Original paper

Primary ameloblastic carcinoma: literature review with case series

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Ameloblastic carcinoma (AC) is an extremely rare malignant odontogenic tumour arising from odontogenic epithelium. It was classified into primary type and secondary type. A previous study revealed that primary ameloblastic carcinoma cases were associated with more favourable prognosis than secondary cases. The aim of the present work was: to report the clinical, histopathological, immunohistochemical, and ploidy status, and therapeutic details of four cases of primary AC, and to review the literature with regard to clinical, follow-up, prognosis, histopathological, and immunohistochemical information of primary AC. The Medline database was searched using the term *ameloblastic carcinoma and primary type*. The review of English literature revealed that primary ameloblastic carcinoma favours the posterior mandible with profound male predilection and appears as an ill-defined radiolucency. Metastasis and invasion are more likely to occur in maxillary cases. The treatment of choice is wide surgical resection with or without cervical lymph node dissection. Adjuvant postoperative radiotherapy is beneficial in incomplete resection cases and advanced soft tissue invasion. The most specific diagnostic methods of AC, as concluded from review, are α-SMA in epithelial cells in conjunction with Ki-67 index value and SPF more than 11.5%.

Key words: ameloblastic carcinoma, case series, primary type, review.

Introduction

Ameloblastic carcinoma (AC) is considered a rare malignant epithelial odontogenic neoplasm, which shows the histological features of ameloblastoma (AB) with cytological atypia, regardless of the presence or absence of metastasis [1]. AC was classified into primary type and secondary type. The primary type (*de novo* carcinoma) is not preceded by simple AB, while the secondary type (carcinoma ex AB) is a malignant transformation of a pre-existing benign AB [2].

Casaroto *et al.* in 2012 correlated the demographic and phenotypic aspects of primary AC and secondary AC and found that secondary AC correlated with recurrence and mortality, suggesting it to be more aggressive than primary AC. They explained that result by the too short reported follow-up time of primary AC cases, which associated this tumour with more favourable prognosis when compared with cases of secondary AC [2]. Therefore, the aims of the present work were: to report the clinical, histopathological, immunohistochemical, and ploidy status and the therapeutic details of four cases of primary AC, and to review the literature with regard to clinical, follow-up, prognosis, histopathological, and immunohistochemical information of primary AC.

