Aneurysmal Bone Cyst

Fine-Needle Aspiration Findings in 23 Patients With Clinical and Radiologic Correlation

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Abstract

Aneurysmal bone cyst (ABC) is an osseous mass lesion that accounts for 1% of primary bone tumors. We describe 23 cases of ABC initially evaluated by fine-needle aspiration biopsy (FNAB). In 4 cases, the ABC was secondary to another primary tumor. Aspirates from 6 cases (26%) were insufficient. Twelve aspirates diagnosed as ABC by FNAB were confirmed as ABC by histologic examination. The accuracy of FNAB was 82% when cases insufficient for evaluation were excluded. One case diagnosed as ABC cytologically was subsequently found to be metastatic carcinoma. In another, the specimen was interpreted as ABC vs giant cell tumor. In the remainder, a diagnosis of ABC was favored cytologically. Owing to the nonspecific findings, ABC cannot be definitively diagnosed by FNAB. However, the presence of typical clinical and radiographic features in conjunction with a blood-rich, mesenchymal cell containing aspirate devoid of overtly malignant cells strongly suggests the diagnosis of ABC.

Aneurysmal bone cyst (ABC) is an expansile, destructive lesion of bone first recognized as a pathologic entity in 1942.[1] Historically, ABCs have been considered nonneoplastic cystic masses that have been divided into primary and secondary (histologically indistinguishable) types.[2,3] The former occur de novo, and the latter arise adjacent to and in conjunction with primary neoplasms of bone, eg, giant cell tumors and chondroblastomas. Histologically, ABC is characterized by channels and multiloculated cyst-like spaces filled with blood and lined by fibrous septa that may or may not contain osteoclast-like giant cells, osteoid, woven bone, and chondroid matrix material. ABC represents approximately 1% to 2% of primary bone tumors, occurs predominantly within the first 2 decades of life, and usually involves the long bones or the spine and pelvis, although any bone may be affected. The routine skeletal radiologic features of ABC vary depending on its developmental phase. In the long bones, most cases arise in the metaphysis and produce a lytic lesion that is circumscribed in the early phase and progresses to an expansile mass with cortical destruction. Owing to these radiologic features and its often rapid growth, the clinical differential diagnosis, in addition to ABC, most commonly includes malignant processes such as osteosarcoma and metastases. Because ABC has essentially no metastatic potential, distinction between these entities is of paramount importance.

The use of fine-needle aspiration biopsy (FNAB) for the initial evaluation of primary bone tumors is controversial, although it is gaining popularity at several large medical centers.[4-11] The evolution of less invasive procedures for the initial evaluation of clinically primary bone tumors has evolved out of necessity to minimize disruption of the tumor bed to prevent potential dissemination of disease. FNAB has gained

popularity over open biopsy or large-bore needle biopsy because it is minimally invasive, relatively easy to perform, and less expensive, and results are generally available much more rapidly. Many cytopathologists are not comfortable evaluating bone tumors by FNAB because they have limited experience in this area. In addition, it is required that data from the clinical examination and radiographic findings be correlated with the FNAB features (triple test). A benefit of bedside clinical FNA is the opportunity to discuss the clinical examination and radiographic attributes with the clinician, a practice that has been demonstrated to increase the accuracy of FNAB.[4] In our experience of evaluating conventional biopsy specimens, it may be much more time consuming to review radiographic and clinical findings with the appropriate clinicians after the biopsy has been performed and the specimen has been decalcified and processed.

To our knowledge, no large series has assessed the value of FNAB in the initial evaluation of ABC. We present a retrospective analysis of clinical, radiologic, and FNAB findings in a large series of patients with ABC who underwent FNA as the initial diagnostic modality.

Materials and Methods

The case files from Wake Forest University Baptist Medical Center, Winston-Salem, NC, and Duke University Medical Center, Durham, NC, were searched for cytology specimens in which the diagnosis of ABC was made on FNAB or on a subsequent histologic specimen. The cytologic features of 23 specimens obtained from 23 patients with a diagnosis of ABC were reviewed. Histologic specimens were available for review in all but 2 cases. The 2 cases without histologic specimens had classic clinical and radiologic features and, thus, are included herein, even though surgical specimens were not available for review, even after a follow-up period exceeding a decade. Clinical information, including initial symptoms, treatment modalities, and pertinent clinical follow-up data were obtained from the patients' medical records. One patient with an associated chondroblastoma has been previously described.[12]

Tumors were aspirated by a cytopathologist, a surgeon, or a radiologist under computed tomographic guidance, using 18- to 23-gauge needles attached to a 10- or 20-mL syringe with or without the assistance of an aluminum syringe holder. FNAB smears were fixed in 95% ethanol and stained using the Papanicolaou technique and/or air-dried and stained using the rapid Romanowsky method. The remainder of the aspirate material was rinsed into saline, and cytocentrifuged preparations and/or paraffin cell blocks were prepared in the usual manner. The experience level of cytopathologists varied from more than 25 years to only a few years. A total of 12 pathologists were the primary interpreters of these specimens. In many cases, more than 1 pathologist reviewed the specimens before they were signed out.

