



# Low-grade spindle-cell ameloblastic carcinoma: report of an unusual case with immunohistochemical findings and review of the literature

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## ABSTRACT

Spindle-cell differentiation in ameloblastic carcinoma is a rare event. Although reported by many authors, it was first described as a separate entity in 1999 by Slater under the heading “low-grade spindle-cell ameloblastic carcinoma.” Here, we report a case of low-grade spindle-cell ameloblastic carcinoma arising in pre-existing unicystic ameloblastoma.

The patient, a 60-year-old Indian woman, had a large irregular swelling in the left mandibular region. Histologically, the lesion was composed of a large cystic cavity with an ameloblastomatous lining and areas showing spindle-cell proliferation. The spindle cells showed hyperchromatism, nuclear pleomorphism, and scattered mitotic figures. To our knowledge, 6 cases of spindle-cell ameloblastic carcinoma have been published to date, and this case appears to be the first reporting malignant transformation with spindle-cell differentiation in unicystic ameloblastoma.

## KEY WORDS

Spindle cells, ameloblastic carcinoma

## 1. INTRODUCTION

Ameloblastoma is a true neoplasm of enamel-type organ tissue that does not undergo differentiation to the point of enamel formation. It was very aptly described as being a tumour that is “usually unicentric, non-functional, intermittent in growth, anatomically benign and clinically persistent”<sup>1</sup>. It arises from dental embryonic remnants (possibly the epithelial lining of the odontogenic cyst), dental lamina or enamel organ, stratified squamous epithelium of the oral cavity, or displaced epithelial remnants<sup>2</sup>.

The question of malignancy has been a subject of considerable discussion and controversy for many years. Although ameloblastic carcinoma was recognized very early by others<sup>3-5</sup>, the World Health Organization (WHO) classifications of 1971<sup>6</sup> and 1992<sup>7</sup> did not include the term in the section on odontogenic

carcinomas. Only in the updated WHO classification of 2005 was ameloblastic carcinoma listed as one of the odontogenic malignancies<sup>8</sup>.

Ameloblastic carcinoma is defined as a rare malignant epithelial tumour that retains the histologic features of ameloblastic differentiation and yet also exhibits cytologic features of malignancy<sup>1</sup>. This malignant epithelial proliferation can be either carcinoma ex ameloblastoma or *de novo* ameloblastic carcinoma<sup>1,7</sup>.

Here, we describe a case of spindle-cell ameloblastic carcinoma in a 60-year-old woman, with details of clinical, radiographic, and unusual histologic features suggesting that the tumour probably arose in a pre-existing unicystic ameloblastoma. To our knowledge, only 6 cases of ameloblastic carcinoma with spindle-cell histology have been published<sup>4,9-11</sup>, and of those, only 2 were diagnosed as spindle-cell ameloblastic carcinoma<sup>12,13</sup>. This third published case appears to be the first spindle-cell ameloblastic carcinoma arising in a pre-existing unicystic ameloblastoma.

## 2. CASE DESCRIPTION

In March 2009, a 60-year-old woman presented in our department with a 19-year history of left mandibular swelling. She had first noticed a small swelling on the left side of the mandible for which she received surgical treatment in a government hospital in 1990, but no histology was done at that time. After 2 months, the swelling reoccurred, and the patient was again treated surgically, but she got no relief. The swelling gradually increased, reaching a size that had been causing the patient difficulty in eating and swallowing for 2–3 months before her presentation to us.

Extraoral examination revealed a large irregular swelling in relation to the body of mandible on left side, extending to involve the ramus of mandible on the same side and across the midline to involve the parasymphiseal and right-side body of the mandible (Figure 1). The approximate size of the swelling was 15×9 cm. The overlying skin was smooth and normal in color, with a shiny surface. A sinus opening was

seen in the submandibular region 4–5 cm from the midline on the left side of the chin. The swelling was non-tender, variable in consistency, nonfluctuant, non-compressible, and fixed to underlying structures. The submandibular lymph nodes on the side of the lesion could not be examined because of the extent of the lesion, and those on the other side were nonpalpable.