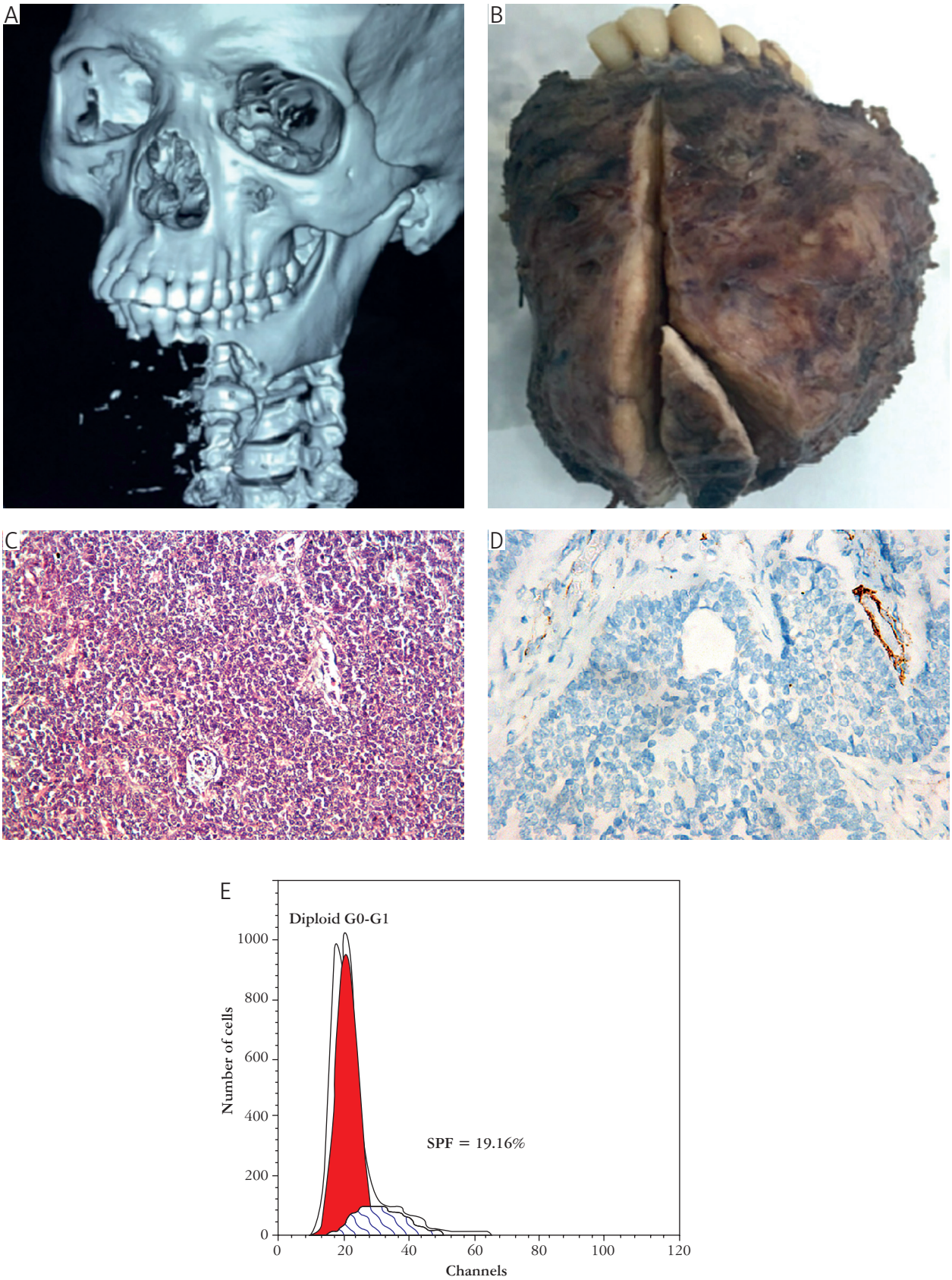

Fig. 1. Case I: A) constructed CT revealed an osteolytic multilocular radiolucency at anterior mandible. B) gross picture of the resected mandible showing well circumscribed soft tissue mass. C) histopathological examination of HE stained section revealed loss of architecture and atypia (200 ×). D) immunohistochemical staining of α-SMA revealed positivity of few stromal cells (400 ×). E) histogram showing diploidy and increased SPF

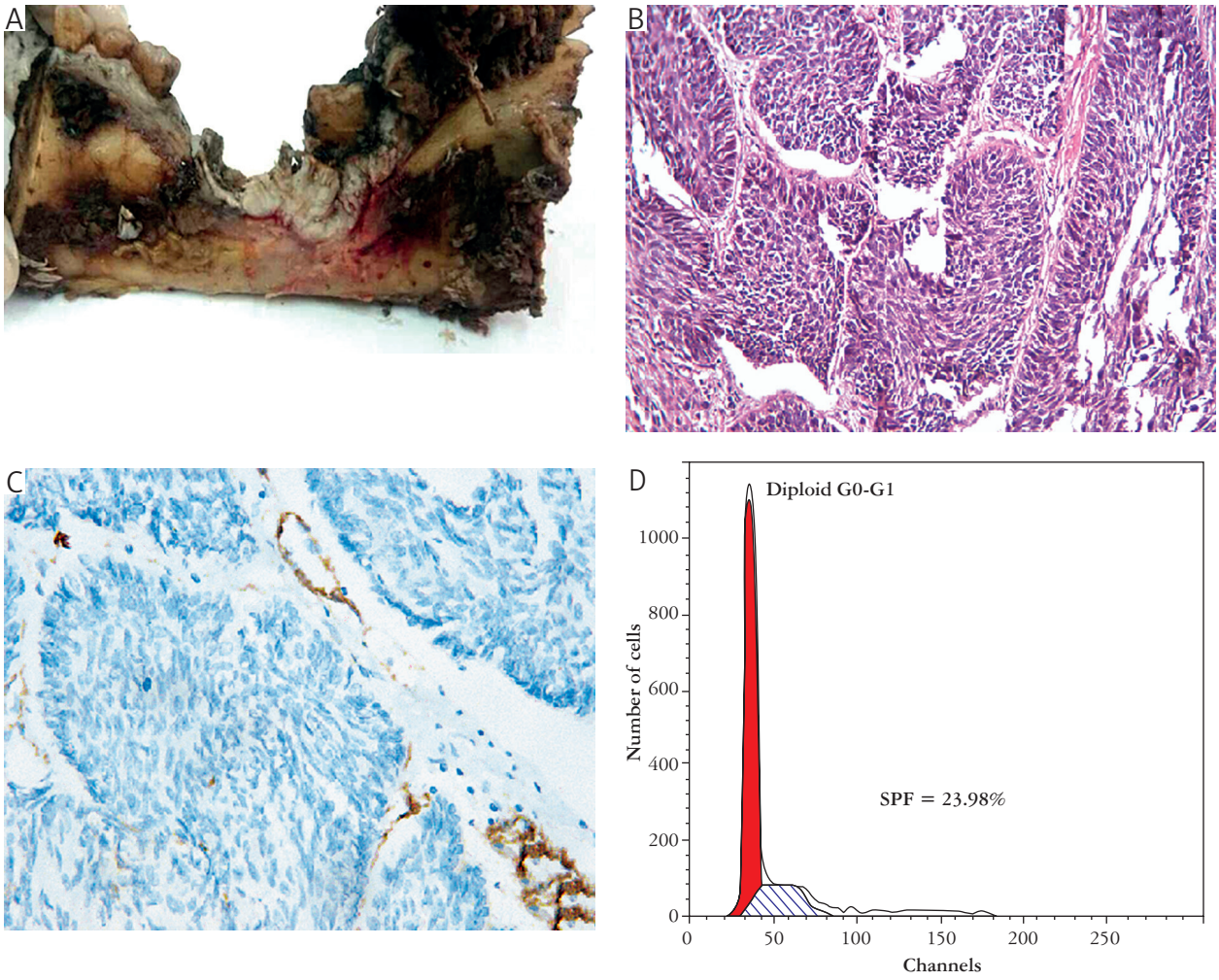

Fig. 2. Case II: A) Gross picture of the resected mandible showing perforation and soft tissue invasion. B) Histopathological examination of HE stained section revealed spindling of the central cells (200 ×). C) immunohistochemical staining of α-SMA revealed positivity of few stromal cells (400 ×). D) histogram showing diploidy and increased SPF

Case reports

Case I

A 25-year-old African male presented to our unit with paraesthesia of the lower lip and non-painful chin swelling. Incisional biopsy showed islands of odontogenic epithelium with ameloblastomatous character. The tumour cells showed frequent mitosis, pleomorphism, and loss of reverse polarity of ameloblast-like cells. Areas of necrosis and others with loss of follicular architecture were evident. Diagnosis of AC was reached (Fig. 1).

