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RESEARCH ARTICLE

Clinicoradiological spectrum of primary aneurysmal bone cysts of the maxillofacial region: A series of 31 cases

[1]Chané Smit, [1]Liam Robinson, [2]Elena Roman Tager, [2]Ana Luiza Oliveira Corrêa Roza, [3]André Caroli Rocha, [2]Alan Roger Santos-Silva, [1,2]Pablo Agustin Vargas, [4]Mário José Romañach, [1,5]Felipe Paiva Fonseca, [6]Román Carlos and [1]Willie FP van Heerden

[1]Department of Oral Pathology and Oral Biology, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa; [2]Department of Oral Diagnosis, Piracicaba Dental School, University of Campinas (UNICAMP), Piracicaba, Brazil; [3]Medical School, Clinics Hospital, University of São Paulo (USP), São Paulo, Brazil; [4]Department of Oral Diagnosis and Pathology, School of Dentistry, Federal University of Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil; [5]Department of Oral Surgery and Pathology, School of Dentistry, Federal University of Minas Gerais (UFMG), Belo Horizonte, Brazil; [6]Pathology Section, Centro Clínico de Cabeza y Cuello/Hospital Herrera Llerandi, Guatemala City, Guatemala

Objectives: The aim of the current study was to analyse the demographic, clinical and radiological features of primary aneurysmal bone cysts (ABCs) involving the maxillofacial region.
Methods: Histologically confirmed cases affecting the maxillofacial region were retrospectively reviewed over a 21-year period (2000–2021). Cases were collected from the archives of five Oral Pathology laboratories from three countries: South Africa, Guatemala and Brazil. The information was analysed, with emphasis on the clinical and radiological spectrum.
Results: Following the inclusion criteria, a total of 31 cases of primary ABCs were included in the study. A nearly equal male-to-female distribution was seen, with ABCs occurring in males at an earlier age compared to females. Localised swelling was the main clinical presentation. ABCs had a mandibular predominance, particularly in the posterior regions. All ABCs presented as blow-out expansile well-demarcated radiolucent lesions with the majority having a multilocular appearance. Cortical expansion was seen in 91% of cases with loss of cortical integrity being common (78%).
Conclusion: Primary ABCs involving the maxillofacial region are extremely rare with the majority of current published literature consisting of isolated case reports. The current study is the first large series detailing the radiological features.
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Introduction

Aneurysmal bone cysts (ABCs) were first reported by Jaffe and Lichenstein in 1942.[1] ABCs are pseudocystic expansile lesions that histologically have no epithelial lining and contain multinucleated giant cells with areas of haemorrhage.[2] The fourth edition of the World Health Organisation (WHO) Classification of Head and Neck Tumours categorise primary ABCs as cystic neoplasms that contain fibrous septae separating numerous blood-filled spaces.[2]

ABCs have different proposed pathogenic mechanisms and can occur as primary neoplastic lesions or secondary reactive lesions in conjunction with pre-existing pathology. Primary ABCs are associated

Correspondence to: Dr Chané Smit, E-mail: chane.smit@up.ac.za

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with mutations in oncogenes that are not detected in secondary ABCs, supporting a different pathogenic mechanism.[3] The mesenchymal neoplastic nature of primary ABCs is characterised by genetic abnormalities in the osteoblast cadherin 11 gene (*CDH11*) that results in the upregulation of the ubiquitin protease *USP6* gene transcription. These alterations have been detected in two-thirds of primary ABCs and were absent in secondary ABCs.[3] Since its initial description in ABCs, other entities including nodular fasciitis, myositis ossificans, giant cell lesion of the small bones, fibro-osseous pseudotumour of digits, and some fibromas of tendon sheath have been added to the list of *USP6*-rearranged lesions.[4] Secondary ABCs of the jawbones most commonly occur in the setting of cemento-ossifying fibromas or central giant cell granulomas.[5] The most accepted theory behind secondary ABC formation is that the pre-existing lesion results in disruption of the normal osseous hemodynamics, resulting in an enlarging intraosseous accumulation of haemorrhage with concurrent osteolysis.[6] Other reported pathogenic theories include aberrant healing with intrabony haemorrhage after trauma or in association with vascular malformations.[7] Approximately 40% of reported ABCs affecting the maxillofacial region were seen in association with pre-existing pathological entities.[5] Unfortunately, most studies group primary and secondary ABCs in the same sample,[5,8,9] limiting accurate analysis. The postulated different pathogenic mechanisms between primary and secondary ABCs is enough evidence to warrant separate studies allowing for more accurate diagnosis, management and prognosis prediction.