Intraoral examination was restricted, being that the mouth opening was compromised because of the extent of the swelling. On retraction of the lips, a single irregular ulcerated swelling that obliterated the mandibular labial and lingual vestibule was seen (Figure 2). The overlying mucosa was, in places, deep red in color. The right second premolar (non-carious) was the only tooth seen in the mandibular region. No sign of nerve involvement was present.

### 2.1 Radiographic Features

A panoramic view showed a multilocular radiolucent lesion mainly in the left-side body and ramus of the mandible, extending across the midline to involve the right parasymphiseal and anterior regions of the right mandibular body and ramus of the right side of the mandible. Destruction of the lingual cortex of the mandible in the affected area and of paracortex in some areas was seen.

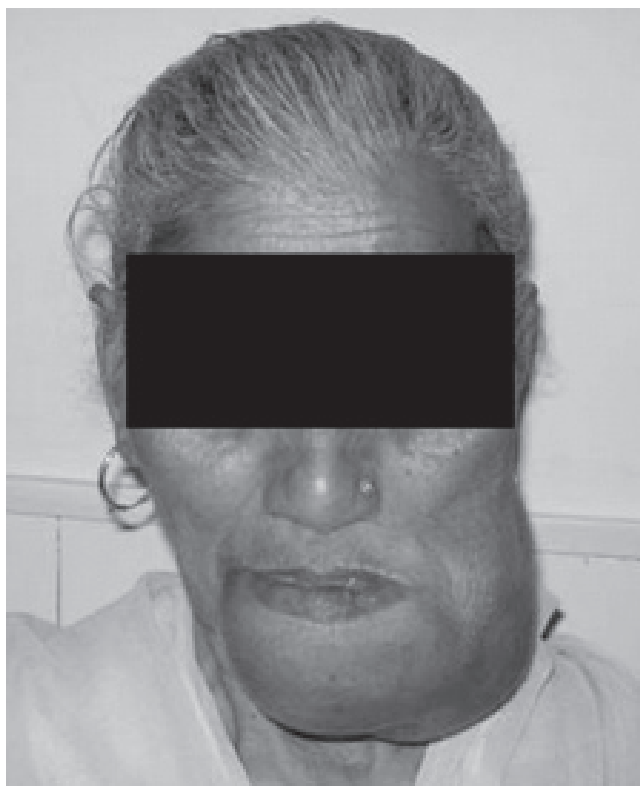


FIGURE 1 Ameloblastic carcinoma involving entire left side of the mandible and extending to the right side.

The computed tomography imaging report revealed a very large expansile multiloculated cystic lesion 99×93×93 mm (medial–lateral × anterior–posterior × superior–inferior) seen mainly in the left-side body and ramus of the mandible (Figure 3). The mass was seen hanging in submandibular area, involving submental and submandibular soft tissue. Superiorly, the mass extended into the oral cavity with destruction of the lingual cortex of the mandible and displacement of the tongue posteriorly, mildly compressing the airway in the oropharyngeal area.



FIGURE 2 Irregular ulcerated swelling in the mandibular region.

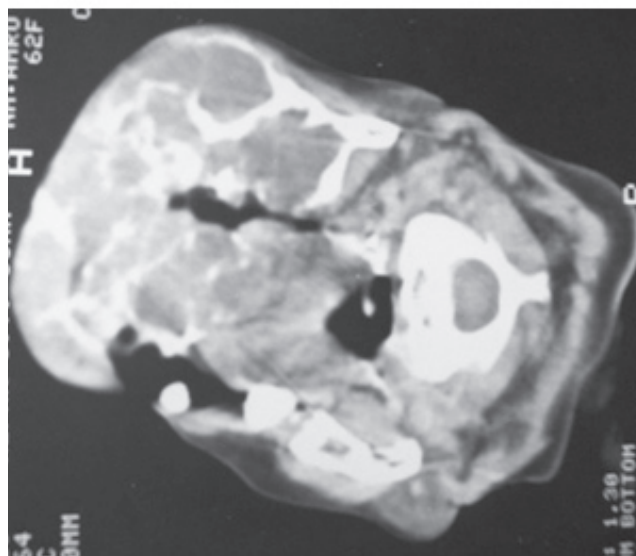


FIGURE 3 Computed tomography image showing large, expansile, multiloculated cystic lesion of the mandible.