Results

Clinical Data

The clinical findings, cytologic features, and histologic diagnoses of the 23 cases are summarized in **Table 1**. Patients' average age was 29.5 years (range, 3-74 years). The most common radiographic finding was a destructive and/or expansile lytic mass that involved a long bone in 10 cases (43%), a flat bone in 8 cases (35%), a vertebra in 3 cases (13%), the mandible in 1 case (4%) and the finger in 1 case (4%). When long bones were involved, the majority manifested as a metaphyseal-centered lesion with a smaller fraction demonstrating diaphyseal origin. In most cases of primary ABC, the radiographic differential diagnosis included a primary bone malignancy, most commonly a telangiectatic osteosarcoma (TOS) vs an ABC (Table 1). The division between primary and secondary ABCs was based largely on the histologic sample and not on the cytologic specimen.

Pathologic Data

Of the 23 cases in our study, 21 had histologic confirmation. Of the 16 cases with a histologic diagnosis of primary ABC, 4 aspiration specimens were considered inadequate for diagnosis at the time of initial interpretation. Of the remaining 12, 11 were diagnosed as consistent with an ABC and 1 was interpreted as ABC vs giant cell tumor. This last sample was quite cellular compared with many of the others. The smears were typically dominated by blood. The number of nonerythrocytic elements typically varied from scant to somewhat moderate and included dispersed or loosely cohesive, spindle-shaped, fibroblast-like cells; histiocytes, the cytoplasm of which occasionally contained hemosiderin; multinucleated osteoclast-like giant cells; fragments of collagen; and, at times, small pieces of bone. Although the relatively stagnant blood in ABCs could conceivably alter the morphologic features of the sampled erythrocytes, we could find no consistent alteration.

One specimen considered to be an ABC cytologically was metastatic carcinoma associated with a small ABC-like lesion histologically. It is unlikely that this vascular component was an ABC for several reasons, including the patient's age and the location of the lesion. This patient was 55 years old, an age group in which ABC is uncommon. The clavicle is also an unlikely site for ABC. Furthermore, the radiographic impression included metastatic neoplasm. A bloody aspirate contained rare, benign, spindle-shaped mesenchymal cells;

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multinucleated histiocytes; and no malignant cells. Because the clinical impression of malignancy was high, a repeated aspirate and open biopsy were performed, and both demonstrated metastatic poorly differentiated non–small cell carcinoma. The lack of tumor cells on the initial aspirate was the result of sampling error.

In 4 cases, the ABC was secondary to another primary bone tumor (2 giant cell tumors, 1 osteoblastoma, and 1 chondroblastoma; this last case has been previously reported).[12] In these cases, the radiographic differential diagnosis included a primary bone tumor and ABC. The giant cell tumors were correctly diagnosed by FNAB. The other 2 samples were considered inadequate for diagnosis.

In cases with primary and secondary ABCs, inadequacy was based on specimens consisting solely or largely of blood, with only rare, benign mesenchymal elements in the smears. Overall, the inadequacy rate was 26% (6/23) and deemed related to sampling error.

If the specimens considered inadequate for diagnosis are excluded, there was 1 false-negative case in which malignant cells were not present in the smears and 2 cases in which a false diagnosis of giant cell tumor was made on the cytologic material. Thus, of the 17 adequate samples, a correct diagnosis was made cytologically in 14, for an accuracy of 82%. If one excludes case 23 in which the diagnosis was "ABC" vs giant cell tumor, the accuracy is 81% (13/16). For lesions with a final diagnosis of primary ABC with an adequate aspirate, the cytologic diagnosis "consistent with ABC" was made in 88% (14/16) of the cases. For primary ABC, if one includes inadequate aspirates, the accuracy falls to 74% (14/19).

