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● *Original Contribution*

DIAGNOSTIC IMPACT OF COLOR DOPPLER ULTRASOUND-GUIDED CORE BIOPSY ON FINE-NEEDLE ASPIRATION OF ANTERIOR MEDIASTINAL MASSES

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Abstract—Although lymphoma and thymoma are common etiologies of anterior mediastinal masses (AMMs), smaller percentages and numbers of patients with these diseases have been enrolled in previous ultrasound-guided biopsy studies. To date, there has been no study of color Doppler sonographic features to support the differentiation of AMMs. For this retrospective cohort study, a search of the database of the China Medical University Hospital using the clinical coding "ultrasound-guided biopsy" was conducted for the period December 2003 to February 2013. We selected patients diagnosed with AMMs (not cysts) using radiographic records. This search yielded a list of 80 cases. Real-time ultrasound-guided core needle biopsy (CNB) was performed in all but 5 patients without a sufficient safety range. In 89% (67/75) of these ultrasound-guided CNB cases, the diagnostic accuracy achieved subclassification. Fine-needle aspiration cytology achieved subclassification in only 10% of cases. On color Doppler sonography, 71% of lymphomas were characterized as "rich vascular with central/crisscross collocations" and 29% as "avascular or localized/scattered peripheral vessels." However, decreased proportions of "rich vascular with central/crisscross collocations" were found in lung cancer (4% [1/23], odds ratio = 0.018, 95% confidence interval: 0.002–0.154, $p < 0.001$) and thymoma/thymic carcinoma (25% [4/16]; odds ratio = 0.133, 95% confidence interval: 0.035–0.514, $p = 0.003$) compared with the lymphoma group. We conclude that the vessels in lymphoma AMMs have specific patterns on color Doppler sonography. Ultrasound-guided CNB of AMMs had an accuracy of ≤89% in diagnosis and subclassification. Fine-needle aspiration cytology itself cannot aid in the diagnosis. Color Doppler sonographic evaluation of AMMs followed by real-time CNB is a more efficient method. (E-mail: hsuwh@mail.cmuh.org.tw) © **2014 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Anterior mediastinal mass, Color Doppler ultrasound, Core needle biopsy, Fine-needle aspiration, Vascularization.**

INTRODUCTION

Anterior mediastinal masses (AMMs) are due to a variety of diseases, such as lymphoma, thymoma, thyroid goiter and metastatic carcinoma (Mullen and Richardson 1986; Nasit et al. 2013; Yu et al. 1991). Moreover, 5% of lung cancers present as mediastinal masses (Koegelenberg et al. 2011; Quinn et al. 1996; Yu et al. 1991). Treatment strategies for AMMs are diverse and include medical treatment for lymphoma and germ cell tumors and multimodality treatment (surgery, radiotherapy and/or chemotherapy) for thymoma and thymic carcinoma; AMMs such as lung cancer and metastatic carcinoma have a poor prognosis. In all cases, however, an exact histopathologic diagnosis is needed.

Several tools are available for tissue diagnosis in AMMs. These include image-guided transthoracic fine-needle aspiration cytology (FNAC), core needle biopsy (CNB) and surgical mediastinoscopy. Each technique has its advantages and disadvantages in terms of accuracy, degree of invasion, cost and risk. An ideal diagnostic method would have a high diagnostic rate and be as least invasive as possible. Mediastinoscopy requires general anesthesia. Image guidance by computed tomography (CT) has the drawback of higher cost and lacks the "real-time" monitoring afforded in biopsies. However, ultrasound-guided (UG) FNAC and CNB have the

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advantages of being radiation free, real time and inexpensive and are able to assess vessel signals (Gorguner et al. 2003; Wang et al. 1995). Because of potential complications such as hemorrhage and pneumothorax in CNB (Arakawa et al. 1997; Hsu et al. 1995; Yang et al. 1992), many clinics recommend the use of UG-FNAC as the initial procedure (Hsu et al. 1995; Koegelenberg et al. 2011; Morrissey et al. 1993).

Malignant lymphomas, however, are a heterogeneous group and can be classified as Hodgkin's disease and non-Hodgkin's lymphoma (NHL). In NHL, classification as T or B cell is a basic requirement for treatment (Sabattini et al. 2010). Thymomas are classified as lymphocytic, epithelial, spindle cell or cancer variants based on their different tumor invasion abilities and prognoses (Okumura et al. 2002). Patients with lung adenocarcinoma should undergo tumor testing for epidermal growth factor mutations (Maemondo et al. 2010) and anaplastic lymphoma kinase rearrangement (Shaw et al. 2009). Whether FNAC is sufficient to subclassify AMMs is doubtful (Gong et al. 2004; Hsu et al. 1995; Yu et al. 1991).

