 19 cases are reported in maxilla till date and one of my case was in maxilla. Corio[1] et al reported 1:1 male : female ratio while my cases showed 3:2 ratio. The mean age of my patients was 32 years while Corio[1] et al reported a mean age of 30 years . Only very less number of reported cases showed metastasis. All these five cases were diagnosed before metastases. All our cases were in dentulous arch like most of the reported cases. The patients showed the features of rapid growth and pain of the swelling. S Akrish[15] in his review reported multilocularity and ill defined borders radiographically. The radiographic features of my cases included destructive radiolucency with multilocularity in one case and impacted teeth in three cases.

The histopathologic features are shown in Table no III. A predominantly follicular growth pattern was seen in three cases and plexiform growth pattern was seen in two cases. Stellate reticulum like cells were minimal in all the five cases. Squamous metaplasia and keratin pearls were zresent in two cases, but three cases showed only squamous metaplasia. No osteoid, dentinoid or calcified tissues were present in any of the cases. Necrosis was present in three cases and cystic degeneration in two cases. Peripheral cells were multilayered in all cases with cuboidal in three cases, squamous in one case and cuboidal and columnar in one case. Reversal of polarity was absent in four cases and present in one case. Cells in the central areas were predominantly spindle shaped in one, spindle and squamous in two cases, squamous in one case and undifferentiated in one case. Hyperchromatism and pleomorphism with increased nuclear **C**ytoplasmic ratio were present in all the 5 cases. In other areas the nuclei were vesicular. Spindle cells were present in all the cases with two cases showing abundance. Clear cells were seen in two cases. Vascular invasion was present in all the five cases with only one case showing neural invasion. Infiltration into the surrounding connective tissue was seen in all the five cases, but infiltration of the malignant cells into the surface epithelium was present only in two cases.

Bruce and Jackson[3] stated the difficulty in differentiating the histologic appearance of primary intra alveolar carcinoma and the ameloblastic carcinoma. Corio et al[1] stated: "Although the primary intra-alveolar carcinoma and the ameloblastic carcinoma exhibit some clinical differences, their histologic features are similar enough to suggest a histogenetic relationship. It is possible that the primary intra-alveolar carcinoma may represent a less differentiated, usually non keratinizing form of ameloblastic carcinoma, both lesions being derived basically from odontogenic epithelial remnants". In our series, there was no ambiguity as all lesions showed clear evidence of ameloblastic carcinoma.

Among the differential diagnosis, carcinomas metastazing from distant primaries mimicking ameloblastic carcinoma and primary intra alveolar carcinoma are the important ones.

Treatment and Prognosis

Surgical resection was the primary modality of treatment in all the five cases. Hemimandibulectomy was performed in the four mandibular lesions and maxillectomy was done for the maxillary lesion. No neck dissection was performed in any of the cases. Surgical treatment decisions were made on the clinical background that all lesions were N0 with no evidence of metastasis. The patients showed good healing in the post operative period, justifying the treatment plan of oral surgeon.

The rarity and unusual behaviour make the prognosis of the ameloblastic carcinoma difficult. Recurrences and metastatic spread can be expected with inadequate treatment. Clear cell type of ameloblastic carcinoma is seen to have the worst prognosis. None of our series were of the clear cell type. Maxillary ameloblastic carcinomas have been stated to have more unfavourable prognosis.

The two patients treated in 2002 were followed up for a year and were then lost to follow up. The patient treated in 2005 was HIV positive and has not reported after his first post operative visit. The two of the patients treated in 2007 are currently being followed up with no signs of recurrence. Survival of ameloblastic carcinomas should be evaluated over a long period of time due to the possibility of loco-

Patient no	Age	Sex	Duration of symptoms	Site	Signs and symptoms
Case 1	35	Female	3 months	Right mandible- ramus and body	Swelling, Pain, Restricted mouth opening
Case 2	32	Female	5 months	Right mandible-ramus and body, Intraoral ulcer	Swelling, Pain, Ulceration
Case 3	40	Male	6 months	Right mandible -ramus and body	Swelling
Case 4	25	Male	3 months	Left maxilla posterior-alveolus and palate	Swelling, Intra oral ulceration
Case 5	26	Female	2 months	Left mandible-ramus and body, Intraoral ulcer	Large swelling, Pain

Table no: I Clinical Features of the 5 patients with Ameloblastic Carcinoma

NO	YEAR	AUTHOR	ARTICLE	Age	Sex and Race	Site
1	1987, Triple O	Corio[1] et al	8 cases of ameloblastic carcinoma	15-84 yrs. Mean-30 yrs	M: F=1:1,	7 in Mandible (4 posteriorly, 1anteriorly and 1 in coronoid) & 1 in maxilla.
2	1991, J of Oral Pathol & Med	Nagai[4] et al	Reviewed the literature- 46 cases of ameloblastic carcinomas after reclassifying the 69 reported cases of both malignant ameloblastomas and ameloblastic carcinoma.	50 yr	Male	Mandible
3	1995, J of laryngeal Otology	Lolachi[5] et al	Reported that there was a total of 34 cases of ameloblastic carcinomas in English Literature. And reported 12th case of ameloblastic carcinoma in maxilla	82 yr	White female	Right maxilla
4	1998, Annals Dent Univ Malaya	SP Khoo[6] et al	Reported a case with cervical node and pulmonary metastases.	59	Malay male	From the right to the left edentulous mandible
5	2000, Triple O	D P Cox[7] et al	Multiple recurrences of ameloblastoma, with subsequent malignant transformation presenting with malignancy-associated hypercalcemia.	25	Male	Left mandible