Discussion

Evaluation of primary bone tumors by FNAB is controversial, although it is gaining popularity. FNAB is minimally invasive compared with open biopsy and has a low complication rate and high diagnostic value. Complications such as poor wound healing, inappropriate placement of the incision, and contribution of open biopsy to unnecessary limb amputation have been cited as disadvantages of open biopsy procedures and can be avoided by using closed biopsy procedures

Table 1
Clinical and Pathologic Features in 23 Cases of Aneurysmal Bone Cyst

Case No./ Age (y)	Cyst Location	Plain Film		Diagnosis	
		Differential Diagnosis	Features	Cytologic	Histologic
1/43	Proximal phalanx	ABC	Expansile; lytic	Inadequate	ABC
2/32	Proximal tibia	GCT	Lytic	GCT	GCT with secondary ABC
3/14	Pubic ramus	ABC vs osteosarcoma	Expansile; lytic	Inadequate	ABC
4/18	Distal tibia	ABC vs osteosarcoma	Lytic	C/W ABC	ABC
5/25	Vertebral body (T1)	ABC vs osteosarcoma	Lytic	C/W ABC	ABC
6/28	Vertebral body (C2)	ABC vs osteoblastoma	Expansile; lytic	Inadequate	Osteoblastoma with secondary ABC
7/21	Mandible	Langerhans cell histiocytosis	Expansile; lytic	Inadequate	ABC
8/55	Clavicle	Metastatic carcinoma	Destructive; lytic	C/W ABC	Metastatic carcinoma
9/74	Rib	ABC vs metastasis	Expansile; lytic	Inadequate	ABC
10/64	Femur	Metastatic carcinoma	Expansile; lytic	C/W ABC	ABC
11/18	Acromion	ABC vs chondroblastoma	Destructive; lytic	Inadequate	Chondroblastoma with secondary ABC
12/14	Distal tibia	ABC vs osteosarcoma	Expansile; multilobulated; lytic	C/W ABC	ABC
13/11	Pubic ramus	ABC vs Ewing sarcoma	Expansile; lytic	C/W ABC	ABC
14/11	Distal femur	Nonossifying fibroma	Expansile; lytic	C/W ABC	ABC
15/9	Distal fibula	ABC vs osteosarcoma	Expansile; lytic	C/W ABC	ABC
16/19	Clavicle	ABC vs osteosarcoma	Expansile; lytic	C/W ABC	ABC
17/12	Proximal tibia	ABC	Expansile; lytic	C/W ABC	ABC
18/60	Vertebral body (L1)	ABC vs osteosarcoma	Expansile; lytic	C/W ABC	ABC
19/40	Rib	Plasmacytoma; ABC; metastasis; chondrosarcoma	Expansile; lytic	C/W ABC	ABC
20/49	Proximal tibia	Giant cell tumor	Lytic	GCT	GCT with secondary ABC
21/3	Distal fibula	ABC vs osteosarcoma	Bubbly; lytic	C/W ABC	NA*
22/45	Rib (multiple)	Metastasis; sarcoid; enchondroma	Expansile; multilobulated; lytic	C/W ABC	NA†
23/13	Distal tibia	ABC	Cystic; lytic	ABC vs GCT	ABC

ABC, aneurysmal bone cyst; C/W, consistent with; GCT, giant cell tumor; NA, not available.
* No histologic follow-up available for >10 years.
† No histologic follow-up available for >8 years.

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such as FNAB.[13] Although the complications of FNAB are rarely reported, the potential impact of therapeutically important diagnostic error has been evaluated by Layfield et al.[5] The value of FNAB in the distinction between malignant and benign primary bone processes and in diagnosing bone metastases has been well documented.[6-11,14,15] However, little attention has been directed specifically toward the findings and use of FNAB in the evaluation of ABC.

Historically, ABCs have been considered nonneoplastic entities that account for 1% to 2% of clinically significant, noninflammatory mass lesions. They are divided into primary and secondary types, the former unassociated with another primary bone tumor. Today, however, we recognize that, in all likelihood, primary ABCs (but not secondary ABCs) are clonal in origin and, thus, neoplastic.[16-19] Most often, this involves a translocation between the *USP6* on the 17p13 locus and promoter regions on other chromosomes, most frequently the *CDH* 11 gene located at 16q22.[19] In other cases, a translocation is not identified, but rearrangements of these genes, especially *USP6,* are present.[18]

Any institution that routinely evaluates bone tumors by FNAB will eventually encounter an ABC. Radiologic correlation is a critical factor in evaluating any bone tumor by FNAB, just as it is with histopathologic examination. Because the diagnosis of ABC is made largely by exclusion of other processes and the cytologic features are nonspecific, correlation with clinical and imaging studies is of absolute paramount importance in this setting. Still, not all classic clinical, radiographic, and gross pathologic attributes are present. At least 5% are considered solid variants, with little or no cystic change.[20-22] We also appreciate the rare occurrence of soft tissue (nonosseous) ABCs.[23]

