Ultrasound in Med. & Biol., Vol. ■, No. ■, pp. 1–7, 2016

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2016.05.012

● *Original Contribution*

USEFULNESS OF MICROVASCULAR ULTRASONOGRAPHY IN DIFFERENTIATING METASTATIC LYMPHADENOPATHY FROM TUBERCULOUS LYMPHADENITIS

INSEON RYOO,* SANGIL SUH,* SUNG-HYE YOU,† and HAE YOUNG SEOL*

* Department of Radiology, Korea University Guro Hospital, College of Medicine, Seoul, Korea; and † Department of Radiology, Korea University Anam Hospital, College of Medicine, Seoul, Korea

(*Received* 1 *December* 2015; *revised* 22 *March* 2016; *in final form* 16 *May* 2016)

Abstract—This study was undertaken to evaluate the usefulness of vascular pattern analysis on microvascular ultrasonography in distinguishing metastatic lymphadenopathy from tuberculous lymphadenitis, compared with conventional power Doppler ultrasonography, and to evaluate inter-observer agreement for microvascular ultrasonography. Thirty-four patients with metastatic lymphadenopathy and 27 patients with tuberculous lymphadenitis were included. The level of inter-observer agreement was excellent or good for all aspects of vascular pattern analysis on both ultrasonographic examinations. Vascular distribution, internal vascularity and internal vascular features of lymph nodes on microvascular ultrasonography differed significantly different ($p \leq 0.002$) between metastatic lymphadenopathy and tuberculous lymphadenitis. A central vascular pattern with displacement was prevalent in metastasis, and an avascular pattern was more frequent in tuberculosis. Internal vascularity of metastasis was higher than that of tuberculosis. Vascular patterns on power Doppler ultrasonography did not differ significantly. Vascular pattern analysis using microvascular ultrasonography can be helpful in differentiating metastatic lymphadenopathy from tuberculous lymphadenitis with good inter-observer agreement. (E-mail: sangil.suh@gmail.com) © 2016 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Microvascular ultrasonography, Superb Microvascular Imaging, Power Doppler ultrasonography, Cervical lymph node, Metastasis, Tuberculosis, Vascular pattern.**

INTRODUCTION

Metastatic lymphadenopathy and tuberculous lymphadenitis are among the major causes of cervical lymphadenopathy (Ahuja et al. 1997; Ying et al. 1998). Tuberculous lymphadenitis is prevalent in Asian countries. Even in non-Asian countries, tuberculosis becomes an important cause of disease because of the increasing number of immunocompromised patients.

Ultrasonography is the primary non-invasive diagnostic modality for cervical lymphadenopathy used to characterize and measure lesions, determine location, evaluate perfusion patterns and guide tissue biopsy. The role of gray-scale ultrasonography is relatively well established (Ahuja et al. 1997; Asai et al. 2001; van den Brekel et al. 1990; Ying et al. 1998). Many prior studies have reported the added value of vascular pattern analysis with power Doppler ultrasonography, especially for differentiating benign lymph nodes from malignant lymph nodes (Chang et al. 1994; Gupta et al. 2011; Na et al. 1997; Steinkamp et al. 1998; Wu et al. 1998a, 1998b; Ying et al. 2004). However, results have been inconsistent from study to study. Studies including many cases of tuberculous lymphadenitis in benign lymphadenopathy (Wu et al. 1998a, 1998b; Ying et al. 2004) had lower specificity (76%–87%) than other studies (91%–100%) (Ahuja and Ying 2004; Ariji et al. 1998; Sato et al. 1998; Tschammler et al. 1996). Some studies reported that distinguishing tuberculous lymphadenitis from metastatic lymphadenopathy on ultrasonography can be difficult not only on gray-scale ultrasonography because of the similarity in nodal distribution, shape, size and internal architecture (Ahuja et al. 1995, 2001a), but also on power Doppler ultrasonography, because of the significant overlap in the vascular patterns of those two diseases (Ahuja and Ying 2004; Na et al. 1997; Wu et al. 1998a, 1998b).

Address correspondence to: Sangil Suh, Department of Radiology, Korea University Guro Hospital, College of Medicine, 148, Gurodong-ro, Guro-gu, 152-703, Seoul, Korea. E-mail: sangil.suh@gmail.com

Conflict of interest disclosure: All authors have no conflicts to disclose.

