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Lung nodules in pediatric oncology patients: a prediction rule for when to biopsy

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Abstract

Purpose: The purpose of the study was to develop a prediction rule regarding the factors that most accurately predict the diagnosis of a malignancy in a lung nodule in the pediatric oncology patient.

Methods: A retrospective review of pediatric oncology patients that underwent lung nodule resection between 1998 and 2007 was performed. Multivariable logistic regression was used to create a prediction rule.

Results: Fifty pediatric oncology patients underwent 21 thoracotomies and 48 thoracoscopies to resect discrete lung nodules seen on computed tomographic scans during workup for metastasis or routine surveillance. The mean nodule size was 10.43 ± 7.08 mm. The most significant predictors of malignancy in a nodule were peripheral location (odds ratio [OR], 9.1); size between 5 and 10 mm (OR, 2.78); location within the right lower lobe (OR, 2.43); and patients with osteosarcoma (OR, 10.8), Ewing sarcoma (OR, 3.05), or hepatocellular carcinoma (OR, 2.38).

Conclusions: Lesions that are between 5 and 10 mm in size and peripherally located in patients with osteosarcoma, Ewing sarcoma, or hepatocellular carcinoma are most likely to be malignant. Use of a prediction rule can help guide clinical practice by determining which patients should undergo surgical resection of lung nodules and which patients may be closely observed with continued radiologic studies.

Primary solid tumors of childhood most commonly metastasize to the lungs. In the pediatric oncologic patient, contrast-enhanced computed tomography (CT) scanning is routinely used to assess for metastases and monitor potential disease recurrence. Technical advances in CT imaging and data processing have improved the detection of small pulmonary nodules. Thoracotomy and video-assisted thoracoscopy are the 2 primary means used to perform a biopsy of these lung nodules [1-3]. These techniques have been proven to be both safe and effective for resecting these lesions [4-8]. Because these nodules may represent benign or malignant disease [9,10] (Figs. 1 and 2), an accurate tissue diagnosis could significantly change the management of these patients and, ultimately, their overall survival. Managing pediatric oncology patients is a multidisciplinary process often requiring several surgical procedures and radiologic studies on the same patient for biopsies, staging, and resections [3]. To help decrease the number of negative biopsies performed on these patients, a retrospective analysis was performed to determine which factors most accurately predicted the diagnosis of a malignancy. By

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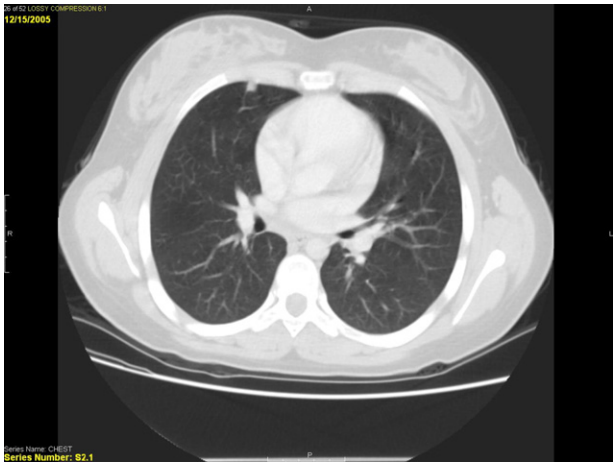

Fig. 1 Axial CT image of a patient with Hodgkin lymphoma showing a peripheral right middle lobe lesion measuring 6 mm. Biopsy showed a hyalinizing granuloma.

decreasing the number of unneeded procedures, we may decrease the morbidity of surgery and delays in chemotherapy and thereby improve overall outcome in the pediatric solid tumor patient.

