

# Solitary Bone Cyst: Traumatic Cyst, Hemorrhagic Cyst, Extravasation Cyst, Unicameral Bone Cyst, Simple Bone Cyst, and Idiopathic Bone Cavity

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## ABSTRACT

**Introduction:** Solitary bone cyst (SBC) of the maxillofacial region is an uncommon lesion. In spite of this, it still remains to be very frequent in the dental literature.

**Purpose:** To review the published literature on SBC for insight on its etiopathogenesis and cytogenetic factors with a brief review on the main characteristics of this lesion.

**Materials and methods:** The data were analyzed from electronic database searches of published literature from PubMed.

**Results:** Following the literature search for the topic, 50 papers were considered eligible for the inclusion into the review. All the literature review and studies were analyzed, coined, and summarized. Based on this available literature, SBC appears to be a very rare entity with typical clinical and radiographic details. Surgical removal being the treatment of choice provides a satisfactory diagnosis.

**Conclusion:** Based on the evidence of available literature, SBC is a very rare lesion that can affect all skeletal bones, a majority of which occur in the long bones with < 10% seen involving the jaw bones. It is mainly diagnosed in young patients during the second decade of life.

**Keywords:** Extravasation cyst, Hemorrhagic cyst, Idiopathic bone cavity, Simple bone cyst, Traumatic cyst, Unicameral bone cyst.

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## HISTORY

Virchow<sup>1</sup> was the first to describe a bone cyst on autopsy in the humerus of a 54-year-old patient. In 1880, Sonnenberg documented a bone cyst due to trauma in an adolescent,

and Schlange in 1887 described a similar case.<sup>2,3</sup> In 1891, the specimens of both of these cases were examined by von Recklinghausen. He detailed the fibrocystic degeneration in the long bones which was termed "von Recklinghausen's disease."<sup>4</sup> The condition was first studied on X-ray by Heineke.<sup>5</sup> The histological, bacteriological, and radiographic details of this lesion were added by Pfeifer (1907).<sup>6</sup>

The solitary bone cyst (SBC) is an uncommon pseudocyst (lacks an epithelial lining) and makes up about 1% of all jaw cysts. In 95% or more cases, the long bones like the proximal humerus and femur are involved. It can manifest elsewhere in the skeleton but the pathogenesis and etiology of these lesions remain unknown. It was first termed a "traumatic bone cyst" by Lucas, and finally defined by Rushton as "solitary bone cyst."<sup>7,8</sup> The term "traumatic bone cyst" has been recognized as a misnomer, since the incidence of prior trauma in patients with this condition is same as in the general population.<sup>9</sup>

## ETIOPATHOGENESIS

Different theories of etiopathogenic processes in SBC have been proposed and this has resulted in various synonyms of the lesion. The trauma-hemorrhagic theory, which has been widely discussed,<sup>10</sup> considers a state of bone which after trauma does not undergo remodeling, but liquefaction predominates and replaces the normal repair mechanism, resulting in a bony defect.<sup>11</sup> The traumatic theory postulates that the clot breaks down and leaves an empty cavity within the bone. Steady enlargement then occurs due to impaired lymphatic or venous drainage. The cavity may be empty or filled with blood, serum, or fluid containing both. The cyst stops enlarging when the pseudocystic cavity reaches the cortical layer of bone. Bony expansion is not a common finding in the SBC.

Cystic fluid is a transudate (low-protein content) devoid of microorganisms.<sup>12</sup> It has significant concentrations of enzymatic factors, which indicate osteoclastic activity.<sup>13</sup> Presence of metalloproteinases is also significant, because they contribute to osteogenesis and osteoclastic reactions.<sup>14</sup>

Other theories of proposed origin have included:

- Cystic degeneration of primary bone tumors.
- Faulty calcium metabolism, such as that induced by parathyroid disease.

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- Ischemic necrosis of fatty marrow.
- End result of low-grade chronic infection.
- Altered bone turnover due to disturbed circulation caused by trauma.
- Osteoclastic resorption due to decreased tissue pH in an area of bone necrosis that has occurred owing to venous stasis because of pressure from a hematoma.<sup>15</sup>

An injury that the patient cannot even remember causes lesion. In the series of reports by Howe, over 50% of patients gave a positive history of trauma, and the time lag between injury and the diagnosis of the lesion varied from 1 month to 20 years.

According to a recently proposed concept, SBC is considered to be a synovial cyst arising from a juxta-epiphyseal error with intraosseous incorporation of synovial tissue.<sup>16,17</sup>

**CYTOGENETIC FACTORS**

Mirror-image SBCs of the humerus in a pair of monozygotic twins have been described.<sup>18</sup> One twin was right handed and had SBC at the left humerus. The other twin was left handed and had SBC at the right side of the humerus. The directions of the whirl of hair on their heads were opposite to each other. These findings suggest cytogenetic factors in the etiology or pathogenesis of SBC.

