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Initial diagnostic management of pediatric bone tumors

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ABSTRACT

Background: Osteosarcoma (OS) and the Ewing sarcoma family of tumors (ESFT) are the most common primary pediatric bone malignancies. We sought to assess the diagnostic accuracy of initial tumor biopsies in patients with OS or ESFT at a pediatric cancer center.

Methods: All biopsies performed at initial presentation of patients with OS or ESFT at our institution from 2003 to 2012 were retrospectively reviewed. Diagnostic accuracy and incidence of complications were correlated with study variables using logistic regression analysis.

Results: One hundred forty-two biopsies were performed in 105 patients (median age 13.4 years, range: 1.8–23.0), 104 (73.2%) OS and 38 (27.8%) ESFT. Thirty-one (21.8%) were performed on metastatic sites. Eighty-five (76.6%) of 111 primary site biopsies were open procedures, and 26 were percutaneous (23.4%). Primary site biopsies were successful in 94.1% of open and 73.1% of percutaneous procedures. Odds of obtaining a successful diagnostic specimen were 7.8 times higher with open approach (CI: 1.6–36.8). Metastatic site biopsies were successful in 66.7% of percutaneous and 100% of open and thoracoscopic procedures.

Conclusion: Biopsy of metastatic sites was equal to primary site in obtaining diagnostic material with the added benefit of accurate staging, with few adverse events and high diagnostic yield.

Osteosarcoma (OS) and Ewing sarcoma family of tumors (ESFT) are the two most common primary pediatric bone malignancies, accounting for 56 and 34% of bone cancer in children, respectively [1]. While studies incorporating the use of neoadjuvant and adjuvant chemotherapy in standardized treatment regimens have improved the outcomes for patients with localized bone malignancies, 5- and 10-year survivals for these patients continue to be below 75% [2–5]. Metastatic disease fares worse for both histologies, with 5-year survival rates of less than 30%. An even worse survival has been seen in patients who present with extra-pulmonary metastatic disease at initial diagnosis [6–8]. Rapid diagnosis and accurate staging are critical to stratifying patients into appropriate therapeutic regimens.

Procurement of adequate diagnostic pathologic specimens is key to determining the correct diagnosis, whether collected from the primary lesion or a suspected metastatic site. As recently noted by several collaborative groups, the most important prognostic factor for OS and ESFT is presence of metastases, with the lungs being the most common metastatic site in both histologies [2,7,9]. Biopsy of suspected metastatic lung nodules may be performed by an open, minimally-invasive (e.g. thoracoscopy), or percutaneous approach [10–11]. Staging these patients with tissue samples and appropriate imaging will help delineate the appropriate treatment plan depending on the spread of these tumors [12–13]. OS is somewhat unique in that resection of metastatic sites has been shown to provide an improvement in survival; therefore, biopsies of suspected metastatic sites must be considered for accurate staging [3,7,14–17].

Recently, we performed a large, retrospective review of all tumor biopsies performed at our institution over a 10-year period [18]. In this review, we noted a high success rate of obtaining a successful pathologic specimen. A subgroup analysis was then performed to assess the initial diagnostic management of bone tumors in children and adolescents. We sought to assess the diagnostic accuracy and describe the initial approach to tumor biopsies in patients diagnosed with OS or ESFT.

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Table 1
Univariate analysis of patient characteristics associated with occurrence of inadequate or non-diagnostic biopsy result and post-operative complications.

Characteristic	No. of initial procedures	Inadequate/non-diagnostic result		Post-procedural adverse events	
Patient characteristics					
All patients	142	14 (9.9)		4 (2.8)	
Categorical variables	***n* (%)**	***n* (%)**	***P***	***n* (%)**	***P***
Gender			0.9491		0.2336
Male	62 (43.7)	6 (42.9)		3 (75.0)	
Female	80 (56.3)	8 (57.1)		1 (25.0)	
Ethnicity			0.1580		0.7717
White	97 (68.3)	12 (85.7)		3 (75.0)	
African-American	43 (30.3)	2 (14.3)		1 (25.0)	
Others	2 (1.4)	0 (0)		0 (0)	
Obese[a]			0.0967		0.1017
Yes	27 (19.0)	4 (28.6)		3 (75.0)	
No	115 (81.0)	10 (71.4)		1 (25.0)	
Continuous variables	**Median (range)**	**Median (range)**	***P***	**Median (range)**	***P***
BMI	19.7 (13.3–42.1)	22.7 (17.5–28.4)	0.7966	27.0 (18.9–29.1)	0.2082
Weight (kg)	53.6 (11.8–115.1)	58.2 (39.6–94.1)		71.0 (59.7–90.8)	
Height (cm)	159.0 (83.7–188.0)	165.0 (129.6–182.6)		171.3 (158.0–177.8)	
Age at biopsy (years)	13.4 (1.8–23.0)	15.1 (8.3–20.0)	0.2656	14.0 (11.8–20.0)	0.3604

[a] Body mass index of >30 if age greater than or equal to 20 or BMI percentile greater than 95% if age less than 20.