Smears are predominated by blood with scattered giant cells, a variable number of spindle cells as single cells or in small groups, histiocytes with or without cytoplasmic hemosiderin, and degenerated RBCs **Image 1**.[11] Fibrous septa lined by osteoclasts and/or reactive stromal cells and bone spicules may be seen **Image 2**. Because these findings are nonspecific, the main problem is deciding when they are representative of the mass in question. In the present series, the qualitative findings observed in cases in which the diagnosis of ABC was strongly suggested were similar to the cases deemed insufficient for evaluation, approximately 30% of cases. Others have reported an insufficient rate of approximately 30% in the evaluation of bone and soft tissue tumors by FNAB, and this percentage is consistent with the insufficient rates for ABC at our institutions.[5] Given that the diagnostic features of ABC are essentially identical to those for cases deemed insufficient for evaluation, how can we hope to make an accurate diagnosis by FNAB? Clearly, there are factors that are useful in making the distinction between an inadequate sample and one representative of an ABC because an accuracy of 88% was obtained in the present study when the diagnosis of primary ABC was suggested.

Radiologic correlation is the most critical factor, and, in general, it has been demonstrated that the ability to review

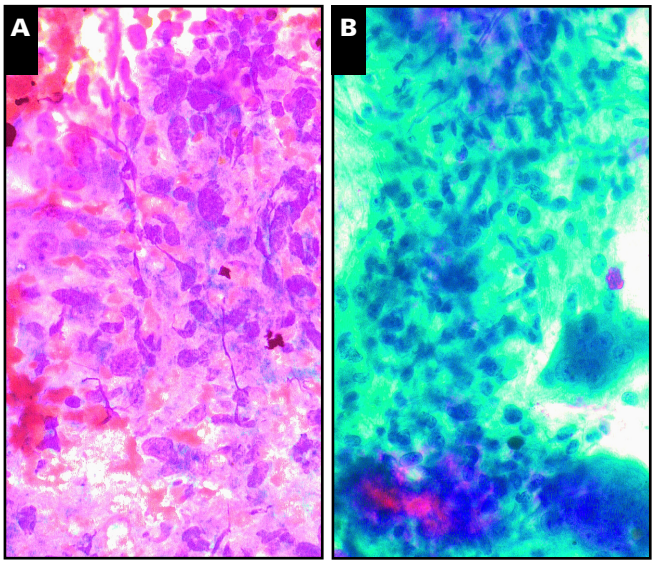

Image 1 An aspirate smear of an aneurysmal bone cyst. Groups of reactive spindled cells, osteoclast-like giant cells, and occasional macrophages containing partially degraded RBC products are observed in a blood-rich background (**A**, rapid Romanowsky, ×400; **B**, Papanicolaou, ×400).

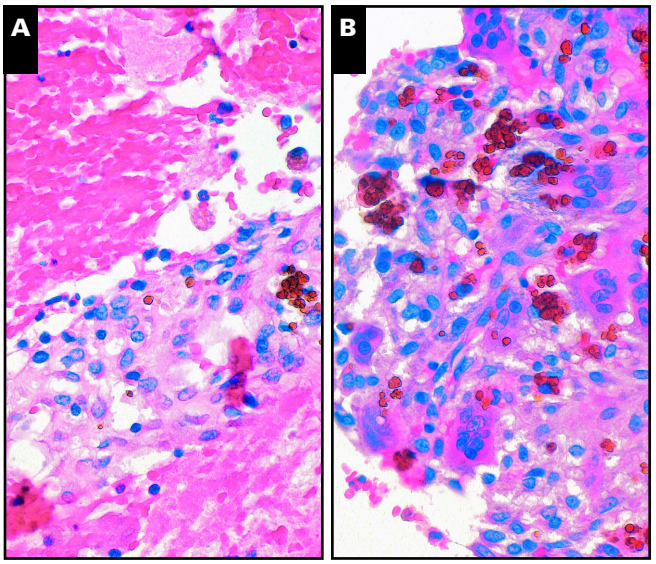

Image 2 **A**, A cell block from an aspirate of aneurysmal bone cyst. Reactive spindle cells, osteoclast-like giant cells, and macrophages containing partially degraded RBC products are shown (H&E, ×200). **B**, A cell block from an aspirate of aneurysmal bone cyst demonstrates a fibrous septum containing reactive stromal cells (H&E, ×200).

