Review article

A comparative study of simple bone cysts of the jaw and extracranial bones

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Running title: Simple bone cyst lesions

Abstract

Objectives: To improve the interpretation of simple bone cyst (SBC) lesions of the jaw.

Methods: A comparative study of SBC lesions of the jaw and extracranial bones was performed through a literature survey.

Results: In extracranial SBC, the cavities were always filled with fluid, and a high recurrence rate was shown through extensive research. Aneurysmal bone cyst was included in the differential diagnosis owing to some clinicopathologic similarities. Fluid, gas, and blood were found in the cavity in jawbone SBC, and recurrence was believed to be rare. Differential diagnosis was rarely discussed in the literature.

Conclusions: Based on reports, the cavity normally did not contain gas because no air-fluid level was observed on panoramic radiographs and no density/intensity area indicating gas was seen on CT/MRI. A blood-filled cavity should be examined carefully, and the possibility of an aneurysmal bone cyst should be considered. The recurrence rate needs to be re-estimated because an extensive survey has not been performed to clarify the treatment outcomes of jawbone SBC.

Keywords: Bone Cysts, Aneurysmal Jaw Cysts Diagnosis, Differential

Introduction

Simple bone cyst (SBC) lesions were first recognized by Virchow in 1876. Jaffe and Lichtenstein provided a detailed discussion of the topic in 1942 (1). In dentistry, Blum reported the first three cases in 1932 (2). SBC of the jawbone was relatively rare, but had been frequently reported in the dental literature and had become familiar to dentists. However, the investigations were restricted to lesions of the jawbones, which is not sufficient for the complete characterization of SBC. Even a peculiar finding may be accepted without suspicion. Consequently, we conducted a study comparing jawbone SBC with SBC of other bones to clarify and discuss the different characteristics.

Materials and Methods

This study was based on a literature survey of English-language studies, which were divided into two groups: those that described SBC lesions of the jawbones and those that described SBC lesions of bones other than the jawbones. In this article, we refer to the SBC cases in each group as jawbone SBC or extracranial SBC. The diagnostic criteria, etiologies, diagnostic terms, some clinicopathologic features, prognoses, and differential diagnoses were compared between the two groups.

The literature survey was initially conducted using PubMed, a database created by the National Center for Biotechnology Information (NCBI: http://www.ncbi.nlm.nih.gov/). The term “simple bone cyst” and several synonyms for SBC (traumatic bone cyst, haemorrhagic/hemorrhagic bone cyst, extravasation cyst, unicameral bone cyst, solitary bone cyst, idiopathic bone cyst/cavity/cavities, and progressive bone cavity/cavities) were used as search terms. In the survey for jawbone SBC, all of the studies found on PubMed were collected except for eight case reports. Including the literature cited in the studies obtained through PubMed, a total of 185 references were used for the assessment. The total number of SBC cases studied in the

collected literature was 881. In the study of extracranial SBC, 110 references concerning SBC and related lesions were collected for assessment. To obtain comprehensive information about extracranial SBC, a WHO classification book (3), seven textbooks on surgery, orthopedics, and radiology (4–10), and nine review articles (1, 11–18) were included. In the collected literature, 1923 SBC cases were studied.

Results

Diagnostic criteria

The diagnostic criterion of extracranial SBC is that of a serous or serosaguineous, fluid-filled, unilocular cavity surrounded by a thin connective tissue wall without an epithelial lining (3). In the dental literature, Rushton advocated the following criteria in 1946: the cyst should be single, with no epithelial lining, and should principally contain fluid (19). In 1974, Hansen et al. modified the criteria to the following: the lesion should be essentially an empty cavity; on occasion, the cavity may contain some fluid and/or small amounts of soft tissue (20). The presence of gas (empty cavity) was accepted among dentists without argument and was believed to be a pathognomonic finding of jawbone SBC. Blood in the cavity was also reported and accepted, and currently intra-bone, non-epithelial-lined cavities are diagnosed as SBC irrespective of the contents (21).

