Aneurysmal bone cysts (ABCs) were first described in 1942 by Jaffe and Lichtenstein, who coined the term aneurysmal cyst because of the pathologic appearance of the lesion within bone. These bone lesions are benign and are typically associated with pain, swelling, or the presence of an expansile mass. ABCs are considered primary lesions in approximately 70% of cases, with the remaining 30% arising secondary to different primary tumors.

The patient with ABC most commonly presents in the first two decades of life. Common lesion sites include the femur, tibia, fibula, humerus, skull, and posterior elements of the spine. Multiple theories have been proposed regarding the pathophysiology of ABC, including vascular, traumatic, and genetic etiologies. Primary ABC has a low incidence rate, ranging from 0.14 to 0.32 per 100,000 individuals. The goal of management is to eradicate the lesion completely while simultaneously preserving as much of the normal host bone as possible.

Pathophysiology

Much debate exists regarding the nature of ABCs. Dabska and Buraczewski were among the first to comment on the pathophysiology and natural history of the ABC. They divided its progression into four phases, with the initial phase described as osteolysis of the marginal part of the bone with discrete elevation of the periosteum. The growth phase is characterized by the progressive destruction of bone. Demarcation of the lesion is poor during this phase; bony shells and septations may not be obvious on plain radiographs. The stabilization phase is defined by the classic ABC appearance: an expansile lesion with a distinct bony shell and osseous septations. In the healing phase, progressive ossifi-
cation of the lesion is obvious and results in a bony mass with a somewhat irregular structure.

Campanacci et al described the lesion as a response to local hemorrhage. An initial insult produces intraosseous bleeding, leading to the formation of a cyst. The cyst walls may house capillaries that hemorrhage into the newly formed cavity, producing osteolytic and reparative tissue, which may ultimately explain the lesion's predilection for rapid, aggressive expansion. Lichtenstein proposed that the ABC is a reactive lesion rather than a true neoplasm and that vascular disturbances in bone lead to increased intraosseous pressure, causing local destruction and distension of bone. Ratcliffe and Grimer described the formation of an ABC at a fracture site in a previously normal tibia. Like Capanacci et al and Lichtenstein, the authors postulated that the fracture altered the intraosseous blood flow and subsequently led to formation of the lesion.

Recently, genetics have been implicated in the etiology of ABC, leading some to believe that ABC is a true neoplasm rather than a reactive process. In a histopathologic study, Oliveira et al reported that gene rearrangements localized to t(16;17) in 36 of 52 primary ABCs (69%) in which the ubiquitin-specific protease 6 oncogene was placed under the regulatory influence of the highly active cadherin-11 promoter. They found no such translocations in 17 cases of secondary ABC. The authors concluded that these findings confirm a true neoplastic etiology. Others have shown that upregulation of ubiquitin-specific protease 6 may induce matrix metalloproteinase production by activation of nuclear factor κ-light-chain-enhancer of activated B cells, which ultimately leads to tumorigenesis.

Leithner et al reported the results of immunohistochemistry and in situ hybridization in 19 specimens of ABC. They found insulin-like growth factor-I or mRNA coding for this growth factor primarily localized in multinucleate giant cells in all of the specimens. Insignificant levels of expression were found in normal human bone tissue. These findings support the theory that genetic factors may play a significant role in the development of primary ABC.

Clinical Presentation

In patients with ABC, age of onset ranges from 1 to 59 years, with the greatest prevalence between ages 12 and 13 years. Typically, males are affected more often than females, with reported ratios ranging from 1:1.04 to 1.8:1. In a population-based analysis of 110 surgically treated ABC patients listed in the Vienna Bone Tumor Registry, 73 ABCs (66%) occurred in patients younger than age 20 years.

The patient with primary ABC typically reports pain and may present with soft-tissue swelling or a palpable expansile mass. As with most benign bony malignancies, secondary symptoms such as fever, weight loss, malaise, nausea, or vomiting are not common.