Cytogenetic studies of SBCs are extremely limited. Highly complex clonal structural rearrangement of the chromosomes 4, 6, 8, 16, 21, and 12 in a resected SBC of an 11-year-old boy has been reported.<sup>19</sup> Richkind et al<sup>20</sup> have mentioned a simple translocation involving the short arm of chromosome 16 and the long arm of chromosome 20 in a curetted specimen of a 9-year-old boy with SBC. There have been a large number of reports of mirror-image manifestations of SBC or congenital anomalies, dental anomalies, and the first and second branchial arch syndromes in monozygotic twins.<sup>21-23</sup>

**EPIDEMIOLOGY**

In a recent report, 322 patients with cystic lesions of the jaws (192 males and 130 females) were diagnosed and treated by Manor et al,<sup>24</sup> and they recorded 16 (5%) cases of SBC (traumatic bone cyst). The mean age of occurrence of cyst was 14 years and the mean diameter was 1.7 cm. The most common SBC locations were the long bones (90%) with predominance in the metaphyseal region of the humeral (65%) and femoral (25%) shafts in their proximal region.<sup>25</sup> A centrifugal expansion of the cyst toward diaphysis is noted, while the bone undergoes linear extension. Solitary bone cyst of the jaw bones appears to be far less common (10%) within the body of the mandible, the premolar and molar regions (75%) being the most usual site. Despite primary location in either long bones or jaws,

SBC is diagnosed predominantly in the first two decades of life (75%). The jaw location is distributed almost equally between the genders, although a male predominance for extrafascial variants is noted. An ethnic predisposition, being most prevalent among white persons, has been reported and most often affect the posterior mandible.<sup>17</sup>

**CLINICAL PRESENTATION**

Solitary bone cysts are typically found as discrete lesions, although a review of the literature found multiple synchronous lesions reported to occur in about 11% of cases. Most SBCs present no clinical symptoms of swelling or other functional signs and are found during panoramic radiographic examination (Fig. 1). Solitary bone cyst evolution in long bones is asymptomatic initially, but clinical signs, such as sporadic limb in the case of the femoral location are elicited. Severe pain due to spontaneous fracture occurring in 90% of the humeral SBC locations is another feature observed.<sup>13</sup>

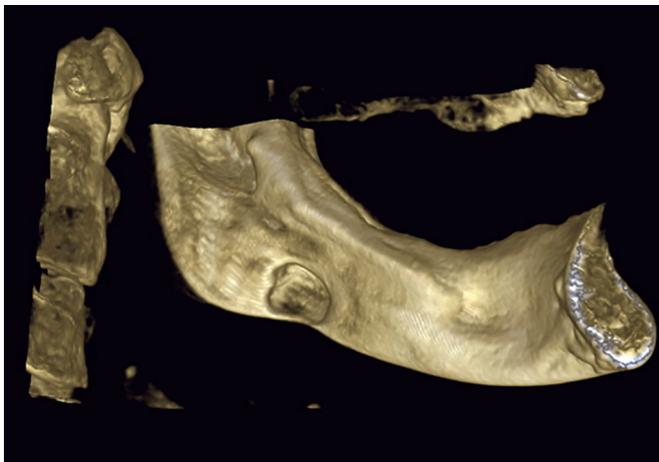
Pain is the most frequent presenting symptom of jaw lesion, affecting 10 to 30% of patients. Tooth sensitivity, fistulas, paresthesia, delayed tooth eruption, and pathological fracture of the mandible have also been reported. In the majority of cases, the pulp of the teeth in the involved area is vital, and swelling or rare pain may be the presenting complaint.

When the cystic cavity is opened surgically, it is found to contain either a small amount of serosanguinous fluid, shreds of necrotic blood clot, fragments of fibrous connective tissue or nothing but a naked, raw, and empty bony cavity without an apparent cystic lining (Fig. 2). It was reported in one case that the hydrostatic, intracystic pressure was exceptionally low compared with capillary pressure, and quite unlike than in other cysts of the jaws.<sup>26</sup>

An important clinical sign that aids in the differential diagnosis of SBC is the apparent lack of bony cortical



**Fig. 1:** Panoramic radiograph showing a solitary bone cyst in the mandible of an edentulous patient



**Fig. 2:** Cone beam computed tomography reconstruction of the mandible, sagittally split, and exposing the cystic lesion. Note the raw cystic lumen without trace of a lining and/or cystic contents. The cortication of the periphery is apparent (Courtesy: Figures 1 to 3, Professor Sujata S Reddy, Oral Medicine and Radiology, Faculty of Dental Sciences, MSR University of Applied Sciences, Bengaluru, India)

expansion relative to the size of the lesion. With more clinically aggressive cystic lesions or neoplasms, expansion of cortices is usually the chief complaint and the primary clinical presentation. Extensive bony destruction of the mandible may also occur, leading to pathologic fracture and tendency to overdiagnose the lesion as a more aggressive condition.