The surgical decision was marginal resection with placement of the reconstruction plate through an extra oral apron approach; level I and II neck lymph nodes were removed. Histological evaluation of the excised part confirmed the diagnosis of AC, with free margins and free lymph nodes. Upon flow cytometric (FCM) analysis of formalin-fixed paraffin-embedded (FFPE) sections, the tumour was diploid with an S-phase fraction (SPF) of 19.16%. Immunohistochemical staining with α-smooth muscle actin (α-SMA) revealed positivity of few stromal cells in close proximity to tumour islands and negative epithelial cells (Fig. 1). Follow-up of the patient for six months revealed no recurrence. The patient then travelled to South Africa.

Case II

A 29-year-old female presented with a non-healing socket after extraction of her lower left third molar three months previously. There was evident swelling both extra- and intraorally. CT scans revealed a multilocular radiolucency extending from the lower left second premolar up to the ipsilateral condyle with perforations medially and laterally.

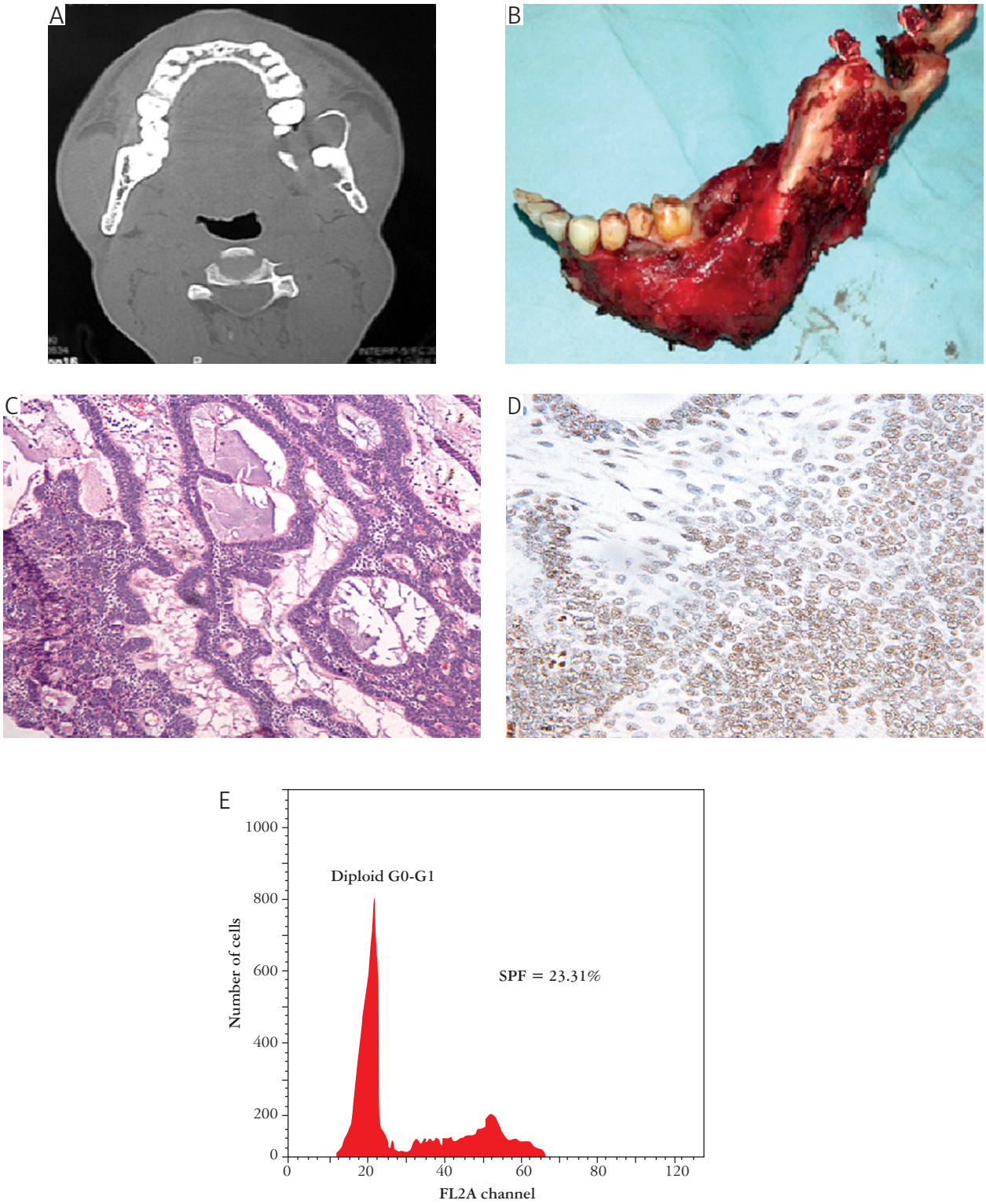

Fig. 3. Case III: A) CT revealed an osteolytic multilocular radiolucency at posterior mandible. B) gross picture of the hemimandible showing buccolingual expansion. C) histopathological examination of HE stained section revealed hyperchromatism and atypia (200 ×). D) immunohistochemical staining of α-SMA revealed positivity of epithelial and stromal cells (400 ×). E) histogram showing diploidy and increased SPF