Due to the rarity of aneurysmal bone cysts (ABCs) involving the maxillofacial region, the majority of current published literature comprises of isolated case reports. Studies on extragnathic ABCs seem to be more common.[10] More recently, Richardson et al[5] published a thorough literature review of primary and secondary ABCs involving the head and neck region. Unfortunately, the radiological features were not a focus point of this review. Other studies on ABCs have documented variable clinical presentations, an eccentric location in the bones and atypical radiological features.[7,11,12] ABCs may present in unusual locations or as uni- or multilocular lesions, well- or poorly demarcated, and in some instances exhibit a fluid level or periosteal reaction.[7,9,13]

ABC typically present as a blood-soaked sponge intraoperatively. Surgical treatment of ABCs via enucleation and curettage is associated with significant bleeding, resulting in many authors advocating lesion resection.[2,5] A pre-operative suspicion of ABC may advise clinicians to proceed with a more cautious approach such as preoperative aspiration in order to confirm the vascular component of the tumour.[14] As an adjunct, preoperative embolisation may assist in managing excessive bleeding encountered intraoperatively.[15] Recurrences have been reported in approximately 16% of cases, depending on the treatment approach.[7] Resection of ABCs has yielded a low tendency for recurrence,[5] whereas, cases treated by curettage alone have a high propensity for recurrence.[3,8]

The aim of the current study was to analyse the demographic, clinical and radiological features of histologically confirmed primary ABCs involving the maxillofacial region. This study is the first of its kind focusing on the clinicoradiological presentation of ABCs and will be advantageous to clinicians in the diagnostic process, surgical planning and overall prognosis.

Methods and materials

The study was conducted following approval by the University of Pretoria, Faculty of Health Sciences Research Ethics Committee (Reference number: 579/2021). All procedures followed the ethical standards of the Helsinki Declaration of 1975, as revised in 2008.

Histologically confirmed cases of primary ABCs affecting the maxillofacial region were retrospectively reviewed in a 21-year period (2000–2021). Cases were collected from the archives of five Oral Pathology laboratories from three countries: South Africa (University of Pretoria), Guatemala (Centro Clinico de Cabeza y Cuello) and Brazil (Federal University of Rio de Janeiro, Federal University of Minas Gerais and the University of São Paulo). The histopathological diagnosis of included cases was confirmed by an experienced Oral and Maxillofacial Pathologist at each institution and reviewed by two other Oral and Maxillofacial Pathologists (LR and WvH). Additionally, ABCs associated with other lesions (secondary ABCs) were excluded from this study by histological and radiological confirmation. Cases with insufficient clinical data or inconclusive histological features to render a diagnosis of primary ABC were excluded from the study. The prevalence of ABCs from all diagnosed oral and maxillofacial lesions was calculated at each institution.

Demographic and clinical data, including age, sex, duration, site and clinical signs and symptoms for each case, were retrieved from the clinical records of each institution. Radiographic examinations utilised in this study included all available imaging modalities, including panoramic radiographs, computed tomography (CT), cone-beam CT (CBCT) and magnetic resonance imaging (MRI). The borders, density, locularity and effects on surrounding teeth and anatomical structures were obtained from available radiographic examinations. The mean size of the lesion was calculated by measuring the maximum diameter of the lesion after calibration of radiographic magnification. The radiological features were analysed by two clinicians with experience in the field of Maxillofacial Radiology (CS and LR), with any disagreements resolved via consensus. Follow-up and recurrence information was recorded when available. The information was analysed, with an emphasis on the clinical and radiological spectrum of included cases.