Although mandibular SBC and that of long bone have some similarities with respect to diagnosis and etiopathogenesis, caution in management is advised as their prognoses and treatment modalities differ. For jaw bone lesions treatment is straightforward, consisting of curettage, and frequently lead to complete healing with no recurrence reported. Resolution of the cyst without treatment has been reported. However, this option is not advisable due to risk of undue enlargement with pathologic fracture or progression to a symptomatic lesion.

## CHALLENGES IN DIAGNOSIS

At times, SBC poses extreme difficulty in diagnosis and prediction of clinical outcome due to the potentially life-threatening lesions it mimics. Arterio-venous malformations (AVMs) and SBC of the mandible are common lesions. The latter could be fairly innocuous, but AVMs require careful management. Trauma induced by a biopsy or an extraction in the region of an AVM can lead to serious intraoperative bleeding, which could be life-threatening. Usually, SBCs of the jaws are incidental during radiographic examination of the mandible and are not a risk to human life.

In a case of a 9-year-old Greek boy, the initial histologic diagnosis of a unicameral bone cyst (SBC) was, on reanalysis of the slides 3 years later, found to have the

cyst wall lined by an Ewing's sarcoma.<sup>27</sup> According to the published literature, Ewing's sarcoma presents with benign radiographic features in less than 2% of cases and with sharp endosteal margins in 10%.<sup>28</sup> However, presentation with a cystic appearance of the tumor is reported to be rare. It is, however, difficult to exclude the possibility that Ewing's sarcoma may have arisen in the lining of a unicameral bone cyst as has been reported only once.<sup>29</sup>

## RADIOLOGICAL FEATURES

Radiographic examination usually reveals unilocular radiolucent area(s) with an irregular but well-defined border, sometimes with a thin sclerotic margin, depending on the duration of the lesion. Some SBCs may measure only a centimeter in diameter, whereas others may be so large that they involve most of the molar area of the body of the mandible as well as part of the ramus. Radiographically, SBC mimics other common jaw lesions posing difficulty in diagnosis. When the radiolucency appears to involve the roots of the teeth, the cavity may have a lobulated or scalloped appearance extending between the roots of these teeth ("scallop effect"). Usually there is no displacement of teeth and in many cases the lamina dura appears intact, and occasionally root resorption may be noted. Multilocular lesions are rarely seen.

An entity that mimics the radiographic appearance of SBC which deserves consideration is the lingual salivary gland depression of the mandible occurring in the molar area and appears as a round or ovoid radiolucent area associated with vital teeth. However, the latter lesion is usually located below the mandibular canal, whereas the SBC usually lies above it.

A clinically and radiographically atypical case of large radiolucency involving the mandibular ramus was reported.<sup>30</sup> It presented as a multilocular, multilobular lesion with irregular but well-defined borders without a clear sclerotic lining. The differential diagnosis included odontogenic keratocyst, odontogenic tumors like ameloblastoma, odontogenic myxoma, giant cell granuloma, and aneurysmal bone cyst. Another atypical characteristic of the lesion was the reported perforation of the cortex. The nearly complete ossification of the defect within 6 months after surgery confirmed the diagnosis in favor of SBC.

An association between SBC volume and recurrence was assessed using conventional radiological examination in response to varied treatments like bone curettage and grafting or steroid therapy. The frequency of complete healing of SBC treated with bone curettage and grafting decreased with an increase in the cyst volume.<sup>31</sup> By using standard radiographs, it is possible to obtain data on accurate cyst volume to evaluate cyst remodeling, total healing, and cyst recurrence in an objective manner (guided by calibration).