ABC commonly arises at sites such as the femur, tibia, humerus, and fibula; these sites account for approximately 52% of ABC sites. Other common locations include the skull and spinal column, with ABC being one of the most common malignancies (along with osteoid osteoma and osteoblastoma) that affect the posterior elements of the spine. In children, the most common sites of extremity ABC are the femur and tibia. ABCs in these areas are typically confined to the metaphyseal regions of the bone.

Classification

Several classification systems have been developed to categorize ABCs. Enneking divided lesions into three stages: inactive, active, and aggressive. The inactive tumor is the most benign because the lesion is contained. Expansion is rare, and there is minimal inflammation or periosseous reaction. An active lesion typically produces mild symptoms such as pain, with expansion and cortical thinning as well as a layer of reactive bone separating the lesion from normal bone visible on radiographs. Aggressive tumors are rapidly expansile and destroy surrounding tissues. This subtype is typically the most symptomatic.

Capanna et al based their system on five morphologic subgroups (Figure 1). Type I lesions are centrally located and well contained, with either no outline or a slightly expanded outline. Type II lesions have marked expansion and cortical thinning with involvement of the entire bony segment. Type III lesions are eccentric and metaphyseal and typically involve only one cortex. Type IV lesions are the least common subgroup and develop subperiosteally, expanding away from the bone. Type V lesions occur periosteally and expand peripherally, ultimately penetrating cortical bone.

Imaging

Suspected ABC can be evaluated initially with plain radiography. The classic radiographic appearance of ABC is a radiolucent cystic lesion within the metaphyseal portion of the bone. The lesion is destructive and may expand into the surrounding cortical bone. The mass may elevate the periosteum, but it typically remains contained by a thin shell of cortex. Typically, ABCs are eccentric
but may also be central or subperiosteal. Lesions in the epiphysis should raise suspicion of secondary changes caused by a different neoplastic process. Occasionally, CT is used preoperatively to better define the bony limits of the lesion. MRI with contrast typically demonstrates internal septations that may contain characteristic fluid-fluid levels, signifying layering of solid blood components within cystic areas of the lesion (Figures 2 and 3). This finding is highly suggestive of an ABC but is not pathognomonic because it is also a radiographic characteristic of telangiectatic osteosarcoma (TOS), giant cell tumor, secondary ABC, and fracture through a simple cyst. In a study of the value of radiography and MRI for diagnosis of ABC, Mahnken et al compared the sensitivity and specificity of MRI alone with that of conventional radiography with MRI. They found that MRI was superior to conventional radiography in terms of specificity. However, the sensitivity, specificity, and positive predictive value were greatest when both modalities were used in concert.

Figure 1

Figure 2
AP (A) and lateral (B) radiographs demonstrating an expansile metaphyseal lesion of the distal ulna with thinning of the bony cortices and internal septations in a 46-year-old man who presented with a painful mass on the distal forearm. C, Axial fat-saturated T2-weighted magnetic resonance image demonstrating fluid-fluid levels consistent with an aneurysmal bone cyst (ABC). Histology confirmed ABC. D, Postoperative AP fluoroscopic image of the distal ulna following en bloc resection.
Histology

Dabska and Buraczewski\textsuperscript{11} were among the first to describe the histopathology of ABCs as that of a cavernous vascular tumor ranging from a few millimeters to 1 to 2 cm in diameter, with intraslesional communicating cavitations without blood clots. Typically, microscopic analysis of ABC reveals hemorrhagic tissue with cavitory spaces separated by fibrous septa composed of spindle cells, inflammatory cells, and a smaller percentage of giant cells (Figure 4). Osteoid formation with or without osteoblastic rimming may be noted. In a clinicopathologic study of 238 patients with ABCs, 5% to 10% of lesions were solid with little to no cystic formation.\textsuperscript{16} These lesions, however, are histologically similar to the solid portion of the classic ABC.