## 2.2 Macroscopic Features

A hemimandibulectomy was done under general anesthesia, and the resulting specimen was received for histopathologic examination. The specimen was creamish white to brown in places and hard in consistency, measuring 14×12×10 cm. On gross inspection, it was found to be filled with large amount of blood-tinged fluid. Tissue for histopathology was taken from four representative sites (Figure 4).

## 2.3 Microscopic Features

Microscopically, the lesion consisted of a large cystic space lined with ameloblastomatous epithelium (Figure 5). The hyperchromatic columnar cells from the epithelial lining showed luminal growth. The tumour growth pattern occurred in cohesive sheets and nests, with peripheral palisaded columnar cells and central spindle-shaped cells. The proliferation was dominated by sheets of densely cellular spindle cells forming broad interwoven bands (Figure 6). The spindled nuclei were cytologically bland and had fine powdery chromatin and small nucleoli often located at the nuclear perimeter. Some spindled cells showed hyperchromatism and nuclear pleomorphism. Few mitotic figures were observed (counted as 2–3 mitoses in 5 high-power fields). Connective tissue showed dense collagen fibres with scanty inflammatory infiltrate. Some areas showed infiltration of the tumour cells into surrounding tissue. Immunohistochemically, these spindle-shaped cells were found to be nonreactive to cytokeratin and vimentin (data not shown).

The overall features were suggestive of a diagnosis of low-grade spindle ameloblastic carcinoma.

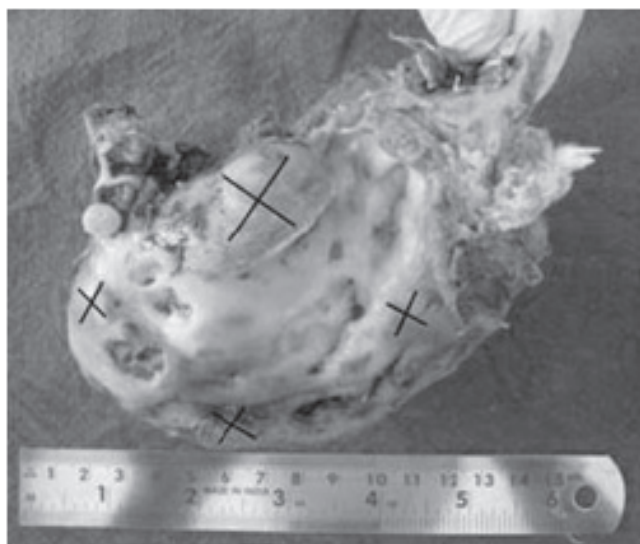


FIGURE 4 Macroscopic appearance of the mandible: creamish white to brown in places. The Xs are the areas from which sections were taken.

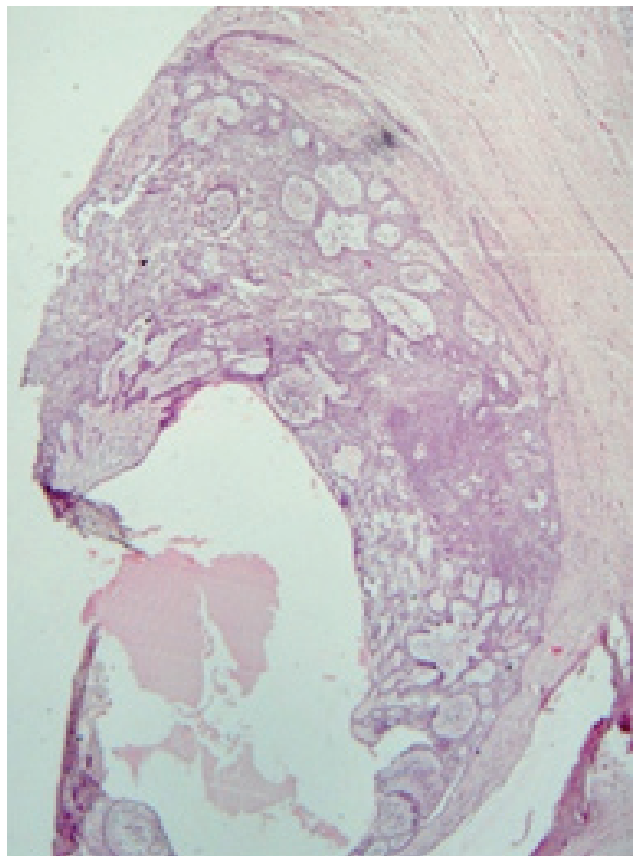


FIGURE 5 Photomicrograph showing cystic lumen lined with ameloblast-like cells. Hematoxylin and eosin stain, 4× magnification.