Etiology

In 1942, Jaffe and Lichtenstein reviewed six proposed causes in a study of extracranial SBC (1). Since that time, clinical behavior studies, electron microscopic examinations, and biochemical analyses of cyst fluid have been performed to clarify the etiology. Despite intensive research, the etiology remains unknown (15). In a study of jawbone SBC, Blum initially proposed trauma as a cause (2). He stated that a history of trauma was one of the three most important factors contributing to a correct diagnosis. His belief was based on the theory advocated by Pommer that SBC results from the encapsulation and alteration of a focus of intramedullary hemorrhage, and trauma was considered the causative agent of the hemorrhage (1). The traumatic theory was widely accepted among dentists. Other possible causes, such as thrombosis, infarction, and a small focal area of infection, were suggested by some authors (22, 23), but these did not obtain widespread acceptance by other researchers.

Diagnostic terms and synonyms

Table 1 presents the number of literature sources that used each diagnostic term in the

titles of articles included in the PubMed database. The terms traumatic bone cyst, hemorrhagic bone cyst, and extravasation cyst were only used in jawbone SBC studies.

Clinical features

There was a male predominance in extracranial SBC, but no gender predilection was confirmed in jawbone SBC (Table 2). Our recent review of reports that dealt with more than ten SBC cases disclosed a total of 205 males and 204 females, resulting in a 1:1 ratio (20, 24–35). The increased ratio of female jawbone SBC patients was considered to be attributable in part to the presence of florid cemento-osseous dysplasia (FCOD), which predominantly affects the jawbone in females and was often accompanied by SBC (29, 36).

Jawbone SBC is rarely symptomatic and is usually discovered accidentally. On the other hand, extracranial SBC is usually discovered as a result of symptoms, such as pain and limited limb movement, attributable to a fracture. In a survey by Bensahel et al. of 105 cases, 98% of the cysts were discovered at the time of a fracture (37).

Radiographic features

Solitary, unicameral, cyst-like radiolucency was a common finding of jawbone and extracranial SBCs. The bone ridge on the wall sometimes formed a multilocular appearance. Radiographic findings of jawbone SBC were initially presented by Blum and consisted of the following: a well-circumscribed bony cavity without a dense cortical rim, preservation of the lamina dura adjacent to the lesion, and bone expansion. He suggested that the findings of the margin and the lamina dura were typical (2). Thereafter, various other radiographic features were presented: resorption of the lamina dura, tooth dislocation, root resorption, multilocular appearance, and multiple lesions (28, 38, 39). As Morris et al. pointed out, there has been a great variance of opinion in the literature on the radiographic appearance of jawbone SBC (40). In the radiographic studies of extracranial SBC, the lesions were often similar to and undifferentiated from other benign osteolytic lesions, but a fallen fragment sign was pathognomonic (4, 41), and a lesion extension confined to the metaphysis juxtaposed to the growth plate (growing epiphyseal plate) was characteristic (10, 42).

Long bone SBCs were radiographically divided into active cysts and inactive cysts. The active cysts were situated close to the growth plate, were more expansive below the cortex, and recurred more frequently than inactive cysts, which were located away from the growth plate (15). Ovadia et al. suggested that the epiphyseal involvement of SBC should be considered a more aggressive form of an active lesion because of the high recurrence rate and frequent complications, such as growth disturbance and pathologic fracture (43). In a long bone SBC study, Campanacci et al. confirmed a high recurrence rate in cases involving a multilocular appearance (44). Thus, the relationship between radiographic findings and some other clinical behaviors were reviewed for extracranial SBC. In jawbone SBC, a high potential of recurrence was suspected in cases with tumorous bone expansion or multiple cavities (26, 29), but a practical survey has not been performed.