Ultrasonography Doppler technologies have dramatically improved in recent decades. Conventional Doppler imaging uses a single wall filter to remove clutter and movement artifacts by suppressing low-velocity flow. Many research groups and manufacturers are developing improved Doppler modes with increased sensitivity to low-velocity flow and improved resolution. Of all of the efforts in this direction, recently developed microvascular imaging technology (Superb Microvascular Imaging [SMI]) effectively separates flow signals from motion artifacts and clutters, preserving the underlying low-velocity blood flow. This is accomplished by applying a proprietary algorithm that incorporates complex Doppler imaging technologies including wide-band Doppler techniques and Doppler digital imaging optimization (Rice 2003). Consequently, microvascular ultrasonography provides visualization of very low velocity microvascular flow in lymph nodes that is not attainable with conventional power Doppler ultrasonography.

The purpose of this study was to evaluate the usefulness of microvascular ultrasonography for distinguishing metastatic lymphadenopathy from tuberculous lymphadenitis, compared with conventional power Doppler ultrasonography, and to evaluate inter-observer agreement for microvascular ultrasonography.

METHODS

Study population

This retrospective study was approved by our institutional review board, and informed consent was waived.

From December 2014 to August 2015, 123 patients underwent ultrasonography-guided core needle biopsy of cervical lymph nodes at Korea University Guro Hospital. Among them, 15 patients had reactive hyperplasia on pathologic reports, 23 had Kikuchi disease, 27 had tuberculous lymphadenitis, 34 had metastatic lymphadenopathy, 9 had malignant lymphoma and the remaining 15 patients had various other pathologic findings.

A total of 61 patients with pathologically proven metastatic lymphadenopathy (n = 34) or tuberculous lymphadenitis (n = 27) were included in this study. Among the patients with metastatic lymphadenopathy, 23 were male and 11 were female, and their mean age was 61.3 ± 12.1 y (range: 34–79 y). Pathologic subtypes were squamous cell carcinoma (n = 16, from oropharynx [n = 7], oral cavity [n = 2], nasopharynx [n = 1], larynx [n = 3], esophagus [n = 1], lung [n = 1] and unknown origin [n = 1]); adenocarcinoma (n = 10, from lung [n = 4], colon [n = 3], salivary duct [n = 1], prostate [n = 1] and bile duct [n = 1]); small cell carcinoma (n = 2, from lung); metastatic hepatocellular carcinoma (n = 1, from liver); metastatic melanoma (n = 1, from orbit); poorly differentiated carcinoma (n = 1, from ureter); and undifferentiated carcinoma (n = 3, from nasopharynx [n = 2] and unknown origin [n = 1]). Among the patients with tuberculous lymphadenitis, 10 were male and 17 were female, and their mean age was 47.4 ± 15.1 y (range: 24–79 y).

Ultrasonography and core needle biopsy

All 61 patients underwent gray-scale ultrasonography, power Doppler ultrasonography and microvascular ultrasonography with SMI (Toshiba Medical Systems, Tochigi, Japan) technique of the neck node using high-resolution ultrasonography units and high-frequency linear transducers (Aplio 500, 7.0–18.0 MHz, Toshiba Medical Systems). Two head and neck radiologists (with 4 y and 16 y of experience in this field) performed ultrasonography-guided core needle biopsy on the largest pathologic lymph node using a disposable 18-gauge gun biopsy needle (TSK Ace-cut, Create Medic, Yokohama, Japan; or Angiotech, Medical Device Technologies, Gainesville, FL, USA). Power Doppler studies were performed with standardized power Doppler parameters set to high sensitivity and a low wall filter to allow detection of blood vessels with weaker blood flow (frame rate, 7–9/s; scale, 4.9–6.1 cm/s; pulse repetition frequency, 13.7–15.6 kHz). The gain was first increased to a level that registered color noise and then decreased until the noise disappeared, as in the previous studies (Ahuja and Ying 2004). Microvascular ultrasonography was performed in both monochrome and color modes with SMI parameters set to a low-velocity range <2 cm/s to visualize extremely low velocity flow with good resolution and a high frame rate with minimal flash artifacts (frame rate, 25–30/s; pulse repetition frequency, 15.4–20.2 kHz).

Image analysis

The vascular patterns of lymph nodes were evaluated in terms of vascular distributions, internal vascularity (number of internal vessels) and internal vascular features on both power Doppler ultrasonography and microvascular ultrasonography based on transverse planes with the largest axial diameters of lymph nodes. All images were analyzed by two head and neck radiologists (I.R. and S.S. with 4 and 16 y of experience in this field, respectively), independently and blinded to the patients' clinical information and each other's review for the evaluation of inter-observer agreement. In cases in which there was a discrepancy between the two reviewers, the consensus method was used to compare the performance of power Doppler ultrasonography and microvascular ultrasonography.

The vascular distributions of lymph nodes were classified into four categories according to the locations of vascularity that have been commonly used in prior cervical lymph node studies (Ahuja and Ying 2002, 2003; Ahuja et al. 2001a, 2001b, 2001c): avascular = absence of flow