Saito et al. (1988) diagnosed 9 of 11 mediastinal masses by UG-FNAC with UG-CNB in their pioneering study. Yang et al. (1992) subsequently reported that UG-CNB had a diagnostic yield of 88.9% in 54 mediastinal tumors. Using UG-CNB focusing on AMMs, Andersson and Lindgren (1992) successfully diagnosed 27 of 28 cases. Over the past decade, Koegelenberg et al. (2011) reported an 88.2% diagnostic yield in 17 UG-CNBs. Nasit et al. (2013) diagnosed 49 of 50 AMMs by CNB under CT or ultrasound guidance. Although lymphoma and thymoma are common etiologies of AMMs (Mullen and Richardson 1986), smaller percentages and numbers of patients with these diseases have been enrolled in previous UG-biopsy studies (Arakawa et al. 1997; Gorguner et al. 2003, Hsu et al. 1995; Koegelenberg et al. 2011; Nasit et al. 2013; Rubens et al. 1997; Yang et al. 1992; Yu et al. 1991). Therefore, experience with real-time UG-CNB in AMMs remains limited. Although gray-scale ultrasound can differentiate a mediastinal cyst from a solid mass, it fails to reveal characteristic patterns for specific tumors (Wernecke and Diederich 1994; Yu et al. 1991).

Lymphoma is part of the hematopoietic system. Color Doppler sonography (CDS) can identify significant vessels in hilar and/or capsular superficial lymph nodes (Ahuja and Ying 2003; Dudea et al. 2012; Rettenbacher 2014) and AMMs of lymphoma patients (Hsu et al. 2008). However, lung cancer has been found to have sparse single vessels because tumor invasion destroys or displaces the original normal bronchial structure. The vessels are either displaced to tumor margins or disappear completely (Beckh 2008; Civardi et al. 1993; Hsu et al. 1998; Yuan et al. 1994). Thus, we hypothesized that CDS may be useful in the differentiation of AMMs.

This retrospective study was carried out to compare the value of real-time UG-FNAC and UG-CNB in the diagnosis of AMMs. Tumor features revealed by CDS were also evaluated. To the best of our knowledge, this study of the use of UG-CNB in AMMs, for which a large number of patients with lymphoma and thymoma were enrolled, is the first study to evaluate the distinguishing features of AMMs using CDS.

METHODS

Identified patients

A search of the database of the China Medical University Hospital using the clinical coding "ultrasound-guided biopsy" was conducted for the period December 2003 to February 2013 (110-mo period) in this retrospective cohort study. We selected patients diagnosed with AMMs (not cysts) using their radiographic records. The study was approved by the China Medical University Hospital institutional review board (CMUH102-REC1-118).

This search yielded a list of 80 cases. Chest radiography and CT or magnetic resonance imaging studies were available for all patients. Diagnostic techniques, final pathologic diagnoses and clinical records were reviewed retrospectively. There were 54 men and 26 women, ranging in age from 17 to 91 y (mean age: 50 y).

Daily routine of chest ultrasound examination

The patients were examined in the supine position. All examinations were performed using a 3.75-MHz curvilinear color duplex probe (Aplio-80, Toshiba Medical Systems, Tokyo, Japan). AMMs were examined with gray-scale sonography initially, followed by CDS. The size, margin, internal pattern (hypo-echoic, iso-echoic or hyper-echoic; homogeneous or heterogeneous) and necrotic area of the tumor were estimated in the gray-scale mode (Yu et al. 1991). CDS was then carried out to evaluate the blood vessels surrounding and within the AMMs before the transthoracic biopsy.

The Doppler filter was fixed at 100 Hz to eliminate low-frequency signals (Hsu et al. 2007). The color Doppler window was focused on the AMM to detect flow signals. During the respiratory cycle, color signals that were firmly in the same position were reasoned to be blood flow signals and not interference (Yuan et al. 2000).

Ultrasound-guided biopsy

Real-time UG-biopsy was selected when CT (or magnetic resonance imaging) revealed more than 1 cm of interface between the AMM and the chest wall