**PATHOLOGICAL FEATURES**

Gross examination shows an empty bone cavity, which occasionally contains a clear liquid of yellowish color (straw color) or a blood colored liquid. This lesion is remarkable for its lack of surgical tissue and usually the submitted specimen consists of little fragments of fibrovascular connective tissue, extravasated red blood cells, and pieces of reactive vital bone. A conspicuous absence of cystic epithelium is noted, making histological diagnosis difficult. However, the intraoperative finding of an empty or fluid-filled space is supportive of a SBC.<sup>32</sup>

Microscopic examination shows the cystic wall characteristically as connective tissue condensation with numerous collagen fibers and no epithelial lining. Numerous fibroblasts and giant cell-like osteoclasts are sometimes visible with some newly formed bony trabeculae surrounded by numerous active osteoblasts. Congested capillaries and cholesterol crystals related to the osseous necrosis may also be present.<sup>33,34</sup>

The histologic features of SBC are nonspecific, but identification of amorphous cementum-like material provides a significant diagnostic clue (Fig. 3).<sup>35</sup> This material is unique to SBC with reported frequency of 10 to 70% and has been described as an immature form of bone. Humerus and femur are the most common sites of cementoid deposition on the cyst wall. This material was seen in different phases of deposition and progression, ultimately transforming into mature bone as seen in four cases of these authors. Cyst wall lining was observed in 70.7% of cases along with several other nonspecific histologic features, including reactive bone formation, hemosiderin macrophages, hemorrhage, multinucleated giant cells, foamy macrophages, fibrin, cholesterol clefts, and

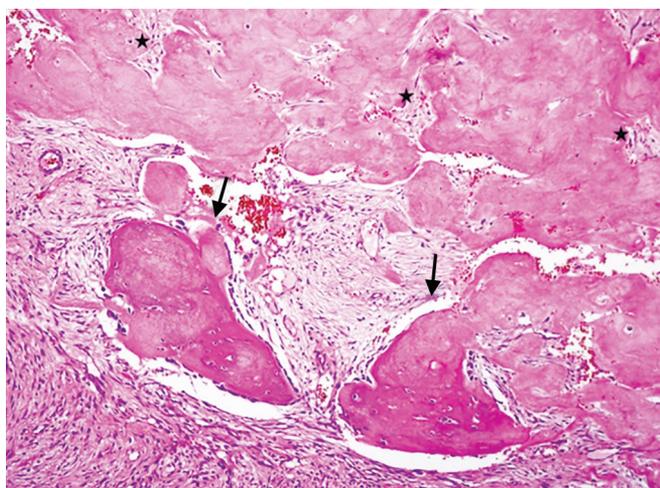
granulation tissue. Cementum-like material (cementoid, Fig. 4) in the connective tissue wall of SBCs is a specific and fairly consistent finding of diagnostic significance in cases where cyst wall lining is deficient. Histologic evidence for the transformation of cementum-like material into reactive and mature bone further validates the immature osteoid nature of the deposit.

The recent edition of the WHO classification of soft tissue and bone tumors has described this material as “collagen deposits sometimes resembling fibrin.”<sup>36</sup> Although proposed, based on ultrastructural and immunohistochemical studies, the osteoid origin of this material has not been histologically demonstrated yet.<sup>37</sup>

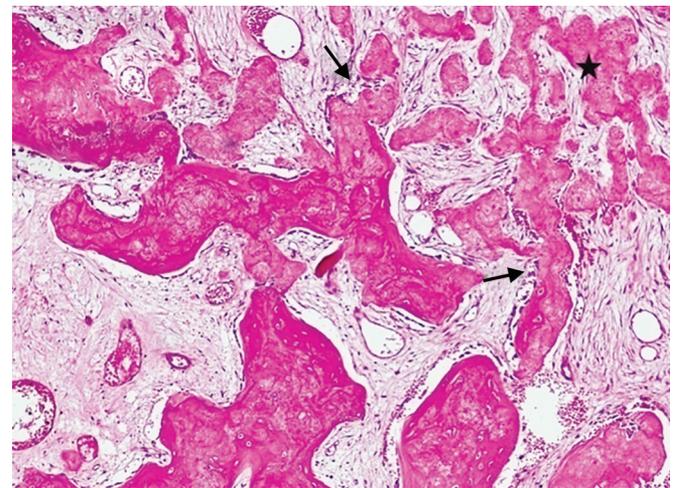
**TREATMENT**

The treatment of SBC is mainly focused on establishing bleeding in the lesional cavity. Hemorrhage either due to surgical curettage or during the explorative procedure may induce a reparative process. It has been found that healing and filling of the space by bone occur in most cases within 6 to 12 months. The prognosis is usually better when the lesion is treated by fenestration and packing the cavity; healing or recurrence can be confirmed within 3 years of treatment. The recurrence rate of SBC is between 20 and 30%, but it has been suggested that those cases of SBC which are associated with cemento-osseous dysplasia or other lesions have a high probability of recurrence.<sup>38</sup> The rarity of this lesion in adults supports the hypothesis of spontaneous resolution. Current treatment calls for complete exploration of the area with curettage of the bony defect.<sup>39</sup>