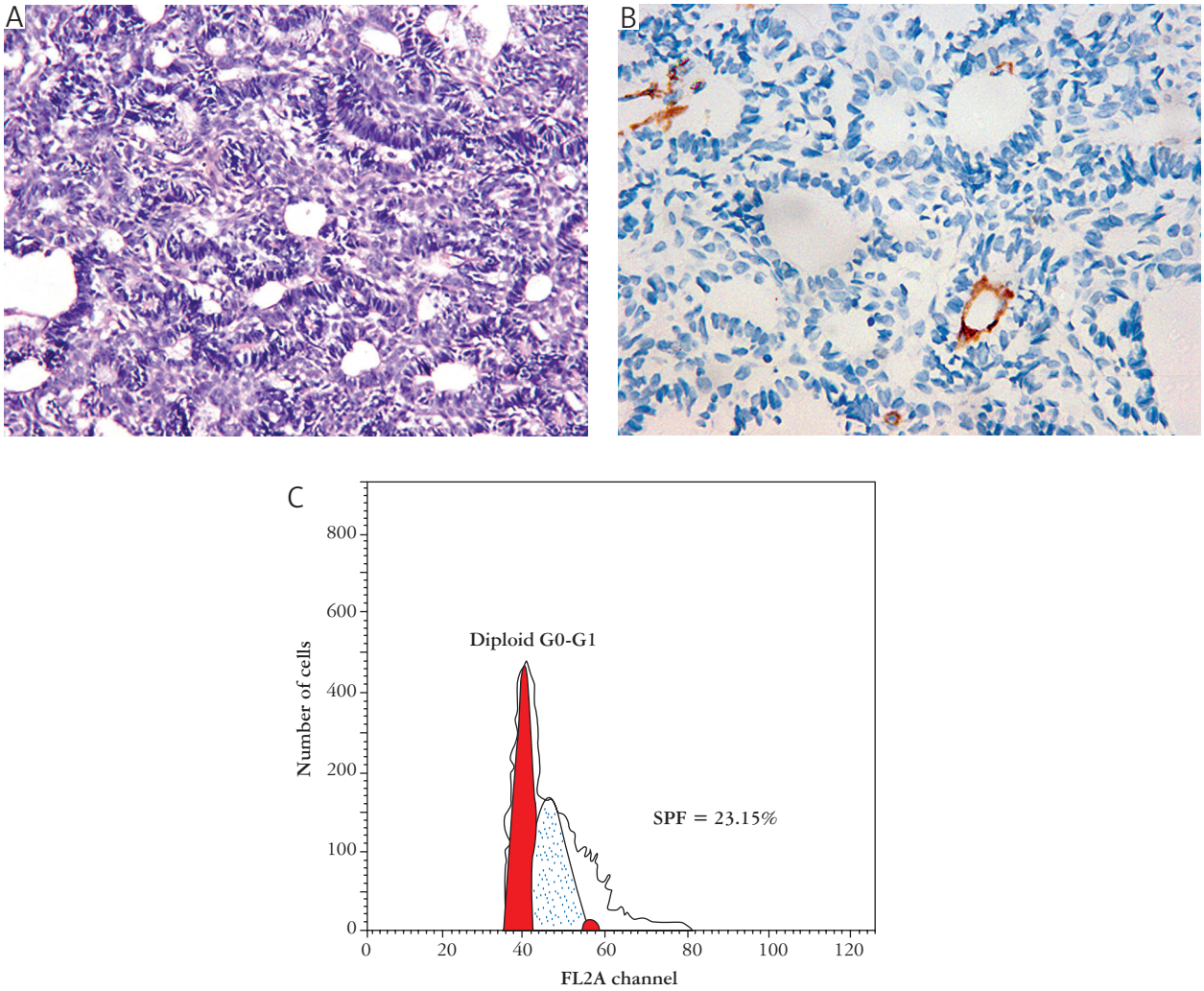

Fig. 4. Case VI: A) histopathological examination of HE stained section revealed loss of architecture, hypercellularity and atypia (200 ×). B) immunohistochemical staining of α-SMA revealed positivity of few stromal cells (400 ×). C) histogram showing diploidy and increased SPF

Incisional biopsy revealed histopathological features of AB. The surgical decision was resection of the left hemimandible with a safety margin of 1 cm; the deep part of masseter and lateral part of medial pterygoid muscle were included in the safety margin as a second anatomical barrier.

Histopathological examination of the excisional biopsy demonstrated dysplastic features, loss of nuclear polarisation and stellate reticulum like cells, nuclear pleomorphism, and increased mitosis. Moreover, sheets of spindle cells, areas of acanthomatous differentiation, and areas of necrosis were observed. Thus, a correction of the diagnosis to AC was performed. Tumour invasion was also observed in the masseter muscle, medial pterygoid, and the medial bony margin. The tumour was diploid with SPF of 23.98%. α-SMA immunohistochemical staining revealed negativity of tumour cells and positivity of stromal cells in close proximity to tumour islands (Fig. 2). The patient died two weeks after surgery.