Currently, incisional biopsy with histologic evaluation is the standard for diagnosis of ABC. Creager et al\textsuperscript{17} retrospectively reviewed 23 histologic specimens from 23 patients with ABCs who were initially evaluated with fine needle aspiration biopsy (FNAB). In 6 cases (26%), the aspirates were insufficient for diagnosis. They concluded that FNAB was associated with an unacceptably high risk of missed diagnosis and found that radiologic correlation of the findings increased the accuracy of FNAB.

Differential Diagnosis

Differential diagnosis of ABC includes benign lesions, such as unicameral bone cysts, or tumorous lesions, such as chondromyxoid fibroma, chondroblastoma, giant cell tumor, or osteoblastoma. It is necessary to distinguish ABCs from these benign lesions because up to 30% of ABCs are ABC-like lesions arising from other primary tumors.\textsuperscript{2} ABC must be differentiated from TOS, given their radiographic and histologic similarities (Table 1). In a retrospective review of 40 pathologically confirmed cases of TOS, Murphey et al\textsuperscript{18} reported thick, nodular enhancement of the tissue surrounding cystic spaces on contrast MRI and CT consistent with TOS. This nodular enhancement was associated with high-grade sarcomatous tissue and hemorrhagic, necrotic spaces. These identifying features could also be seen before contrast was administered in 32 cases (80%). In contrast, ABC has a thin peripheral rim and septal enhancement without significant nodularity. Histologically, TOS is characterized by blood-filled lakes, areas of necrosis, and giant cells. Most importantly, TOS has areas of

\begin{figure}[h]
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\caption{A, AP radiograph of the distal femur demonstrating a well-defined metaphyseal lytic lesion in a 26-year-old man who reported left knee pain and swelling for 6 months. Axial noncontrast CT (B) and axial fat-saturated T2-weighted magnetic resonance image (C) of the same lesion demonstrating internal septations, fluid-fluid levels, and thinning and erosion of the posterior cortex with minimal soft-tissue expansion. Curettage with cryotherapy and subsequent bone grafting, cementing, and internal fixation were performed. D, Postoperative AP radiograph of the distal femur following curettage, grafting, and internal fixation.}
\end{figure}
pleomorphism and atypical mitotic figures that are visible under high-power microscope magnification (Figure 5). Osteoids may or may not be present. Accurate diagnosis is essential because the prognosis and treatment of ABCs are significantly different than those of TOS and other malignant lesions of bone.

**Management**

Diagnosis of ABC must be confirmed histologically before initiating definitive treatment. Once the diagnosis is established, management generally consists of intralesional curettage and bone grafting, with or without adjuvant therapy. Adjuvant treatment is intended to treat microscopic disease contamination within the tumor bed to lower the incidence of local recurrence.

Wide resection and reconstruction can be considered for lesions that have destroyed the metaphyseal bone in periarticular areas. For large tumors in the axial skeleton and pelvis, preoperative embolization can be considered to minimize intraoperative bleeding; embolization may not be required for small, peripherally based tumors. Lesions that involve the spine should be treated in consultation with an experienced spine surgeon. Long-term clinical and radiographic follow-up is required to assess for recurrence and to monitor function. Spontaneous resolution of ABCs has been reported.19

**Curettage and Bone Grafting**

Currently, curettage and bone grafting with or without adjuvant therapy is the accepted method for management of ABC.16 In the literature, the description of curettage ranges from creation of either a small fenestration or large cortical windows in the cyst...
to complete saucerization. Saucerization is preferred when a strut of cortical bone may be preserved to allow maintenance of the structural integrity of the bone. Cottalorda and Bourelle found that curettage through a small fenestration in the cyst led to a higher rate of recurrence and should be avoided. Gibbs et al found that curettage with a high-speed burr reduced the incidence of recurrence independent of the type of graft (eg, cancellous autograft, cancellous allograft, polymethyl methacrylate) used. The authors reported that 4 of 34 patients with ABCs (12%) who underwent curettage had a local recurrence, whereas no patient who underwent complete excision of the cyst had a recurrence. The authors found that recurrence was associated with young age and open growth plates.