Contents of the cavity

Gas and blood were often reported only in jawbone SBCs (38, 45) (Table 2). Based on radiographic findings that an air-fluid level was not observed on panoramic

radiographs and that a low-density area indicating the presence of gas was not observed on CT images, Suei et al. recently pointed out that the presence of gas in the cavity was an erroneous interpretation (24, 46). MRI examinations have shown the same results (47, 48). Despite these findings, empty cavities have still been emphasized in recent reports (49, 50).

Histopathology

In the soft tissue of jawbone and extracranial SBCs, new bone formation and giant cells may have been observed. These findings were also seen in anuerysmal bone cysts (ABCs) and giant cell granulomas (GCGs), both of which had similar histopathology and were presented as the same entity in a recent classification system (3). In studies of extracranial bone lesions, the close relationship between SBC and ABC (GCG) was mentioned. Clough and Price described tissue simulating an ABC occasionally forming part of the wall of an otherwise typical SBC (51). In the investigation by Levy et al. involving 57 secondary ABCs, the coexistence of SBC was confirmed in 18 cases (52). Some ABCs were unilocular (53) and strikingly cystic with only a small amount

of soft tissue, and the diagnosis of ABC based on the material from curettage was difficult (54, 55). In the jawbone cases, reports stated that SBC arose after surgery for ABC (56) or GCG (45) and that GCG arose after surgery for SBC (57). Despite these results, the relationship with ABC was scarcely discussed in the studies of jawbone SBC (58); only a wide variety of histopathology was noted (30).

Cementum-like tissue was observed in the soft tissue wall of extracranial SBC. Amling et al. detected the cementum-like substance (so-called cementoma of long bones) in approximately 70% of cases (278/402 cases) (59). The pathogenesis of the substance was obscure, but microscopic differentiation from odontogenic cementum was difficult (60). This cementum-like substance was not reported in the soft tissue wall of jawbone SBC, but there was a relationship with cemento-osseous lesions. Horner et al. presumed some common etiological factor between jawbone and extracranial SBCs based on an association between the lesions and the production of cementum-like calcified tissue (61).

Concomitant disease

It was well known that jawbone SBC occurred together with FCOD and another type of cemento-osseous dysplasia (36). In a few cases, the combination of jawbone SBC with fibrous dysplasia was reported (62, 63); however, in the jawbones and extracranial bones, fibrous dysplasia accompanied ABCs rather than SBCs (64, 65). In extracranial SBC, associated entities were ABC (52) and so-called cementoma of the long bones.

Treatment modalities and prognosis

The most common management of jawbone SBC was curettage of the bone wall. The application of Gelfoam, the grafting of allogenic bone with platelet-rich plasma, and the injection of a mixture of blood, hydroxyapatite, and bone fragments were reported to produce good results (23, 66-68), but the number of reported cases was small. In extracranial SBC, several treatments, such as curettage, bone grafting, injection of bone marrow, cryosurgery, and injection of methylprednisone (a steroid), were applied independently or concomitantly (17, 44, 69).

In extracranial SBC, treatment outcomes were assessed by the evaluation of a

large number of cases that received long-term follow-up, and a high recurrence rate was often reported (17, 44, 69) (Table 2). In a review by Schreuder et al. (17), the recurrence rate was 29% (range, 12–48%). In contrast, in studies of jawbone SBC, little attention was paid to the prognosis. An extremely low recurrence rate of less than 2% was found (45, 70), but the studies included many cases that did not receive follow-up after treatments.

Differential diagnosis

As described above in the *Histopathology* section, the possibility of ABC was included in the differential diagnosis of extracranial SBC. In the studies of jawbone SBC, however, differential diagnosis was scarcely discussed.

Discussion

Some differences between jawbone SBC and extracranial SBC were clarified. Noticeable differences were found regarding the etiology, cavity contents, prognosis, and differential diagnosis.