Within the orthopedic literature, intralesional injection of methyl prednisolone has been described as a treatment



**Fig. 3:** Extensive deposition of cementum-like material as globular masses (upper half) with intervening fibrovascular stroma (stars) transforming into mature bone (arrow heads) (H&E, 200× magnification)



**Fig. 4:** Small deposits of cementum-like material (star) with intervening fibrovascular stroma. Transformation into mature bone is evident (arrow heads) (H&E, 200× magnification) (Courtesy: Figures 3 and 4 by Muhammad Usman Tariq and NasirUd Din, Department of Pathology and Microbiology, Aga Khan University Hospital, Karachi, Pakistan)

modality for SBC in the long bones.<sup>40,41</sup> It has been proposed that the healing is not solely a response to the corticosteroid treatment but rather results from mechanical disruption of the cavity. In a randomized, multicenter clinical trial, intralesional injection of steroid produced superior rates of healing compared with intralesional injection of bone marrow.<sup>42</sup> The steroid method may have equal efficacy but less morbidity compared with surgical treatment. The mechanism of action of corticosteroid is complex, with both anti-inflammatory properties and significant reduction of the cellular metabolism via modulation of the nuclear transcription. Methyl prednisolone has been shown to influence synovial cells to secrete less prostaglandins, resulting in a decrease in bone resorption, while allowing other cells to rapidly reproduce.<sup>43</sup>

Recently, endoscopy-assisted techniques have been implemented by different surgical specialties, following the new concept of minimally invasive surgery. Report of a rare case of condylar lesion of SBC in the mandible treated with an intraoral, endoscopy-assisted approach is reported.<sup>44</sup> The clinical evaluation, radiographic features, and operative techniques are described. Histologic diagnosis of the lesion showed a SBC. When benign lesions of the mandible are not easily and completely removed through a transoral approach, endoscopy-assisted approaches can be used successfully.

The potential wide application of beta tricalcium phosphate (TCP) as a reliable and safe bone substitute in the treatment of lacunar bone defects like SBC was tried and it performs as good as allogenic bone grafts.<sup>45</sup> Most of the beta-TCP could be resorbed and remodeled into new bone. The degradation of beta-TCP was not affected in most individuals, promising a broad application scope in the lacunar bone defect repair.

Recurrences with progression from benign bone lesions are possible, but long intervals being reported suggest a different pathogenesis for sarcomas. This is an extremely rare case, accounting for only 0.26% of all bone sarcomas. This incidence is the same as that of sarcomas arising on fibrous dysplasia and is lower than those arising on bone infarcts or on Paget's disease. This possible event must be considered during follow-up of benign lesions.

## RESEARCH

The acid and alkaline phosphatase activity in fluid aspirated from SBC in six patients was measured and large increases in the concentration of acid phosphatase were found.<sup>9</sup> In some cases this increase was reflected in venous blood concentrations as well. The significance of these findings in the pathogenesis and management of SBC need to be followed. The increased concentration of acid

phosphatase may be related to bone destruction by osteoclastic activity in the walls of the cyst, but the mechanism is uncertain, particularly whether osteoclastic activity initiates bone destruction or only attacks previously damaged bone. The cause for the marked acidosis which is required for acid phosphatase activity remains uncertain, and the fluid within the cyst does not show such a marked acidosis.

To better elucidate the pathophysiology of the SBC, the activity of nitric oxide (NO) and cytokines in the cyst fluid as well as in the cyst membrane were analysed.<sup>46</sup> The levels of nitrate and nitrite were significantly higher in the cyst fluid than in serum. Immunostaining of cells in the stroma and lining cells of the cyst wall was strongly positive for inducible nitric oxide synthase. The levels of interleukin (IL)-6 and IL-1-beta in the cyst fluid were elevated, and cells in the cyst membrane were positive for tumor necrosis factor-alpha, IL-6, and IL-1-beta. Cultured cells from the cyst membrane were induced in the production of nitrate and nitrite in response to cytokine treatment. These findings suggest that the SBC was in a state favorable for the production of NO. From these results, a proposal for the mechanism of bone destruction in SBC is outlined. The degradation of the extracellular matrix components of collagen and proteoglycans is attributed to matrix metalloproteinases (MMPs) whose production is stimulated by NO and IL-1 $\beta$ . In reaction with superoxide, nitric oxide forms peroxynitrite, which leads bone cells to apoptosis. Nitric oxide has an important role in the advancement of the SBC. Steroid might have a blocking effect in the production of MMPs and an anti-inflammatory effect against IL-1 $\beta$ .

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