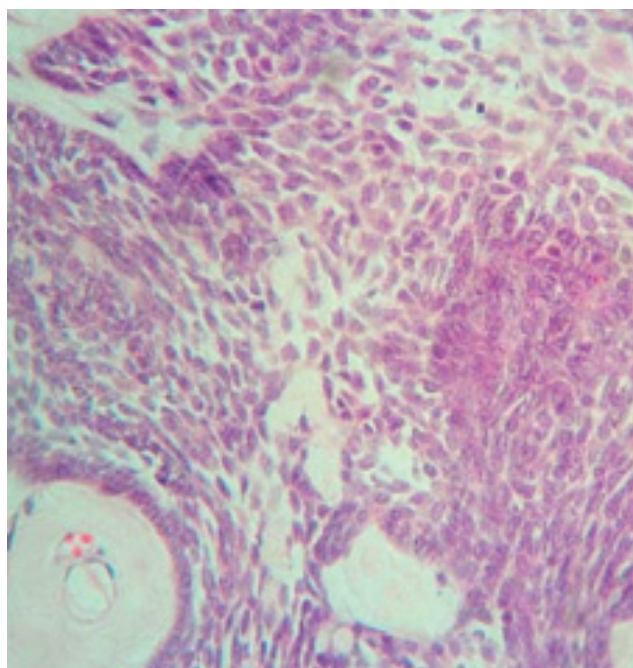


FIGURE 6 Photomicrograph showing hyperchromatism and nuclear pleomorphism in spindle-cell component. Hematoxylin and eosin stain, 40× magnification.

**3. DISCUSSION AND CONCLUSIONS**

Carcinomas derived from ameloblastomas have been designated by a variety of terms, including malignant ameloblastoma, ameloblastic carcinoma, metastatic ameloblastoma, and primary intra-alveolar carcinoma<sup>6,7</sup>. In 1974, Shafer introduced the term “ameloblastic carcinoma” to describe ameloblastomas in which histologic malignant formation occurs<sup>7</sup>. The term “metastasizing (‘malignant’) ameloblastoma” was applied to an ameloblastoma that metastasizes and yet reveals a benign or typical appearance in both the primary and the metastatic lesions<sup>8</sup>.

Elzay<sup>3</sup> in 1982 and Slootweg and Müller<sup>4</sup> in 1984 proposed classifications for ameloblastic carcinoma; however, it was only in the WHO’s 2005 histologic classification of odontogenic tumours<sup>8</sup> that ameloblastic carcinoma was included as an odontogenic carcinoma with histologic features of ameloblastoma, but with cytological atypia with or without metastasis. More recently, Kruse *et al.*<sup>5</sup> recommended a modified classification in which a primary ameloblastoma is followed by secondary metastasis with histopathologic features of malignancy and without evidence of malignancy in the primary location.

Ameloblastic carcinoma is a rare malignant tumour. Adebisi *et al.*<sup>14</sup> analyzed 197 Nigerian cases of odontogenic tumour and reported that 15 cases (7.6%) were malignant. Ameloblastic carcinoma was the most prevalent malignant tumour, with 11 cases (5.6%); primary intraosseous carcinoma, with only 3 cases (1.5%), was next. Spindle-cell ameloblastic carcinoma, a histologic variant of ameloblastic carcinoma, is extremely rare, and thus no epidemiologic or prognostic data are available in the literature. This variant is usually considered together with ameloblastic carcinoma. To date, only 6 cases with the histologic features of spindle-cell ameloblastic carcinoma have been reported in the literature. Ours is the 7th case.

In 2007, Akrish *et al.*<sup>15</sup> reviewed 37 cases of ameloblastic carcinoma in patients ranging in age from 15 years to 84 years (mean age: 52 years). The male:female ratio was 2:1. Table 1 shows the clinical data for reported cases of ameloblastic carcinoma showing spindle-cell differentiation. The male:female ratio is 5:3, and the age range is 20–75 years, with most cases occurring in the 6th decade of life. The case reported here involved a 65-year-old woman.