1. Materials and methods

Institutional review board approval was obtained for this study. A retrospective chart review of pediatric oncology patients who had undergone a resection of a pulmonary nodule between November 1998 and December 2007 was included in the study. All lung nodules were identified on preoperative CT imaging for the evaluation of metastatic disease or for routine surveillance, and were resected by either thoracotomy or thoracoscopy. Excluded from the study were those patients that underwent resection of chest wall, mediastinal, or pleural lesions; patients undergoing formal lobectomy; or those patients undergoing random biopsies. Patient demographics, initial diagnosis, location of the lung nodule, procedure performed, and pathology of the lesion were recorded. The data were examined with SAS system software version 9.2 (SAS Institute, Cary, NC). All data were expressed as mean ± SD for normally distributed data and median or range for skewed data. A multivariate logistic regression model was developed to create a prediction rule. The model was constructed with 9 variables: age, sex, tumor type, size, stage, chemotherapy, grade of tumor, location of lung nodule (peripheral vs central), and lung lobe involved. The model was validated by bootstrap methodology and with the Hosmer-Lemeshow goodness-of-fit test.

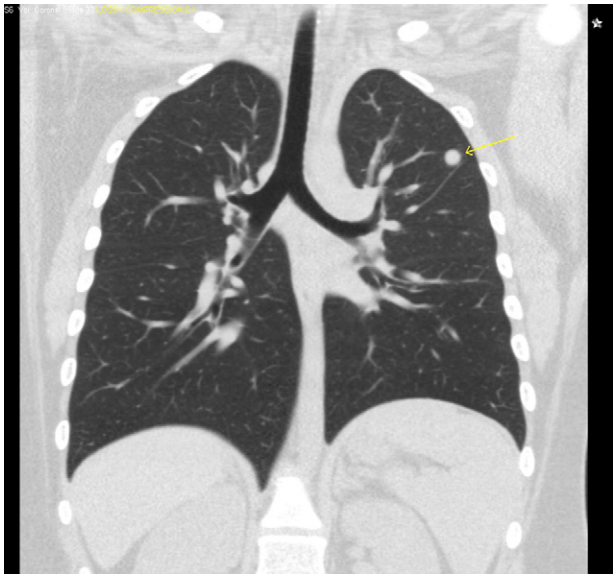

Fig. 2 Coronal CT images of a patient with osteosarcoma showing an enlarging left upper lobe lesion measuring 8 mm. Biopsy was positive for metastatic osteosarcoma.

2. Results

2.1. Patient demographics

Fifty patients were identified who developed lung nodules while being followed in the pediatric oncology clinics at our institution and who subsequently underwent 68 surgical procedures. The ages ranged from 9 months to 22 years (median, 13 years). There were 27 male and 23 female patients. The oncologic diagnoses of these patients included osteosarcoma (11), Ewing sarcoma (6), rhabdosarcoma (3), other sarcomas (5), non-Hodgkin lymphoma (4), Hodgkin lymphoma (4), leukemia (3), Wilms tumor (4), hepatic tumors (2), aplastic anemia (2), germ cell tumors (2), melanoma (1), and other tumors (3). Ten patients had repeat procedures for recurrent or new pulmonary nodules.

All nodules were identified on preoperative CT scans. Positron emission tomography (PET) scanning was used in 19 (38%) of 50 patients to further define the lesions within 3 weeks of their CT scans and before their surgical procedure. Nine were PET positive, 2 were indeterminate, and 8 were negative. The PET-positive lesions had a mean size on CT scan of 13.2 ± 5.19 mm, and the PET-negative lesions had a mean CT scan size of 7 ± 4.60 mm (P = .020). Surgical pathology revealed that all 9 PET-positive scans were true positives, 2 of the indeterminate PET scans were also positive for malignancy, and 4 (50%) of the 8 negative PET scans were true negatives. The 4 false-negative PET scan patients all had metastatic osteosarcoma. The 2 indeterminate PET scan patients had metastatic melanoma and Hodgkin lymphoma. The 4 true-negative PET scan patients had primary diagnoses of osteosarcoma (3 patients) and B-cell lymphoma (1 patient).