Table 1 Demographic and clinical features of primary ABCs

	Results* n = *31 (%)	
Prevalence	**0.04%**	
Mean age, years (range)[a]	21	(6-65)
Sex (ratio)	14M:17F	(1:1.2)
Mean duration, months (range)[b]	16	(1-60)
Clinical signs and symptoms[c]		
Painless swelling	21	68%
Painful swelling	10	32%
History of trauma	3	10%
After extraction	1	3%
Trismus	2	7%
Proptosis	2	7%
Site		
Maxilla	4	13%
Frontal bone	1	3%
Mandible[d]	26	84%
Corpus	*18*	*69%*
Ramus	*10*	*39%*
Coronoid	4	*15%*
Condyle	4	*15%*

[a]Missing data for one case
[b]Missing data for 14 cases
[c]Patients reported more than one symptom
[d]Due to the size of ABCs, more than one subsite could be simultaneously affected

The data were entered into a data capture sheet using Microsoft Excel Version 2016. A basic descriptive statistical analysis was carried out by the authors and conclusions drawn from the data.

Results

After the initial search, a total of 44 primary ABCs were identified from all included institutions. Thirteen cases were excluded due to insufficient clinical features and/or inconclusive histopathological findings to render a diagnosis of primary ABC. Following the inclusion criteria, a total of 31 cases of ABCs were included in the study. Table 1 summarises the main demographic and clinical features. The final sample included 12 cases from South Africa, 10 cases from Brazil and 9 cases from Guatemala. The calculated prevalence of ABCs from the dataset was 0.04% of all oral and maxillofacial lesions diagnosed in the study period at all institutions. Radiographs were available in 23 cases and included panoramic radiographs (16 cases), CT imaging (12 cases), Cone-beam CT (4 cases) and MRI (one case).

The mean age of presentation was 21 years (range 6–65 years) with a peak incidence in the second decade. The overall sample included 14 male and 17 female patients (1:1:2 ratio). Females presented at a mean age of 24 years, whereas males presented at a mean age of 17 years. The reported mean duration was 16 months (range 1–60 months).

Localised swelling was the main clinical presentation in all cases with the majority being painless (68%), while associated pain was less frequently reported (32%). A history of trauma was reported in three cases (10%) and one case presented after a recent tooth extraction (3%). Trismus was seen in two cases (7%), all involving the ramus and condylar regions. Proptosis was also seen in two cases involving the upper facial skeleton (7%).

The majority of cases were located in the mandible (84%), with the corpus being the most commonly affected subsite, followed by the ramus, coronoid and condyle (Figure 1). Four cases were located in the maxilla (13%) and one case in the frontal bone (3%). Two of the maxillary cases extended to involve the sinonasal region.

The main radiological features are summarised in Table 2. ABCs reached a mean size of 5.9 cm on initial radiological examination, with the largest measuring 10 cm. All ABCs presented with a well-demarcated radiolucent radiological appearance. The majority of cases had a multilocular appearance, seen in 74% of cases (Figure 2). Most cases (47%) did not affect the surrounding teeth. The frequent effects on surrounding teeth included tooth displacement (33%) and root resorption (20%). No cases were seen in association with impacted teeth. In two cases (13%) the region involved by the ABC had associated missing teeth. Cortical expansion was seen in 91% of cases (Figure 3), with loss of cortical integrity being common, either via cortical thinning (78%) or destruction (74%). Displacement of the inferior alveolar nerve was only noted in 27% of cases affecting the mandibular corpus area. Displacement of anatomical structures was common among maxillary cases, with encroachment of the maxillary sinus, nasal cavity and orbit. Encroachment of the sphenoid sinus and cranial base was uncommon, seen only in extensive lesions involving the upper facial skeleton (Figure 4). Recurrence was noted in four cases (13%) occurring two years after enucleation. In the 12 cases where CT imaging was available, fluid levels were only visible in five cases and periosteal reactions were not detected.

Discussion

Aneurysmal bone cysts are rare with a reported overall incidence of approximately 1.7%.[7] They may occur anywhere in the skeletal system, frequently involving the long bones of the lower limbs, vertebrae and humerus.[3] The jawbones are affected in less than 2% of ABC cases.[2] The prevalence in the current sample was estimated as 0.04% from all diagnosed head and neck lesions, confirming their rarity in the maxillofacial region.

