

CHARACTERIZATION OF CONGENITAL LYMPHATIC AND BLOOD VASCULAR MALFORMATIONS IN THE HEAD AND NECK USING BLOOD POOL SCINTIGRAPHY AND SPECT

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ABSTRACT

The purpose of this study was to investigate the usefulness and diagnostic efficacy of blood pool (BP) scintigraphy and SPECT for characterizing congenital vascular malformations (CVMs) in the head and neck area. A total of 154 patients suspected of having head and neck CVMs underwent whole-body BP scintigraphy and head and neck BP SPECT using ^{99m}Tc-labeled red blood cells. Based on SPECT findings, CVMs were classified into lymphatic malformation/non-(blood) vascular disease (LM/NVD, no distinct uptake), arterio-venous malformation (AVM, abnormal uptake in lesions and asymmetrically increased jugular vein uptake on ipsilateral side), venous malformation (VM, strong uptake in lesions with symmetric jugular vein uptake), and veno-lymphatic malformation (VLM, no or mild uptake on lesions with symmetric jugular vein uptake). The sensitivities and specificities of BP SPECT for diagnosing each subtype of head and neck CVM were 100% (13/13) and 97.1% (137/141) for LM/NVD, 61.1% (22/36) and 99.1% (117/118) for AVM, 91.7% (88/96) and 79.3% (46/58) for VM, and 55.6% (5/9) and 93.7% (136/145) in VLM, respectively. The overall accuracy for characterizing CVMs by

head and neck BP SPECT was 83.1% (128/154). In conclusion, BP SPECT is a useful method for classifying CVMs in the head and neck area due to its high diagnostic efficacy.

Keywords: blood pool scintigraphy, blood pool SPECT, ^{99m}Tc red blood cells, congenital lymphatic malformation, vascular malformation, head and neck

Congenital vascular malformations (CVMs) are found frequently in the head and neck, and they present with different functional problems such as pain, bleeding or even life-threatening consequences, as well as significant cosmetic problems (1). Localized vascular malformations are usually located superficially but may involve skeletal muscle. Therefore, detecting visible malformation lesions as well as deep-seated lesions is important in the diagnosis of CVMs.

Based on the predominant component of the vascular defect, CVMs are classified into vascular malformation (VM), arterio-venous malformation (AVM), lymphatic malformation (LM), and veno-lymphatic malformation (VLM) (2-5). Since the treatment and prognosis of CVMs are different according to type, the classification of CVMs is essential.

However, the diagnosis of CVM using clinical examination and diagnostic images can be difficult.

Many imaging modalities such as simple x-ray, ultrasonography, CT scan, and magnetic resonance imaging (MRI) are useful for diagnosing, classifying, and determining the extent of CVMs (6). Among these, MRI is the most useful modality because it can distinguish lesion from soft tissue. However, MRI frequently fails to differentiate LM and VM where lesions appear as solid masses and suggest low-flow type CVMs. Although angiography is still the gold standard method, it has the associated risks for an invasive method.

Nowadays, whole-body blood pool scintigraphy (WBBPS) using ^{99m}Tc labeled red blood cells (RBCs) is used to characterize CVMs due to several advantages including safety, non-invasiveness, and low cost compared to CT/MRI and angiography (7-9). We have also previously shown that a combination of WBBPS and lymphoscintigraphy can characterize various forms of CVMs with high accuracy (10). However, there have not been any studies evaluating WBBPS in CVMs of the head and neck. In addition, blood pool (BP) single-photon emission tomography (SPECT) may be a more suitable imaging method to evaluate deep-seated CVMs in the head and neck area due to several benefits such as providing 3-dimensional images, better lesion localization, and improved sensitivity for detecting a lesion (11,12). Therefore, we investigated the usefulness and diagnostic efficacy of WBBPS and SPECT for characterizing CVMs in the head and neck area.

MATERIALS AND METHODS

Subjects

Between July 2003 and August 2007, 245 patients were referred to our department for suspicion of having CVMs in the head and neck area and underwent WBBPS as a part

of clinical diagnostic evaluation. Among them, 154 patients (61 males, 93 females; mean age: 18.1 ± 13.8 years, range: 1-58 years) also underwent additional BP SPECT of the head and neck. Head and neck MRI was performed in 140 patients who were suspected of having CVM and angiography was done in 106. The final classification in each case was determined by clinical findings, MRI, angiography, and Doppler sonogram.