Case III

A 25-year-old Nigerian male presented with a painful massive left mandibular swelling. Radiographic examination revealed a well-defined multilocular radiolucency related to an impacted third molar (Fig. 3). An incisional biopsy was performed, and it was diagnosed as AB. A hemi-mandibulectomy was planned, and the excisional biopsy revealed features of malignancy: increased mitosis, hyperchromatism, pleomorphism, and areas of necrosis, rendering a diagnosis of AC. FMC revealed diploid tumour with SPF of 23.31%. α-SMA staining showed strong nuclear positivity of epithelial cells (Fig. 3). Upon follow-up for six months, the patient was alive with no recurrence; the patient then travelled.

Case IV

A 62-year-old male patient presented with an exophytic mass appearing from a non-healing socket

Table I. Data analysis of clinical features, management, and outcome

	Age	Gender	Location	Radiograph	Metastasis	Management	Follow-up (months)	Outcome
Casaroto *et al.* 2012 [2]	66	M	Mand	Unilocular	No	Resection+ neck dissection	NS	NR
Chaisuparat *et al.* 2012 (1) [3]	20	M	Mand	NS	No	Resection	48	R
Chaisuparat *et al.* 2012 (2) [3]	24	M	Max	NS	No	Resection	NS	NS
Chaisuparat *et al.* 2012 (3) [3]	35	M	Mand	NS	No	Resection + postoperative irradiation	96	NR
Chaisuparat *et al.* 2012 (4) [3]	47	M	Max	NS	No	Resection	NS	NS
Chaisuparat *et al.* 2012 (5) [3]	35	F	Mand	NS	No	Resection	NS	NS
França *et al.* 2012 [4]	59	M	Max	Multilocular with cortical bone erosion,involving the nasal cavity and the eyeball, focal radiopacities	No	Hemimaxillectomy + radiotherapy	24	NR
Horváth *et al.* 2012 [5]	8	F	Mand	Unilocular with soft tissue invasion	Lung, pleura, bone marrow	Chemotherapy	8	Death
Jaitley and Sivapathasundharam 2013 [6]	45	M	Mand	Multilocular	No	NS	NS	NS
Roy and Garg 2013 [7]	27	M	Mand	Unilocular with cortical erosion	NS	Hemimandibulectomy	NS	NS
Fitzpatrick *et al.* 2014 [8]	37	M	Max	Multilocular mixed	No	Hemimaxillectomy	Half	Progressive healing
Kallianpur *et al.* 2014 [1]	24	M	Mand	Multilocular with cortical erosion	No	Resection + neck dissection	NS	NS
Kar *et al.* 2014 (1) [9]	21	M	Max	Unilocular with cortical erosion	No	Resection+postsurgical radiotherapy	15	NR
Kar *et al.* 2014 (2) [9]	70	M	Mand	Multilocular	No	Hemimandibulectomy	8	R and death
Koca *et al.* 2014 [10]	35	M	Max	Unilocular	No	Postoperative helical tomotherapy	12	Reduction of remaining lesion size
Kumaran *et al.* 2014 (1) [11]	25	F	Mand	Multilocular	No	Resection	32	NR
Kumaran *et al.* 2014 (2) [11]	34	M	Mand	Unilocular	Lymph node	Hemimandibulectomy+neck dissection	23	NR
Kumaran *et al.* 2014 (3) [11]	27	F	Mand	Unilocular	No	Hemimandibulectomy	39	NR
Kumaran *et al.* 2014 (4) [11]	60	M	Mand	Unilocular with cortical erosion	Lymph node	Hemimandibulectomy+neck dissection	Lost	NR

Table I. Cont.

Kumaran *et al.* 2014 (5) [11]	35	M	Mand	Unilocular with cortical erosion	Lymph node	Hemimandibulectomy+neck dissection+ wide excision of skin	24	NR
Kumaran *et al.* 2014 (6) [11]	55	M	Mand	Unilocular	No	Resection	26	NR
Li *et al.* 2014 (1) [12]	61	M	Mand	NS	No	Hemimandibulectomy	108	NR
Li *et al.* 2014 (2) [12]	40	M	Mand	NS	No	Hemimandibulectomy + soft tissue	96	NR
Li *et al.* 2014 (3) [12]	39	F	Mand	NS	No	Hemimandibulectomy	84	NR
Li *et al.* 2014 (4) [12]	42	M	Mand	NS	No	Hemimandibulectomy + soft tissueexcesion	72	NR
Li *et al.* 2014 (5) [12]	46	M	Mand	NS	No	Hemimandibulectomy	60	NR
Li *et al.* 2014 (6) [12]	32	M	Mand	NS	No	Hemimandibulectomy	60	NR
Li *et al.* 2014 (7) [12]	30	M	Mand	NS	No	Resection	48	NR
Li *et al.* 2014 (8) [12]	35	M	Mand	NS	No	Hemimandibulectomy	36	NR
Ansari *et al.* 2015 [13]	60	M	Max	Unilocular with cortical bone erosion	No	Hemimaxillectomy	Lost	NS
Uzawa *et al.* 2015 [14]	22	M	Max	unilocular	No	Resection	22	NR
Takahashi *et al.* 2015 [15]	58	M	Max	Multilocular invading base of skull	NS	Surgical resection + postoperative single fraction helical tomotherapy	19	NR
Kodati *et al.* 2016 (1) [16]	16	M	Mandibular gingiva	Saucerization of cortical bone	NS	Excision	NS	NS
Kodati *et al.* 2016 (2) [16]	33	F	Mand	Multilocular	Lymph node	Hemimandibulectomy	NS	NS
Kodati *et al.* 2016 (3) [16]	25	M	Mand	Unilocular with cortical bone erosion	NS	NS	NS	NS
Kiresur *et al.* 2017 [17]	32	F	Mand	Multilocular with perforation	NS	Hemimandibulectomy	14	NR
Our case (1)	25	M	Mand	Multilocular with cortical bone erosion	No	Resection + neck disection	6	NR
Our case (2)	29	F	Mand	Multilocular with cortical bone erosion and soft tissue invasion	NS	Resection	Lost	Death
Our case (3)	25	M	Mand	Multilocular with cortical bone erosion	No	Hemimandibulectomy	6	NR
Our case (4)	62	M	Max	Multilocular with cortical bone erosion	No	Hemimandibulectomy	Lost	NS