ABCs affect a wide age group, however, 80% of cases occur in the first two decades of life.[2,16] Their reported mean age of presentation is 19 years (range of 5 months to 62 years).[5,8] The mean age of presentation in the current sample was slightly higher than that of reported literature, but the peak within the second decade corresponds to literature.[7] In the

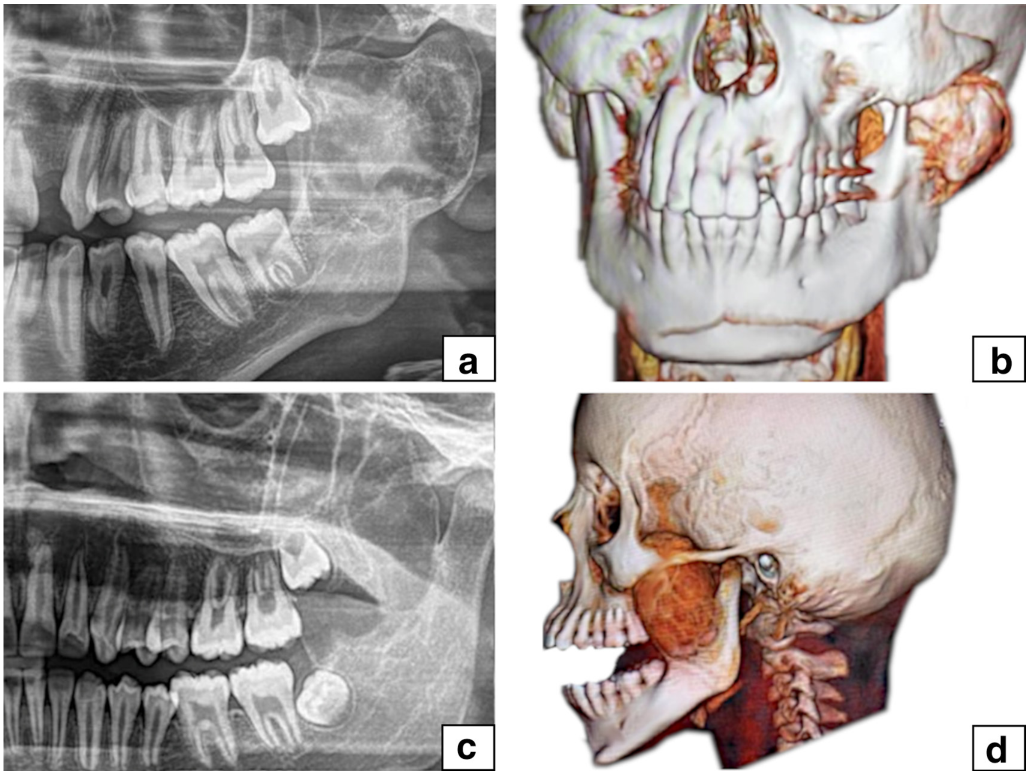

Figure 1 Panoramic radiograph and three-dimensional (3D) reconstructed CT images of ABCs affecting the condyle (A, B) and coronoid process (C, D)of the mandible.

current study, ABCs presented with a near equal gender distribution, in agreement with published literature.[3,5,8] Interestingly, ABCs presented nearly 8 years earlier in males compared to females. This was also noted in the literature, however, it is uncertain if these data reflect primary or secondary cases of ABC.[7,16] The authors postulate that the earlier occurrence of ABCs in males reflects their propensity to traumatic events involving the maxillofacial region.

The clinical duration before diagnosis is often short (19 days to 5 months) due to the rapid growth and highly expansile nature of the lesion.[7,8,12] In the current study, the mean duration before seeking treatment was longer compared to literature. This is possibly due to difficult patient access to specialised healthcare in developing countries.