Garg et al retrospectively evaluated ABCs of the spine and reported no recurrences in eight cases treated with a surgical technique using intraslesional curettage, electrocautery, high-speed burr, and bone grafting compared with four recurrences in four cases treated with curettage and bone grafting alone. Complications associated with curettage are often related to incomplete resection of the lesion and resultant recurrence.

Cryotherapy
Use of cryotherapy has been found to reduce the recurrence rate of ABC. In a retrospective review of 27 ABCs treated with cryotherapy, Schreuder et al reported a 3.7% rate of recurrence. Similarly, Peeters et al reviewed 80 consecutive cases of ABC treated with curettage and cryotherapy. At an average follow-up of 55 months, the authors found only four local recurrences for an overall rate of 5%. These recurrences were all successfully treated with repeat curettage and cryosurgery.

Sclerotherapy
Sclerotherapy is a noninvasive management method based on the theory that ABCs arise as a vascular malformation and would heal if the hemodynamic disturbance were controlled. In a prospective randomized study, Varshney et al evaluated 94 patients treated with either sclerotherapy with polidocanol or curettage with high-speed burr and bone grafting. The average follow-up was 4.4 years. The sclerotherapy group had a 93.3% healing rate compared with 84.8% in the curettage group. The authors determined that the sclerotherapy group had a similar rate of recurrence but better functional outcomes and fewer complications (eg, deep or superficial infection, growth disturbances) than did the curettage group. Complications unique to the sclerotherapy group include local induration at the injection site and hypopigmentation. Patients who underwent sclerotherapy required a higher number of repeat procedures to achieve healing than did those treated with curettage. This finding has been reported in other similar studies, although the underlying mechanism of failure has not been elucidated. In a retrospective study of 72 patients with ABCs treated with percutaneous sclerotherapy with polidocanol, Rastogi et al reported a mean clinical response of 84.5%; however, patients required an average of three injections.

Ethibloc (Ethnor Laboratories/Ethicon, Norderstedt, Germany), a local fibrogenic and thrombogenic agent that was initially used for vascular embolization, is another possible sclerotherapy agent. Adamsbaum et al reviewed 17 patients with ABC who were treated with Ethibloc injection. At a 5-year follow-up, 14 patients (82.4%) achieved complete healing. However, 16 patients (94.1%) had local inflammatory reactions, and 3 (17.6%) developed small cutaneous fistulae. Ethibloc has been associated with severe complications, including pulmonary embolism and aseptic fistulae that require incision and drainage. A fatal
case of cerebellar infarct following Ethibloc injection into a cyst in the atlas has also been reported.\textsuperscript{29} Given the rate of severe complications, some authors consider Ethibloc injection an alternative to surgery rather than a first-line treatment.

Radionuclide Ablation

Recently, radionuclide ablation has been proposed for management of ABC. This method has been used successfully to manage other diseases such as rheumatic synovitis and recurrent hemarthroses associated with hemophilia. Interest in this modality has grown given the radiosensitivity of ABCs and the ability of radionuclide ablation to control disease within a cavity. Bush et al\textsuperscript{30} retrospectively reviewed five patients with large ABCs treated with a CT-guided injection of chromic phosphate P32. The patients were followed for more than 2 years. The authors reported successful control of the lesion with one injection in four patients and a complete success rate after two injections. Although this method is promising, additional research is required before it may be considered as a first-line treatment for ABC.