**NS – not specified, NR – no recurrence, R – recurrence, M – male, F – female, Max – maxilla, Mand – mandible*

Table II. Data analysis of histopathological features

	GP	PP	RP	SR	Mit	CCs	SCs	GCs	Ker	Nec
Casaroto *et al.* 2012 [2]	F	Yes	No	No	Yes	No	No	No	Yes	Yes
Chaisuparat *et al.* 2012 (1, 2, 3, 4, 5) [3]	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
França *et al.* 2012 [4]	NS	Yes	NS	No	Yes	No	No	No	No	Yes
Horváth *et al.* 2012 [5]	F	Yes	NS	Yes	Yes	No	No	No	No	Yes
Jaitley and Sivapathasundharam 2013 [6]	P	Yes	Yes	Yes	Yes	Yes	No	No	No	No
Roy and Garg 2013 [7]	F	Yes	NS	Yes	Yes	No	No	No	Yes	No
Fitzpatrick *et al.* 2014 [8]	F	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes
Kallianpur *et al.* 2014 [1]	P	Yes	NS	NS	Yes	No	No	No	Yes	NS
Kar *et al.* 2014 (1) [9]	F	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Kar *et al.* 2014 (2) [9]	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Koca *et al.* 2014 [10]	P	Yes	Yes	Yes	Yes	No	No	No	No	NS
Kumaran *et al.* 2014 (1, 2, 3, 4, 5, 6) [11]	F	Yes	NS	Yes	Yes	No	No	No	Yes	Yes
LI *et al.* 2014 (1, 2, 3, 4, 5, 6, 7, 8) [12]	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Ansari *et al.* 2015 [13]	F+ cribriform	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes
Uzawa *et al.* 2015 [14]	F	Yes	Yes	NS	Yes	No	Yes	No	No	NS
Takahashi *et al.* 2015 [15]	NS	NS	NS	NS	NS	No	No	No	Yes	Yes
Kodati *et al.* 2016 (1) [16]	F	Yes	No	Yes	Yes	No	No	No	No	No
Kodati et al, 2016 (2) [16]	P	Yes	No	Yes	Yes	No	No	No	Yes	NS
Kodati *et al.* 2016 (3) [16]	F	Yes	No	Yes	Yes	No	No	No	Yes	NS
Kiresur *et al.* 2017 [17]	F	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes
Our case (1)	F	Yes	No	Yes	Yes	No	No	No	No	Yes
Our case (2)	F	Yes	No	No	Yes	No	Yes	No	Yes	Yes
Our case (3)	P	Yes	No	Yes	Yes	No	No	No	No	Yes
Our case (4)	P	Yes	No	Yes	Yes	No	No	No	Yes	Yes
Total	18 F, 6 P	25	7	20	25	3	5	1	16	18

**NS – not specified; F – follicular; P – plexiform*

of an extracted upper 8. The lesion appeared as a maxillary well-defined multilocular radiolucency. Incisional biopsy revealed hypercellular strands of odontogenic epithelium with increased mitosis and loss of polarisation (Fig. 4). Areas of necrosis and areas of acanthomatous metaplasia were evident. A diagnosis of AC was reached. The tumour was diploid upon FMC analysis, with an SPF of 23.15%. α-SMA staining revealed negative epithelial cells and positive stromal cells in close proximity to tumoural cells (Fig. 4). The patient refused to undergo the surgery.

Material and methods

The Medline database was searched using the term *ameloblastic carcinoma* and *primary type*, and all cases of primary AC published in English between 2012 and 2017 were reviewed, including our cases. Data analysis including patient age, gender, location, radiograph, management, follow-up, and histopathological features of tumours have been recorded in Tables I and II.

Results

The review of English literature from 2012 to 2017 revealed 40 reported cases of primary AC, including our cases. The age ranged from (8-70 years) with a mean of 37.5 years. The male : female ratio was 4 : 1 and the ratio of occurrence of AC in mandible : maxilla was 3 : 1. The cases with reported radiographic picture were 27; 14 cases were unilocular

radiolucency (53.8%), 12 cases were multilocular lesion (46.15%), two of them were mixed radiolucent radiopaque lesions, and one case was peripheral AC showing saucerisation of the cortical bone. Cortical bone erosion was demonstrated in 13 cases (50%) and soft tissue invasion was detected in four cases (15.38%).