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these findings with the appropriate clinician increases the accuracy of FNAB.[9] Radiographically, ABCs may have several appearances. In the long bones, the features of ABC evolve and are categorized according to their pattern of progression. Early, a small, frequently eccentric and nonexpansile lytic lesion that may have permeative growth is observed. Rapid destructive growth characterizes the growth period, and Codman triangles may be observed. During this period, fast growth may exceed the ability of the periosteal bone to encompass the tumor, bony circumscription may be lost, and soft tissue may be involved. This phase is the most likely to be confused with malignancy. The stable phase demonstrates the more classic features of ABC, notably expanded bone with a distinct bony shell and internal trabeculations. Finally, a healing phase in which the bony trabeculae become increasingly ossified results in the radiographic appearance of an irregular bony mass with coarse trabeculation. ABCs in vertebral bones may demonstrate the same progression, and most commonly arise in the vertebral arch and spinous processes.

In the present series, of the 16 cases of primary ABC confirmed histologically, ABC was in the radiologic differential diagnosis in 14 cases (88%). Osteosarcoma is usually in the same differential diagnosis, and, in older patients, metastases may be as well. Basically, FNA corroborates the radiographic impression. Computed tomography scanning and, especially, magnetic resonance imaging may be helpful (although not totally sensitive and specific) by demonstrating fluid-fluid levels in ABCs.[24,25] This is generally not useful in distinguishing ABC from TOSs. The cytologic distinction of TOS and ABC may, in some cases, be impossible. One reason for this would be less than satisfactory needle sampling of the TOS such that foci with frankly sarcomatous cells are not punctured. Alternatively, some TOSs are composed of relatively bland malignant cells that may not be recognizable as to their true nature in smears.

ABC aspirates, while generally paucicellular and blood-rich, may show a moderate degree of cellularity with reactive atypia with mitotic figures. However, atypical mitotic figures are not observed. It can be argued that even a blood-rich aspirate may provide useful information by helping to rule out malignancy if sampling is considered adequate. Osteosarcomas and other primary bone sarcomas often yield cellular and diagnostic material in the large majority of cases. Kilpatrick et al[8,10] demonstrated unsatisfactory rates of 7% and 13% for the primary diagnosis of osteosarcoma and other pediatric primary bone tumors. Treaba et al[15] analyzed the usefulness of FNAB in the evaluation of bone lesions in patients with a history of nonosteogenic malignancy. They demonstrated a very high accuracy rate for the diagnosis of metastatic disease and an unsatisfactory rate of only 4.8%.

Despite the high rates of diagnostic adequacy in these studies, insufficient cases still exist and yield blood-rich aspirates devoid of malignant cells, similar to aspirates of ABC. In fact, the only diagnostic error in the present series occurred in a 55-year-old patient with known carcinoma in whom a clavicular lesion thought to be metastatic carcinoma by the radiologist was diagnosed as consistent with ABC on FNAB (case 8). Subsequent examinations demonstrated metastatic carcinoma not sampled in the initial aspirate material. It is important to note that this diagnostic error may have been avoided had the triple test been followed. The patient had a known history of carcinoma, was 55 years old, and had a lytic mass thought to be a metastasis by the radiologist and in an unusual location for ABC.

In the present study, 4 cases of ABC arising secondary to another primary bone tumor were evaluated by FNAB. Half of these cases, both giant cell tumors with secondary ABC, were deemed sufficient for evaluation. Both were thought to represent giant cell tumors by the radiologist and were diagnosed as such specifically by FNAB without any indication in the report of secondary ABC. This typifies the difficulty of diagnosing ABC. When a process with more tangible and specific cytologic findings is present, the relatively nonspecific findings observed in ABC are easily overlooked. Conversely, when the presence of ABC is suspected, one cannot totally exclude the possibility of a primary bone tumor with secondary ABC or that a primary bone tumor or metastasis has been unsampled. TOS or osteosarcoma with secondary ABC may yield a hemodiluted and a bloody aspirate, and care should be taken to evaluate the smears for any significant atypia, no matter how dilute the specimen appears. The cytologic features of the solid variant of ABC have been described, and this diagnosis should be considered in the differential diagnosis.[22] Because therapeutic intervention is usually required for treatment of ABC, erroneous diagnoses will usually be discovered and malignancy, when present, realized.

The FNAB features of ABC are nonspecific, although a high diagnostic accuracy can be obtained when this diagnosis is favored clinically and care is taken to correlate the imaging studies and clinical data with the morphologic findings. Aspiration biopsy thus provides important preoperative data for the surgeon. In many patients, the diagnosis of ABC is confirmed at surgery. Another undiagnosed primary bone tumor will usually be evident at the time of operation. Thus, although FNAB may not be fully diagnostic of ABC or representative of all elements present (as in any body site), the orthopedic oncologist can approach the patient with much greater confidence before entering the operating suite.

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