Clinically, ABCs present as painful swellings with associated tooth mobility being a common finding.[2,5,9] Other authors report that ABCs are frequently painless.[8] In the current sample, the majority of cases presented as painless swellings, with associated pain only reported in less than one-third of cases. Many cases of ABC in literature have a history of trauma preceding development.[9,15–17] Although no reports have included a history of development following tooth/teeth extraction, the bony trauma experienced during such a procedure could warrant classification under trauma in other reports. Other presenting symptoms include trismus, proptosis, airway or nasal obstruction and gingival haemorrhage.[8,15] In the current study, proptosis was reported in two-thirds of maxillary ABCs, whereas trismus was seen in two cases, mainly involving the ramus and condyle regions. This finding also corresponds to the literature.[8,18] ABCs associated with the paranasal sinuses frequently result in clinical signs of proptosis.[9]

Head and neck ABCs have a predilection for the jawbones, in particular, the mandible,[5,7,8] followed by the condyle,[7,18,19]paranasal sinuses,[9,20] cranium,[15]maxilla, orbit[13] and zygoma,[15] in decreasing frequency.[5,16] Other reported sites include the mastoid process and pterygomaxillary fossa.[15] Some cases detailing the involvement of the coronoid process have also been reported previously.[21,22] The results in the literature correspond to the findings of the current study where the mandible was most frequently involved. Additionally, the distribution between the corpus, ramus and condyle regions corresponded to the results of other studies.[16] Additionally, literature regarding the distribution of jaw ABCs is confounding, with some reporting no significant distribution incidence, whilst others report a posterior predominance.[7,16,23]

The term 'aneurysmal' is appropriate, as these lesions usually present with typical 'blow-out' expansion of the associated bone. Lesions reach a mean size of 4 cm, with rare cases reaching a size of up to 10 cm.[5,8] In the current study the mean size of lesions reached 5.7 cm with the

Table 2 Radiological features of primary ABCs

	Results n = 23 (%)	
Mean size, cm (range)	5.9	(2.1–10)
Borders		
Well-demarcated	23	100%
Density		
Radiolucent	23	100%
Locularity		
Unilocular	6	26%
Multilocular	17	74%
Effects		
Tooth displacement[a]	5	33%
Root resorption[a]	3	20%
Missing teeth	2	13%
No effects on teeth	7	47%
Cortical expansion	21	91%
Cortical thinning[b]	18	78%
Cortical destruction[b]	17	74%
No effects on cortex	2	9%
Inferior alveolar nerve displacement[c]	3	27%
Maxillary sinus encroachment[d]	4	100%
Nasal cavity encroachment[d]	3	75%
Orbit[d]	3	75%
Sphenoid sinus[d]	2	50%
Cranial base[d]	1	25%

[a]8 cases not associated with teeth
[b]Some cases exhibited cortical thinning and destruction
[c]Only 11 cases in mandibular corpus area with radiographs
[d]Only four upper face/maxillary lesions with radiographs

largest measuring 10 cm. It is the authors' opinion that pseudocystic spaces without blow-out or extensive bony expansion and devoid of an epithelial lining histologically are better considered simple/solitary bone cysts. Intraoperative findings of a fluid-filled/empty and blood-filled lesion could also differentiate. Similarly, ABC features histologically seen in conjunction with other pre-existing pathologies and without expansion should rather be termed ABC-like changes or a co-existing giant cell lesion.

The radiological presentation of ABCs varies between the different histological subtypes, with the solid variant being more indolent and the vascular variant being more destructive.[7] The solid variant is rare and difficult to distinguish histologically from other giant cell lesions of the jawbones. All cases in the current sample were vascular variants of ABCs and the destructive nature was evident radiologically. Importantly, these lesions often present in young individuals and therefore a mean size of 4 cm results in significant disfigurement.

The typical presentation of an ABC is an eccentrically-positioned lesion with significant expansion and a thin shell of cortical bone.[10] Radiologically, ABCs have various presentations, but typically present as highly expansile, well-demarcated unilocular or multilocular radiolucencies.[2,8] All ABCs in the current sample presented as well-demarcated radiolucencies. Mixed radiolucent-radiopaque lesions and cases with poorly demarcated borders have also been reported in the literature,[8] but were not identified in the current sample. In the current study, multilocular lesions were