Metastatic status was reported in 34 cases: 29 cases with no metastasis (85%), four cases with lymph node metastasis (11.76%), and only one with metastasis in lung, pleura, and bone marrow. The management was reported in 38 cases; all of them treated with resection or hemi-mandibulectomy/hemi-maxillectomy with or without neck dissection, except one case which was treated with chemotherapy. Five cases were subjected to postoperative radiotherapy with two of them subjected to helical tomotherapy.

Follow-up was reported in 26 cases with a period of wide range (half-108 months) and with a mean of 34.5 months. Three cases were lost in follow-up. The outcome was non-specified in 11 cases. Twenty-five cases were alive with no recurrence (86.2%) and two cases showed recurrence (6.9%). Death was reported in three cases (10.34%).

The histopathological analysis revealed that 18 cases were follicular in pattern (75%), one of them with cribriform pattern. Six cases were plexiform (25%), and 16 cases were non-specified. Twenty-five cases showed peripheral palisading and increased mitosis; the remaining 15 cases were non-specified. Reverse polarity was seen in seven cases (46.66%), and 25 cases were non-specified. Twenty cases showed stellate reticulum-like cells (86.95%) and 17 cases were non-specified. Necrosis was detected in 18 cases (85.7%), but 19 cases were non-specified. Acanthomatous metaplasia were detected in 16 cases (61.5%), and 14 cases were non-specified. Clear cells were detected in three cases, spindle cells were detected in five cases, and one case showed ghost cells.

Discussion

AC is an extremely rare odontogenic tumour arising from odontogenic epithelium and accounts for approximately 1% of all jaw tumours [18]. The pathogenesis of AC is controversial, with many genes being associated with malignant transformation. Khojasteh *et al.* in 2013 observed methylation of p16 in AC [19]. Mitochondrial apoptosis-inducing factors have been considered to play a role in malignant transformation in AB [1].

Malignant odontogenic tumours show up-regulation of coronin gene and downregulation of STK19 (Serine/Threonine Kinase) [20]. García-Muñoz *et al.* in 2015 found that PITX2 expression, which participates in cell proliferation, cell migration, cell invasion, and tumour growth, is highly augmented in AC [21].

Similar to AB, the most common site of AC is the posterior mandible [2]. Painful swelling, numbness of lower lip, rapid growth, cortical bone expansion with erosion, perineural invasion, and mucosal ulceration are the typical clinical manifestation of AC [5]. The most common radiographic picture of AC is an ill-defined radiolucency either unilocular or multilocular [11]. Mixed lesions seem to be related to maxilla. Bone erosion was seen in half of the lesions; however, soft tissue invasion is uncommon in primary AC. Maxillary lesions were more aggressive, with invasion to the nasal cavity, eyeball, or base of the skull. Peripheral AC is extremely rare, causing saucerisation of cortical bone [16]. Radiographic differential diagnosis of AC includes odontogenic keratocyst, odontogenic myxoma, AB, and calcifying epithelial odontogenic tumour [11].

Metastasis in AC is infrequent (15%), mainly to regional lymph nodes or lung, originally believed to be due to aspiration from the oral lesion rather than a true hematogenous or lymphatic spread. Few cases have reported metastasis to the brain, bone marrow, and liver [9]. Zwahlen *et al.* reported a case with histologically proven myocardial metastasis of a maxillary malignant AB [22].

AC shows the architectural features of AB with cellular dysplasia, such as: pleomorphism, hyperchromatism, bizarre mitosis, and altered nuclear/cytoplasmic ratio. Squamous metaplasia and keratin pearl formation could be detected in many cases (61.5%). In the second place, spindling of the cells was reported in five cases, including our case. Clear cells detected in three cases, and only one case showed ghost cells resembling ghost cell odontogenic carcinoma.

Histologically, AC should be differentiated from primary intraosseous carcinoma that lack the peripheral palisading and stellate reticulum. Furthermore, this lesion tends to resemble squamous odontogenic tumour, which also lacks stellate reticulum, peripheral palisading, and cytologic atypia [11]. Ameloblastic carcinoma mimics histologically high-grade mucoepidermoid carcinoma (mucicarmine positive) and metastatic carcinoma to the jaws [9]. Spindle cell variant of AC should be differentiated from odontogenic sarcoma and ameloblastic carcinosarcoma; spindle cell areas are negative for vimentin and positive for cytokeratin [1].

Flowcytometric analysis of our cases revealed diploidy of all tumours with a mean SPF of 22.4%, which indicates hyperactive proliferation. These results were in accordance with the previous work of Bello *et al.*, who, in 2009, examined the ploidy of AC and found that all the cases were diploid. They explained that result by the presence of excessive cell debris in paraffin-embedded sections, which may have hidden

small aneuploid peaks [18]. Furthermore, Mahmoud *et al*., in 2017 investigated the diagnostic accuracy of flow cytometric analysis in AC and found that all the examined tumours were diploid with a mean SPF value of 14.05%. They determined the cut off value of SPF as 11.5% [23].