1. Patients and methods

1.1. Patient and procedures

Following Institutional Review Board approval, we retrospectively reviewed the records of all patients diagnosed with either OS or ESFT who underwent their initial tissue biopsies at St. Jude Children's Research Hospital between January 1, 2003 and December 31, 2012. We collected data regarding patient characteristics including age at time of procedure, weight, height, race, gender, primary diagnosis, histologic result of biopsy and pre-procedure laboratory values; and procedure-related characteristics including type of anesthesia used, biopsy site, mode of biopsy and imaging modality if any was used. Percutaneous biopsies were performed by both surgeons and interventional radiologists with imaging modalities being used to acquire the biopsy. We also collected data on whether the biopsy site was a primary versus a distant lesion. Overweight was defined as a body mass index (BMI) ≥85th percentile for children of the same age and sex, while obesity was defined as a BMI ≥95th percentile.

All adverse events occurring within the 30-day post-procedure period were reviewed and graded 1–4 according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 [19]. No patients in this sub-group analysis died within this 30-day post-procedure time period. The diagnostic accuracy of a biopsy has been previously described [20]. Briefly, we assessed the conclusiveness of the pathologist's report, compared congruency of the histologic result obtained at subsequent biopsies, and the patient's clinical course. We considered a biopsy to be "successful" if it was deemed "diagnostic" and the biopsy had acquired an adequate volume of lesional material yielding a definitive histologic diagnosis. The biopsy was deemed "unsuccessful" if it was deemed "insufficient for diagnosis" or "non-diagnostic" where lesional material was either obtained or not obtained, respectively.

1.2. Statistical analysis

Correlation of study variables with diagnostic accuracy and incidence of complications were analyzed using univariate logistic regression. Using stepwise selection, all factors were entered into multivariable logistic regression models at level of $P < 0.2$. The relationship of selected laboratory test values and the occurrences of post-procedural blood transfusions and infections were analyzed using Pearson correlation and univariate logistic regression.

2. Results

2.1. Patient and procedure characteristics

One hundred forty-two biopsies were performed in 105 patients with a median age at biopsy of 13.4 years (range: 1.8–23.0). Patient characteristics are summarized in Table 1. Fifty-eight (55.2%) patients were female, and the majority (65.7%) of the patients were Caucasian (69 white, 34 black, 2 other). Median BMI of these patients was 19.8 (range: 13.3–42.1); however, by BMI percentile adjusted for age and sex, 10 (9.5%) patients were overweight and 22 (21.0%) patients were obese. One hundred four (73.2%) biopsies proved to be OS and 38 (27.8%) proved to be ESFT by final pathology (Table 2).

One hundred eleven (78.2%) procedures were performed on the primary lesion. Procedure characteristics are summarized in Table 2. Of these biopsies, 85 (76.6%) were performed via an open approach, with the remaining 26 (23.4%) procedures done percutaneously. Primary lesions yielded a diagnostic specimen in 80 (94.1%) open procedures and 19 (73.1%) percutaneous biopsies. Distant sites were targeted for biopsy in 31 (21.8%) procedures, while 15 (14.3%) patients were found to have metastatic disease by pathology. Twenty-five (80.6%) biopsies were performed on the lung and 3 (9.7%) were performed on bony skip lesions. The remaining suspected metastatic sites were the following: a liver lesion in a patient with ESFT, a chest wall lesion in a patient with OS from a large, pre-celiac intra-abdominal tumor, and a sacral mass in a patient with a primary distal femoral OS. The approaches for the metastatic sites were open, thoracoscopic, or percutaneous in 10 (32.3%), 15 (48.4%), and 6 (19.3%) procedures, respectively, with success rates of 100, 100, and 66.7%. The odds of obtaining a successful diagnostic specimen were 7.8 times higher when using an open approach at all sites (CI: 1.6–36.8) (Table 2).

Twenty-three (21.9%) patients had biopsies performed of both the primary lesion and a distant site; however only 10 (43.5%) of these patients had procedures performed the same day. Pulmonary lesions in 19 (82.6%) procedures were the most common distant sites approached when both lesions were being biopsied. Thirteen (68.4%) of these biopsies were approached thoracoscopically, whereas the others were open in 5 (26.3%) and percutaneous in 1 (5.3%). The percutaneous biopsy in this group was the only procedure which yielded a non-diagnostic pathologic specimen. Six (5.7%) patients had eight biopsies performed on only a distant site biopsied with presumed malignancy of the primary lesion. Eleven (10.5%) patients were confirmed to have metastatic osteosarcoma at initial diagnosis, while only 2 (1.9%) ESFT patients