The survey of diagnostic terms (Table 1) revealed the preference of dentists for the hypothesis that SBC is caused by hemorrhage after trauma. The terms traumatic bone cyst, hemorrhagic bone cyst, and extravasation cyst were only used in jawbone SBC studies. However, we did not find any persuasive evidence to support the hypothesis of a traumatic origin but instead identified an adverse opinion of some authors (1, 19, 71). Furthermore, the term hemorrhagic bone cyst may cause confusion with other diseases that involve a blood-filled cavity, such as hemophilic pseudotumor and hemorrhagic cyst (72-74). The terms extravasation cyst and idiopathic bone cavity are synonyms of not only SBC but also salivary gland cyst (mucocele) and static bone cavity, respectively. These four terms are inappropriate for diagnosis. In studies of extracranial SBC, the terms solitary bone cyst and unicameral bone cyst have been

used less frequently in recent years, possibly because cases with multiple cysts and a multilocular appearance have been reported (75). At this time, simple bone cyst is considered to be the preferred diagnostic term.

The detailed determination of the contents of the cavity may not be meaningful to the treatment of SBC, but a correct interpretation is essential for an accurate diagnosis and is necessary to estimate the pathogenesis. It was speculated that the amount of fluid in the cavity diminishes with the age of the lesion until the cavity is eventually filled with gas (76) and that cyst enlargement is caused by the gas filling the cavity (77). Such speculation is not valid if gas does not occur in the cavity. In extracranial bone, confirmation of the cavity contents, *i.e.*, fluid or blood, is important to differentiate ABC from SBC. When a blood-filled cavity is encountered, it is highly recommended that clinicians perform a careful histologic examination. In jawbone, however, even cavities with brisk bleeding were diagnosed as jawbone SBC (23, 31). Histologic examination should be performed more carefully while considering the possibility of ABC, especially in cases with a soft tissue mass or blood-filled cavity.

In conclusion, jawbone SBC should be recognized as a fluid-filled cavity lined by

a connective tissue membrane. Gas in the cavity is unlikely. In cases involving a blood-filled cavity, the possibility of another entity should be considered. The etiology is not known, and an extensive survey is required to clarify the prognosis.

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Legends for Tables

Table 1. The number of studies published between 1950 and 2005 using each diagnostic term in the title of the article. The numbers in parentheses are studies from the last 10 years (1995–2005).

Table 2. Clinicopathologic features of jawbone SBC and extracranial SBC. Different findings are underlined.

Table 1: The number of studies published between 1950 and 2005 using each diagnostic term in the title of the article. The numbers in parentheses are studies from the last 10 years (1995–2005).

Diagnostic term	Jawbone SBC		Extracranial SBC	
Simple bone cyst	36	(13)	84	(41)
Solitary bone cyst	18	(3)	77	(11)
Idiopathic bone cavity (cyst)	11	(4)	2	(0)
Unicameral bone cyst	0	(0)	123	(34)
Traumatic bone cyst	76	(14)	0	(0)
Hemorrhagic bone cyst	23	(1)	0	(0)
Extravasation cyst	5	(0)	0	(0)
Progressive bone cavity	3	(0)	0	(0)

Table 2: Clinicopathologic feature of jawbone SBC and extracranial SBC. Different findings are underlined.

	Jawbone SBC	Extracranial SBC
Age	most frequent in the second decade*	most frequent in the second decade
Sex	no gender predilection*	male predominance
Symptom	usually none	often pain, limited limb movement
Radiographic feature	unilocular radiolucency multilocular appearance multiple lesions	unilocular radiolucency multilocular appearance multiple lesions
Cyst wall	thin connective tissue	thin connective tissue
Contents	serous fluid gas (empty) blood	serous fluid
Histologic finding	connective tissue with new bone trabecula, giant cell	connective tissue with new bone trabecula, giant cell cementum-like material
Prognosis	fairly good	high recurrence rate
Concomitant disease	(florid) cemento-osseous dysplasia	aneurysmal bone cyst cementoma of long bone
Differential diagnosis	none	aneurysmal bone cyst

* Lesions accompanied by cemento-osseous dysplasia predominantly occur in females during the fourth or fifth decade of life.