In the study by Akrish *et al.*<sup>15</sup>, 25 of the 37 tumours were located in the mandible, including 11 that extended from the posterior region to the ramus. Expansion or hard mass was the chief complaint, followed by pain or discomfort. Others signs and symptoms included trismus, dysphonia, and paresthesia<sup>11</sup>. Table 1 shows that the reported cases of spindle-cell ameloblastic carcinoma occur more often in mandible than in maxilla, for a ratio of 3:1. In our

TABLE 1 Reported ameloblastic carcinomas with spindle-cell differentiation<sup>a</sup>

Reference	Patient		Site	Duration	Diagnosis	Metastasis	Recurrence	Follow-up
	Age	Sex						
Slootweg and Müller, 1984 <sup>4</sup>	75	Male	Mandible	—	Intraosseous carcinoma with features of ameloblastoma	Not detected	Present	Died after 2 years, 2 weeks
Nagai <i>et al.</i> , 1991 <sup>9</sup>	50	Male	Mandible	11 Months	Ameloblastic carcinoma	—	Present	—
Infante-Cossio <i>et al.</i> , 1998 <sup>10</sup>	69	Female	Maxilla	3 Months	Ameloblastic carcinoma	Not detected	Absent	Free of disease 5 years postoperatively
Lau <i>et al.</i> , 1998 <sup>11</sup>	23	Male	Mandible	—	Ameloblastic carcinoma	—	—	Free of disease 5 years postoperatively
Kawauchi <i>et al.</i> , 2003 <sup>12</sup>	67	Male	Mandible	—	Spindle cell ameloblastic carcinoma	Lung	—	—
Ismail <i>et al.</i> , 2009 <sup>13</sup>	21	Female	Mandible	3 Years	Spindle cell ameloblastic carcinoma	—	—	—
Present case	65	Female	Mandible	19 Years	Spindle cell ameloblastic carcinoma	—	2 Months	Free of disease to time of writing

<sup>a</sup> The term “spindle-cell ameloblastic carcinoma” was introduced in 1999 by Slater<sup>21</sup>; cases reported before 1999 were therefore diagnosed as ameloblastic carcinoma only, even though they showed spindle-cell differentiation in the tumour mass.

case, the lesion was present in the left-side body and ramus of the mandible, extending across the midline to involve the body and reaching the ramus on the opposite side. Swelling and dysphagia were the chief complaints of the patient.

Lung is the most common site for distant metastasis, but regional lymph nodes and bones may be affected as well<sup>15,16</sup>. Interestingly, our patient had a 19-year history of tumour in the mandible with no lymph node involvement on clinical examination, highlighting the low-grade nature of the tumour and suggesting the possibility that the carcinoma may have arisen in a pre-existing benign lesion. Among previous reports, only 1 case of spindle-cell ameloblastic carcinoma metastasized to lung<sup>12</sup>.

Histologically, ameloblastic carcinoma exhibits features of conventional ameloblastoma, but with features of cytologic malignancy<sup>8</sup>. A follicular or plexiform ameloblastoma blends through a narrow transition zone with a hypercellular, poorly differentiated carcinoma that demonstrates sheets of disorderly, mitotically active small basaloid cells with dark nuclei<sup>11,17,18</sup>, larger squamoid or polygonal cells with pale vesicular nuclei<sup>16</sup>, or elongated spindle epithelial cells<sup>9,19,20</sup>. Histologically, the present case showed a large cystic cavity with an ameloblastomatous lining showing luminal growth. The luminal proliferation showed areas of spindle-cell fascicles. Those spindle cells showed hyperchromatism, nuclear pleomorphism, and scattered mitotic figures. In 1999, Slater proposed the term “spindle-cell ameloblastic carcinoma” for a group of odontogenic carcinomas with sarcomatoid spindle-cell components<sup>21</sup>. He proposed that spindle-cell ameloblastic carcinoma can be distinguished from odontogenic carcinosarcoma by a lack of the ameloblastic fibrosarcoma-like pattern in the spindle-cell ameloblastic carcinoma<sup>21</sup>. In the present case, no area in the examined sections showed any resemblance to ameloblastic fibroma.