Head and neck MRI

MRI was performed with a 1.5-T Signa scanner (General Electric Medical Systems) to obtain axial, sagittal, and coronal plane views of the lesions in spin-echo T1-weighted (TR/TE 450 to 600/18 to 30 milliseconds) and fast spin-echo T2-weighted (TR/TE 4,500 to 5,000/80 to 100 milliseconds) sequences.

MRI was used primarily to differentiate between the high-flow and low-flow hemodynamic status of the lesion at first, and then to evaluate the extent of involvement of the lesion in the adjacent organs and tissues (e.g., muscle, tendon, nerves, vessels, bones) to delineate its anatomic relationship with the surrounding structures.

WBBPS and SPECT in head and neck

Patients were evaluated scintigraphically with ^{99m}Tc RBCs labeled by a modified in vitro method. Twenty minutes after the injection of pyrophosphate solution containing SnCl_2 , 5ml of venous blood was sampled. The blood was mixed with 925-1110 MBq of ^{99m}Tc pertechnetate, and centrifuged for 5 minutes at 1300g. Then, 2-3ml of packed red blood cells were withdrawn, and 555-740MBq of ^{99m}Tc -RBCs were re-injected into the patient. Whole body was scanned with a dual head gamma camera (Biad[®], Trionix Research Laboratory, Twinsburg, OH, USA) at least 10 minutes after re-injecting the radiolabeled RBCs.

For BP SPECT in the head and neck, a triple-head gamma camera (Triad XLT[®],

TABLE 1
Diagnostic Results of Blood Pool SPECT for Characterizing Head and Neck CVMs

Final Diagnosis		VM (n=96)	AVM (n=36)	LM/NVD (n=13)	VLM (n=9)	PPV (%)
SPECT Diagnosis	VM	88	9		3	88
	AVM	1	22			95.7
	LM/NVD	3		13	1	76.5
	VLM	4	5		5	35.7
	Sensitivity (%)	91.7	61.1	100	55.6	

Trionix Research Laboratory, Twinsburg, OH, USA) was used for all subjects. The tomographic images were reconstructed using filtered backprojection with a Butterworth filter (cutoff frequency, 0.60 cycle/cm; order, 3) and were displayed in a 128 x 64 matrix (pixel size = 3.56 x 3.56 mm with a slice thickness of 3.56 mm). No attenuation correction was performed.

The images were retrospectively reviewed visually by the consensus of 2 nuclear medicine physicians who were unaware of the results of the final diagnoses and other imaging modalities, except for the location of the lesions. At the last step, a re-evaluation was done together to reach a consensus. The degree of uptake in CVMs was semi-quantitatively scored on transaxial SPECT images displayed on a workstation monitor using a variable upper window threshold; 0 = similar to head and neck background activity, 1 = more than background activity, less than the activity of the contralateral internal jugular vein, 2 = similar to or more than the activity of the contralateral internal jugular vein but less than the cardiac blood pool activity, and 3 = similar to or more than cardiac blood pool activity. On WBBPS, the activity of the jugular vein ipsilateral to the CVM was compared with the activity of contralateral jugular vein to evaluate the increase in venous return suggesting AVM (10). In addition, we evaluated the presence

of other abnormal blood pooling lesions suggesting CVMs besides those in the head and neck area.

Based on BP SPECT findings, CVMs were classified into LM/non-vascular disease (NVD) (no distinct uptake), AVM (abnormal uptake on lesions and asymmetrically increased jugular vein uptake on ipsilateral side), VM (strong uptake on lesions with symmetric jugular vein uptake), and VLM (no or mild uptake on lesions with symmetric jugular vein uptake).

The classification based on SPECT findings was compared with the final diagnosis determined by clinical findings, MRI, angiography, and Doppler sonogram.

Statistical analysis

The chi-square test was used to compare uptake scores between the final diagnostic groups. A p value of < 0.05 was considered statistically significant.