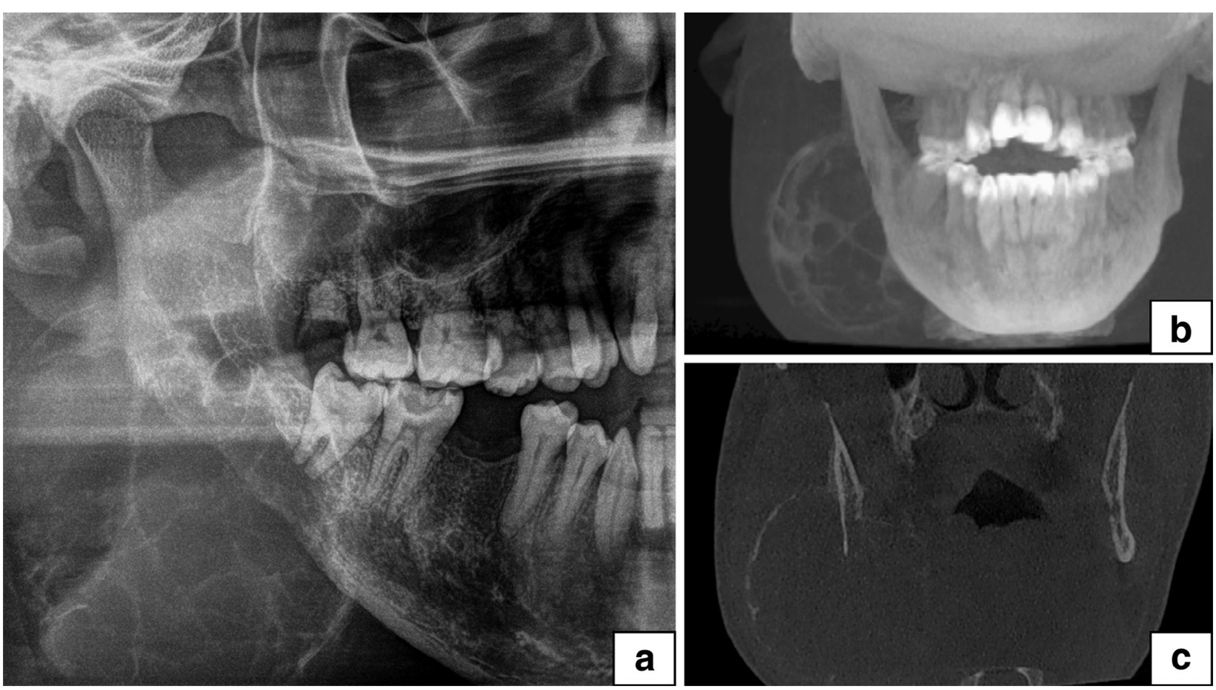

Figure 2 (A) Panoramic radiograph and (B) 3D CBCT reconstruction of a multilocular ABC affecting the posterior mandible withblow-out expansion of the cortical bone. (C) Coronal CBCT image shows an eccentric location in the bone with destruction of the lingual cortical plate.

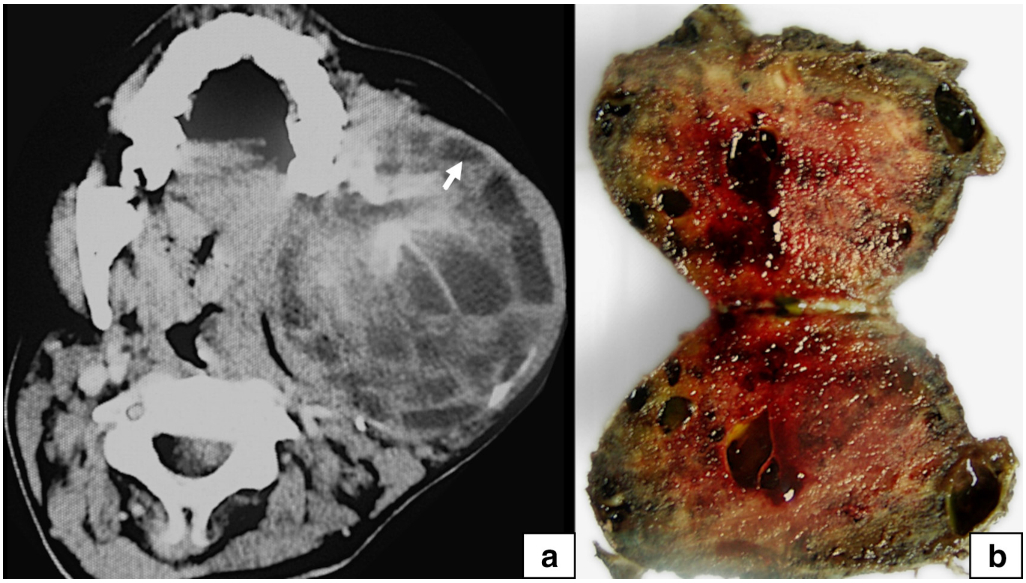

Figure 3 (A) Axial view of a soft-tissue window of CT imaging showing a highly expansile multilocular lesion affecting the ramus complex. Fluid level was visible in some areas of the lesion (arrow). (B) On cut-section, the specimen presented as a blood-soaked sponge containing numerous blood-filled cystic spaces.