Because the cyst cavity in this tumour was lined with ameloblast-like cells and because no areas showed the features of follicular or plexiform multicystic ameloblastoma, the carcinomatous changes might have arisen in a pre-existing unicystic ameloblastoma. To our knowledge, this case might be the first of ameloblastic carcinoma, spindle-cell variant, arising in a pre-existing unicystic ameloblastoma.

The spindle cells in the present case showed no immunohistochemical reactivity to either cytokeratin or vimentin. In 2004, Lau *et al.*<sup>11</sup> authored a case report on two ameloblastic carcinomas in which no immunoreactivity of the spindle cell component to vimentin or cytokeratin was found. Table II summarizes the results of special staining and immunohistochemistry for tumour spindle cells in the cases reported to date. In 2003, Kawauchi *et al.*<sup>12</sup> reported a case of spindle-cell ameloblastic carcinoma in which the epithelial carcinomatous cells were immunohistochemically positive for cytokeratin and negative

for vimentin. In 2009, Ismail *et al.*<sup>13</sup> also reported a case of ameloblastic carcinoma (spindle-cell variant) in which immunohistochemistry was positive for cytokeratin and negative for desmin and smooth muscle actin.

The differential diagnosis of a spindle-cell (sarcomatoid) ameloblastic carcinoma would include true sarcoma and the very rare variants of odontogenic sarcoma<sup>22</sup>. The odontogenic sarcomas would include ameloblastic fibrosarcoma, ameloblastic fibrodentinosarcoma, and ameloblastic fibro-odontosarcoma. The odontogenic sarcomas differ from our case in that they contain benign odontogenic epithelium similar to that seen in ameloblastoma or ameloblastic fibroma, some with odontogenic hard tissues of tooth structure, in conjunction with a malignant mesenchymal component. In contrast to this case of spindle-cell ameloblastic carcinoma, sarcomas will show immunoreactivity to vimentin.

Another entity that may be considered in the differential diagnosis is ameloblastic carcinosarcoma<sup>23</sup>. That tumour is defined as a mixed carcinomatous ameloblastic and malignant mesenchymal spindle-cell proliferation. The current case differs in its bland cytologic appearance and nonreactivity to vimentin, showing that the tumour cells are not of mesenchymal origin.

Differential diagnoses of sarcomatoid lesions include fibrosarcoma, neurofibrosarcoma, leiomyosarcoma, and monophasic synovial sarcoma. Negative immunohistochemical staining for vimentin excludes all the sarcomatous lesions.

TABLE II Summary of results for special staining and immunohistochemistry for spindle-shaped malignant cells

Reference	Result	
	Negative	Positive
Nagai <i>et al.</i> , 1991 <sup>9</sup>	Periodic acid-Schiff, alcian blue	
Lau <i>et al.</i> , 1998 <sup>11</sup>	Cytokeratin (AE1 and AE3), vimentin, desmin, actin, factor VIII, carcinoembryonic antigen	
Kawauchi <i>et al.</i> , 2003 <sup>12</sup>	Vimentin	Cytokeratin, 5q amplification of 5q13 genomic analysis
Ismail <i>et al.</i> , 2009 <sup>13</sup>	Desmin, smooth muscle actin	Cytokeratin
Present case	Vimentin, cytokeratin	

The biologic behaviour of spindle-cell ameloblastic carcinoma is not well characterized. Given the rarity of this tumour and the lack of a known association between its histologic patterns and its clinical course, it is rational to treat the lesion aggressively, with wide excision: that is, margins in all three dimensions should be negative (0.5–1.0 cm clear).

In the reported case, hemimandibulectomy was performed. No postsurgical complications or recurrences have been reported to date. Taking into account this patient's 19-year history, the clinical features, and the radiographic, histopathologic, and immunohistochemical findings, a diagnosis of low-grade spindle-cell ameloblastic carcinoma was made.