Arterial Embolization

The results of selective arterial embolization for management of ABC have also been evaluated. In a retrospective study of 36 patients with ABCs treated with arterial embolization, Rossi et al\textsuperscript{31} found that 32 patients (94\%) had full resolution of the lesion on radiographic and clinical examination. Of these cases, 14 required more than one embolization. Two cases of skin necrosis were reported; one required flap coverage. Risk factors associated with the need for repeat embolization were age <16 years or lesions >5 cm in size. Lesions in the thoracic or upper lumbar spine require a careful approach because inadvertent embolization of the artery of Adamkiewicz could lead to cord ischemia and anterior cord syndrome; therefore, the surgeon must make every attempt to visualize this artery to prevent inadvertent embolization.

Recurrence

In a long-term study of 150 ABCs treated over 20 years, Mankin et al\textsuperscript{34} reported a local recurrence rate of approximately 20\%. Patients in this series were treated primarily with curettage and either implantation of allograft chips or polymethyl methacrylate. Several risk factors have been implicated in the high rate of ABC recurrence. In several clinical series, younger age (ie, <12 years) has been associated with an increased risk of recurrence.\textsuperscript{21,35,36} Dormans et al\textsuperscript{12} however, did not find a significant difference in the recurrence rate in patients older or younger than age 10 years. Open physes also have been associated with an increased risk of recurrence after curettage with a high speed burr; this may be due to less aggressive curettage of the area because of the fear of inducing growth arrest.\textsuperscript{21} Despite the increased risk, some do not believe that more aggressive management is warranted because the risk of complications such as violation of articular cartilage or destruction of the physal could predispose the patient to future angular deformity or limb-length discrepancy.\textsuperscript{36}

Histologic evaluation may serve as a prognostic indicator of recurrence. Docquier et al\textsuperscript{37} determined the likelihood of recurrence based on the proportion of cellular tissue (ie, giant cells, stromal cells) relative to the amount of osteoid (ie, bone matrix) and fibrillar components (ie, fibroblasts, collagen) in 21 biopsy samples. The authors compared the ratio of osteoid and fibroblastic components with the cellular content of each specimen. Recurrent ABCs had a predominantly cellular component. When the osteoid component predominated, the prognosis was good because the cyst was presumed to be in a healing phase.

Mitotic indices may also have prognostic value. Ruiter et al\textsuperscript{38} found that the recurrence rate of ABCs was significantly higher in cases with a mitotic index of ≥7 per 50 fields than in those with a lower mitotic index. Other histologic factors that have been associated with recurrence include the presence of an immature
lace pattern and fibromyxoid nodular fasciitis-like areas.39

Malignant Transformation

A small number of malignant transformations of ABCs have been reported. Some reports were associated with the use of adjuvant radiation in addition to primary treatment.50 Brindley et al49 reported on two cases of malignant transformation that occurred 5.5 and 12 years, respectively, after the ABCs were managed with intralesional curettage without adjuvant radiation. A TOS and fibroblastic osteosarcoma, respectively, were identified at the sites of the ABC. These cases demonstrate the need for continued long-term follow-up, especially if symptoms recur or change.

Summary

ABCs are benign, active lesions that may cause significant morbidity in children and adults. Although the risk of malignant transformation is very rare, these lesions are typically managed surgically, with the primary goals of completely eradicating the lesion and minimizing the risk of recurrence. Secondary goals are improved function and resolution of pain. Compared with other management methods, excision of the primary lesion is associated with the lowest rate of recurrence, although this method is not always feasible from a functional standpoint.

Currently, open curettage with adjuvant therapy and bone grafting is the most widely accepted management option. It has a low rate of recurrence, with minimal risk to the function of the affected area. Recently, other treatments have gained attention, including sclerotherapy, radionuclide ablation, and selective arterial embolization. Excellent success rates have been reported with use of these modalities. However, there is paucity of prospective randomized controlled studies that directly compare treatment modalities; thus, treatment is typically guided by surgeon preference.

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References

Evidence-based Medicine: Levels of evidence are described in the table of contents. In this article, reference 26 is a level II study. Reference 36 is a level III study. Reference 37 is a level IV study.

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