Many proliferation markers had been used to diagnose AC, especially, Ki-67, PCNA, and MCM proteins. Bello *et al.*, in 2009 found that Ki-67 labelling index in AC is three times that of AB [18]. Maya *et al.* in 2012 found that PCNA values of AC were almost five times the value of AB [24]. Casaroto *et al.* in 2012 found that the mean Ki-67 in AC was 42.45% [2]. Bologna-Molina *et al.* in 2013 studied PCNA and Ki-67 expression in AC and found that the mean proliferation index of AC using Ki-67 was 48.7%, and while using PCNA it was 93.3%, significantly higher than AB. Furthermore, they found that Ki-67 was a more specific marker for the proliferation of ameloblastic tumour cells [25]. Carreón-Burciaga *et al.* in 2015 found that Ki-67, MCM2, and MCM3 expression levels were higher in AC than in AB, which indicates aggressive, invasive, and metastatic neoplasm [26].

Among the apoptosis regulators, Bcl-2 expression in AC was investigated by Kallianpur *et al.* in 2014 and revealed strong positivity [1]. Furthermore, Casaroto *et al.* in 2012 investigated the expression of P53 and Bcl-2 in AC and revealed strong positivity [2]. Among the differentiation markers, Ansari *et al.* in 2015 found negative expression of CK19 in AC, while Uzawa *et al.* (2015) found positive expression of vimentin in AC epithelial cells, which indicates dedifferentiation of epithelial cells [13, 14].

Grewal and Sethi in 2014 found that AC showed a significantly higher nuclear expression of Autocrine Motility Factor Receptor in the neoplastic epithelial cells when compared to benign AB, which plays a role in cell motility [27].

Lei *et al.* in 2014 found that diffuse nuclear staining of sex determining region-Y-related high-mobility group box 2 (SOX2) is suggestive of malignant ameloblastic neoplasm [28]. Kamath *et al.* in 2010 found decreased expression of syndecan-1 in AC when compared to various ABs, which indicates aggressiveness [29].

In accordance with Roy and Garg (2013) and Ansari *et al.* (2015), α-SMA immunostaining in our patients revealed only one case with positivity in epithelial cells and stromal cells in close proximity to epithelial cells; the other three cases showed positivity in stromal cells only [7, 13]. The immunoreactivity of stroma is due to the emergence of myofibroblasts caused by the release of TGFβ1 and PDGF from neoplastic cells during the invasion process [7]. Myofibroblasts promote epithelial-mesenchymal transition, which is essential for tumour invasion and metastasis causing immunoreactivity of α-SMA in epithelial cells [6].

Bello *et al.* in 2009 found strong positivity of α-SMA within the tumour islands (in both peripheral and central cells) [18]. Furthermore, Kamath *et al.* in 2010 found definite positivity of α-SMA in stroma in close approximation with the epithelial islands and in the stellate reticulum like cells [29]. Safadi *et al.* in 2016 found that α-SMA expression in epithelial islands provided 100% specificity to favour a diagnosis of AC versus Ki-67 with a specificity of 95% [30].

Furthermore, histochemical staining using Ag-NOR was investigated in AC vs. AB by Kamath *et al.* (2010), Prasanna *et al.* (2014), Da Silva *et al.* (2016), and Mahmoud *et al.* (2017), who found that the mean ANOR count/cell in AC was more than 3 dots/cell, which is twice that of AB [29, 31, 32, 23].

The treatment of choice for AC includes wide surgical resection with 2-3 cm of bony margins with or without cervical lymph node dissection [2]. Various chemotherapeutic agents have been used, including cisplatin, cyclophosphamide, carboplatin, paclitaxel, doxorubicin, methotrexate, prednisone, bleomycin, 5-fluorouracil, and dacarbazine, with varying degrees of response [10]. Horvath *et al.* in 2012 lost an AC patient with pulmonary metastasis, who was treated with chemotherapy, but it may have been due to the advanced stage of disease [5].

In incomplete resection cases and advanced soft tissue invasion, adjuvant postoperative radiotherapy may be considered as a treatment option. This management has been reported in many cases with patients alive and free of disease [3, 4, 9]. Koca *et al.* (2014) used postoperative helical tomotherapy for a patient with incompletely resected maxillary AC and found reduction of remaining lesion size [10]. Furthermore, Takahashi *et al.* (2015) managed a patient with maxillary AC invading the base of the skull with surgical resection and postoperative single fraction helical tomotherapy, and the patient found alive and free of disease [15].

The survival rate of AC depends on medical background, local recurrence, and regional or distant metastasis. Maxillary AC has a worse prognosis than mandibular lesions due to rapid growth and extension into sinuses, orbit, base of the skull, and other vital areas nearby [1].

Conclusions

To sum up, primary AC is a rare malignant epithelial odontogenic tumour that favours the posterior mandible with profound male predilection and appears as an ill-defined radiolucency. Metastasis and invasion are more likely to occur in maxillary cases. The treatment of choice is wide surgical resection with 2-3 cm of bony margins with or without cervical

lymph node dissection. Adjuvant postoperative radiotherapy is beneficial in incomplete resection cases and advanced soft tissue invasion. The most specific diagnostic method of AC, as concluded from review, is α-SMA in epithelial cells in conjunction with Ki-67 index value and SPF more than 11.5%.

The authors declare no conflict of interest.

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