### 3. REFERENCES

1. Shafer WG, Hine MK, Levy BM. Cysts and tumors of odontogenic origin. In: Rajendran R, Sivapathasundharam B, eds. *Shafer's Textbook of Oral Pathology*. 5th ed. New Delhi: Elsevier; 2006: 416–20.
2. Avon SL, McComb J, Croke C. Ameloblastic carcinoma: case report and literature review. *J Can Dent Assoc* 2003;69:573–6.
3. Elzay RP. Primary intraosseous carcinoma of the jaws: review and update of odontogenic carcinomas. *Oral Surg Oral Med Oral Pathol* 1982;54:299–303.
4. Slootweg PJ, Müller H. Malignant ameloblastoma or ameloblastic carcinoma. *Oral Surg Oral Med Oral Pathol* 1984; 57:168–76.
5. Kruse ALD, Zwahlen RA, Grätz KW. New classification of maxillary ameloblastic carcinoma based on an evidence-based literature review over the last 60 years. *Head Neck Oncol* 2009; 1:31.
6. Pindborg JJ, Kramer IRH, Torloni H. *Histological Typing of Odontogenic Tumours, Jaw Cysts and Allied Lesions*. Geneva: World Health Organization; 1971: 35–6.
7. Ameloblastic carcinoma (primary, secondary [dedifferentiated] intraosseous; secondary [dedifferentiated] extraosseous). In: Reichart PA, Philipsen HP. *Odontogenic Tumors and Allied Lesions*. London, U.K.: Quintessence Publishing; 2004: 215–20.
8. Barnes L, Eveson JW, Reichart P, Sidransky D. *Pathology and Genetics of Head and Neck Tumors*. World Health Organization classification of tumours. No. 9. Lyon, France: IARC Press; 2005: 287.
9. Nagai N, Takeshita N, Nagatsuka H, et al. Ameloblastic carcinoma: case report and review. *J Oral Pathol Med* 1991; 20:460–3.
10. Infante-Cossio P, Hernandez-Guisado JM, Fernandez-Machin P, Garcia-Perla A, Rollon-Mayordomo A, Gutierrez-Perez JL. Ameloblastic carcinoma of the maxilla: report of 3 cases. *J Craniomaxillofac Surg* 1998;26:159–62.
11. Lau SK, Tideman H, Wu PC. Ameloblastic carcinoma of the jaws: a report of 2 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004;85:78–81.
12. Kawauchi S, Hayatsu Y, Takahashi M, et al. Spindle-cell ameloblastic carcinoma: a case report with immunohistochemical, ultrastructural, and comparative genomic hybridization analyses. *Oncol Rep* 2003;10:31–4.
13. Ismail SB, Zain RB, Yaacob HB, Abraham MT. Ameloblastic carcinoma (spindle cell variant). *Pathology* 2009;41:292–5.
14. Adebisi KE, Odukoya O, Taiwo EO. Ectodermal odontogenic tumours: analysis of 197 Nigerian cases. *Int J Oral Maxillofac Surg* 2004;33:766–70.
15. Akrish S, Buchner A, Shoshani Y, Vered M, Dayan D. Ameloblastic carcinoma: report of a new case, literature review and comparison to ameloblastoma. *J Oral Maxillofac Surg* 2007;65:777–83.
16. Dhir K, Sciubba J, Tufano RP. Ameloblastic carcinoma of the maxilla. *Oral Oncol* 2003;39:736–41.
17. Andersen E, Bang G. Ameloblastic carcinoma of the maxilla—a case report. *J Maxillofac Surg* 1986;14:338–40.
18. Cox DP, Muller S, Carlson GW, Murray D. Ameloblastic carcinoma ex ameloblastoma of the mandible with malignancy-associated hypercalcemia. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;90:716–22.
19. Yoshida T, Shingaki S, Nakajima T, Suzuki M, Fukushima M. Odontogenic carcinoma with sarcomatous proliferation: a case report. *J Craniomaxillofac Surg* 1989;17:139–42.
20. Tanaka T, Ohkubo T, Fujitsuka H, et al. Malignant mixed tumor (malignant ameloblastoma and fibrosarcoma) of the maxilla. *Arch Pathol Lab Med* 1991;115:84–7.
21. Slater LJ. Odontogenic sarcoma and carcinosarcoma. *Semin Diagn Pathol* 1999;16:325–32.
22. Zarbo RJ, Marunick MT, Johns R. Malignant ameloblastoma, spindle cell variant. *Arch Pathol Lab Med* 2003;127:352–5.
23. Slater LJ. Odontogenic malignancies. *Oral Maxillofac Surg Clin North Am* 2004;16:409–24.

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