Table : II Review of Literature of Ameloblastic Carcinomas

6	2002, J Oral Maxillofac Surg	Jesus Sastre[8] et al	15th case of ameloblastic carcinoma of maxilla	40	White male	Right edentulous anterior maxilla
7	2003, oral Oncol	Kaan[9] et al	18th case of ameloblastic carcinoma of maxilla	72	Caucasian male	Right maxillary sinus
8	2003, Triple O	J Hall[10] et al and 3 pathologists	Reviewed 200 tumours of Mayo clinic and reported 11 cases of ameloblastic carcinomas.			5 maxillary and 6 mandibular
9	2003, Am J Otolaryngol	Rajiv Datta[11] et al	Reported a highly aggressive mandibular lesion with widespread bony metastases to the spine and long bones as well as liver and retroperitoneal lymph nodes	22		Mandible
10	2003, Oncology reports	Shigeto Kawauchi[12] et al	Reported a case of spindle cell ameloblastic carcinoma	67	Japanese Male	Right mandible
11	2006, Triple O	Ann Soomalnen[13] et al	Reported an ameloblastic carcinoma of mandible resembling odontogenic cyst in OPG	21	Caucasian Female	Left angle of the mandible
12	2007, Triple O	James[4] et al	Studied 14 archived cases of ameloblastic carcinoma. the treatment a nd follow up of these patients in Mayo Clinic.	16-63 yrs	10 Male and 4 female	6 Right mand, 2 Left mand, 3 Right max, 3 Left Max
13	2007, J Oral Maxillofac surg	S.J. Akrish[14]	Reviewed 37 cases from the literature and reported one new case of ameloblastic carcinoma.	15-84	25 Males and 13 Females	Ant and Post-Max- 1, Post Max-11, Mand-3, Ant, Post and ramus-3, Unspecified-mand-8, max-1
14	2007, J Oral Maxillofac Surg	Brent B. Ward[15] et al	Reported 19th maxillary case with review of literature	80 64	White male African American man	Left mandible Anterior maxilla
15	2007, Triple O	Adil[16]	Reported single case and reviewed 65 cases of ameloblastic carcinoma	90	male	Left Maxilla

Table : II Review of Literature of Ameloblastic Carcinomas

Sl. No	Feature	Case 1	Case 2	Case 3	Case 4	Case 5
1.	Growth pattern	Predominantly Plexiform	Predominantly Follicular	Predominantly plexiform	Predominantly follicular	Predominantly Follicular
2.	Central areas of tumour islands Stellate reticulum like cells Other types of cells in central areas	+ Spindle cells	+ Spindle cells predominantly And less squamous cells	+ Squamous cells and Spindle cells	++ Predominantly squamous	Absent Undifferentiated
3.	Types of cells in other areas Spindle cells	++	++++	++	++	+++
4.	Clear cells Ghost cells Peripheral cells-Type	- - Cuboidal multilayer	+ - Columnar in some areas and cuboidal in other	- - Squamous multilayer	- - Cuboidal multilayer	+ - Cuboidal multilayer
	Reversal of polarity of peripheral cells	Absent	Present in some areas	Absent	Absent	Absent
5.	Nuclear details	Pleomorphic with increased N/C ratio, Vesicular in some areas and Hyperchromatic in other areas	Pleomorphic with increased N/C ratio, Vesicular in some areas and Hyperchromatic in other areas	Pleomorphic with increased N/C ratio, Vesicular in some areas and Hyperchromatic in other areas	Pleomorphic with increased N/C ratio, Vesicular in some areas and Hyperchromatic in other areas	Pleomorphic with increased N/C ratio, Vesicular in some areas and Hyperchromatic in other areas
6.	Necrosis / Cystic Degeneration	Necrosis Present	Necrosis Present	Absent	Cystic degeneration Present	Both Present
7.	Infiltration of malignant cells into epithelium	Absent	Present	Absent	Present	Absent
8.	Connective Tissue Infiltration of malignant cells into connective tissue	Present	Present	Present	Present	Present
9.	Osteoid /Dentinoid / Calcification	-	-	-	-	-
10.	Squamous metaplasia / Keratin pearls	Both present	Both present	Squamous metaplasia present	Squamous metaplasia present	Squamous metaplasia present
11.	Vascular / Neural invasion	Vascular invasion present	Vascular invasion present	Vascular and neural invasion present	Vascular invasion present	Vascular invasion present

Table III Histopathologic Features of 5 patients with Ameloblastic Carcinoma (- means absent, + means slight, ++ means occasional, +++ means frequent and ++++ means dominant)

regional recurrences and metastases.

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