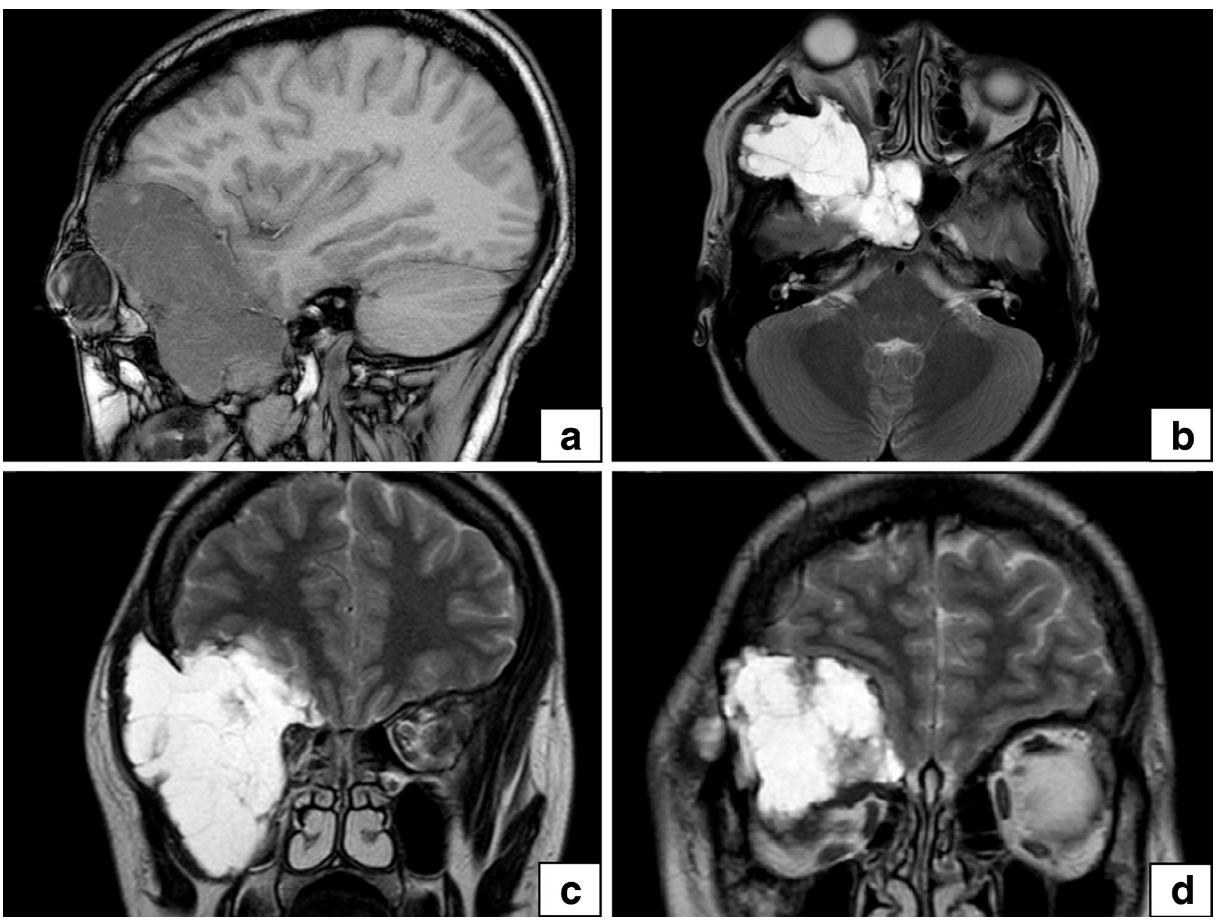

Figure 4 (A) Sagittal T_1-weighted MRI showing a well-demarcated isointense lesion. (B) Axial and (C, D) coronal T_2-weighted images show a hyperintense expansile lesion encroaching the orbit and cranium resulting in significant proptosis.

more common than unilocular, a feature also mirrored in other studies.[16]

Tooth displacement and root resorption are commonly seen in association with ABCs.[2,8] Effects on surrounding teeth were uncommon in the current sample, with tooth displacement only seen in 33% of cases involving the dentition. It is postulated that the association of the lesion with missing teeth could have resulted from bone destruction and root resorption resulting in tooth/teeth mobility and subsequent extractions.

Cortical perforation with soft tissue extension are common findings in cases of gnathic ABC.[2,8] In the current study, the majority of ABCs were associated with cortical expansion. Patients without cortical expansion all presented with clinical signs of swelling, and therefore the lack of radiologically detectable cortical expansion can be explained by being unable to see buccal-lingual expansion in cases where only two-dimensional imaging was available. Loss of cortical integrity was commonly seen in the current sample, corresponding to the fast growth of ABCs. Some authors report periosteal reactions in association with the lesion.[7,11,14] This feature was however not noted in the current sample. Maxillary involvement can extend to encroach on the maxillary sinus, nasal cavity and orbits,[2] a finding mirrored in the current sample. Unfortunately, due to low absolute numbers, an estimate of the frequency of these effects cannot be made. Encroachment of the sphenoid sinus and cranial base were uncommon and mainly seen in extensive ABCs involving the upper facial skeleton.

Advanced imaging of ABCs typically highlights a fluid level or a soft tissue attenuated epicentre.[5,10,13,20] These fluid levels will only be visible when the central beam is perpendicular to the plane of the fluid level and is therefore influenced by patient positioning. Additionally, fluid levels are not commonly seen in cases with prior surgical intervention such as biopsies. These reasons could explain the low prevalence of fluid levels in the current sample. Moreover, fluid levels have also been described in other lesions and are therefore not unique to ABCs.[24] MRI findings of perilesional oedema are considered a feature of ABCs displaying rapid growth.[11] These features were not identified in any of the current cases. Interestingly, ABCs in the current study showed an eccentric bone location, as previously reported in the literature. Often the epicentre of the lesion does not occur centrally within the bone, with asymmetrical expansion involving one of the bony cortices, as illustrated in Figure 2.

The radiological differential diagnosis for ABCs occurring with an epicentre in the alveolar bone includes odontogenic tumours such as ameloblastoma. This is supported by the expansile nature, multilocularity and mandibular predilection.[25] The tendency for ABCs to cause blow-out or eccentric expansion, by affecting one cortex to a greater extend than the other, is unlike ameloblastomas that typically causes symmetrical bucco-lingual expansion. Lesions with an epicentre in the condyle, coronoid or upper facial skeleton, where odontogenic epithelial remnants are typically absent, should raise a high suspicion for non-odontogenic entities such as ABC. Additionally, although not pathognomonic, the fluid-fluid level in a well-defined lesion should support a strong presumptive diagnosis of ABC.[24]

Recurrence rates of ABCs can be as high as 22%, often detected in the first two years after initial surgical intervention.[9] Interestingly, orbit involvement and clinical signs of proptosis were seen in association with poor clinical outcomes, either progression or recurrences.[9] The recurrence rate of the current study corresponds to the current literature.[7] Additionally, the recurrence rate of primary ABCs were reportedly lower than secondary cases probably related to the pathophysiology of the primary lesion.[16]

Conclusion

Primary aneurysmal bone cysts involving the maxillofacial region are extremely rare with the majority of current published literature consisting of case reports. The current study is the first series detailing the radiological features. ABCs often present as blow-out expansile multilocular radiolucencies, commonly involving the ramus complex of the posterior mandible. The results of this study will be advantageous to clinicians in the diagnostic process, surgical planning and overall prognosis.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Ethics approval

This study was approved by the University of Pretoria, Faculty of Health Sciences Research Ethics Committee (Reference no.: 579/2021). All procedures followed the ethical standards of the Helsinki Declaration of 1975, as revised in 2008.

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