RESULTS

Of 154 patients, the final diagnoses were VM in 96 (62.4%), AVM in 36 (23.4%), LM/NVD in 13 (8.4%), and VLM in 9 (5.8%). The clinical manifestations were extremely variable, including head and neck mass, vascular protruding, pulsation, heating sense, or port-wine stain. The mean age when the

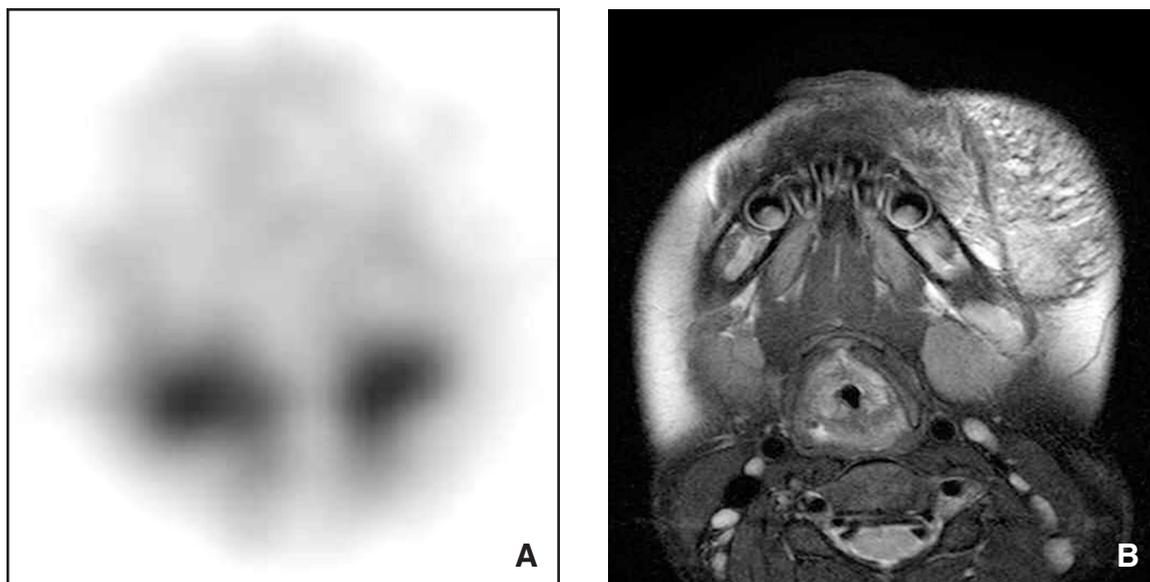


Fig. 1. Transaxial images of BP SPECT (A) and T2-weighted MRI (B) in a 9-year-old female patient with left cheek swelling. Although high signal intensity in the left cheek area suggested a low flow type vascular malformation, there were no abnormal blood pooling lesions in the same area on BP SPECT (visual grading score = 0). This lesion was confirmed as lymphangioma by biopsy.

symptoms appeared was 5 years. The most frequently involved site was the cheek (36%), followed by the neck and upper lip. None of the patients had a history of prior treatment.

Diagnostic results of BP SPECT for characterizing head and neck CVMs are shown in *Table 1*. Using the above mentioned diagnostic criteria, the sensitivities of BP SPECT for diagnosing each subtype of head and neck CVM were 100% (13/13) for LM/NVD, 61.1% (22/36) for AVM, 91.7% (88/96) for VM, and 55.6% (5/9) in VLM. The specificities of BP SPECT for diagnosing each subtype of head and neck CVM were 97.1% (137/141) for LM/NVD, 99.1% (117/118) for AVM, 79.3% (46/58) in VM, and 93.7% (136/145) for VLM. The overall accuracy of CVMs characterized by head and neck BP SPECT was 83.1% (128/154). Representative cases are shown in *Figs. 1-4*.

Visual grading of BP SPECT produced mean scores of 2.45 in VM, 1.92 in AVM, 1.44 in VLM, and 0 in LM/NVD with a significant difference between groups ($p < 0.001$) (*Table 2*).

On WBBPS images, additional abnormal vascular lesions were found in 2.6% (4/154) of patients with CVM, which was not suspected on the initial clinical evaluation (*Fig. 5*). Among these, one patient underwent additional MRI for that lesion, which proved to be CVM.

DISCUSSION

In this study, we investigated whether BP SPECT of the head and neck could be used to classify patients with head and neck CVMs. We found that head and neck BP SPECT had a high overall accuracy (83.1%) for characterizing CVMs of the head and neck, suggesting that BP SPECT is sufficient for routine clinical use. Because incorrect diagnosis of CVMs may lead to inadequate or inappropriate treatment, there have been several studies on methods for improving classification. Although MRI is considered the best modality for categorization, WBBPS and BP SPECT seem to be useful in detection of CVMs because they are simple and

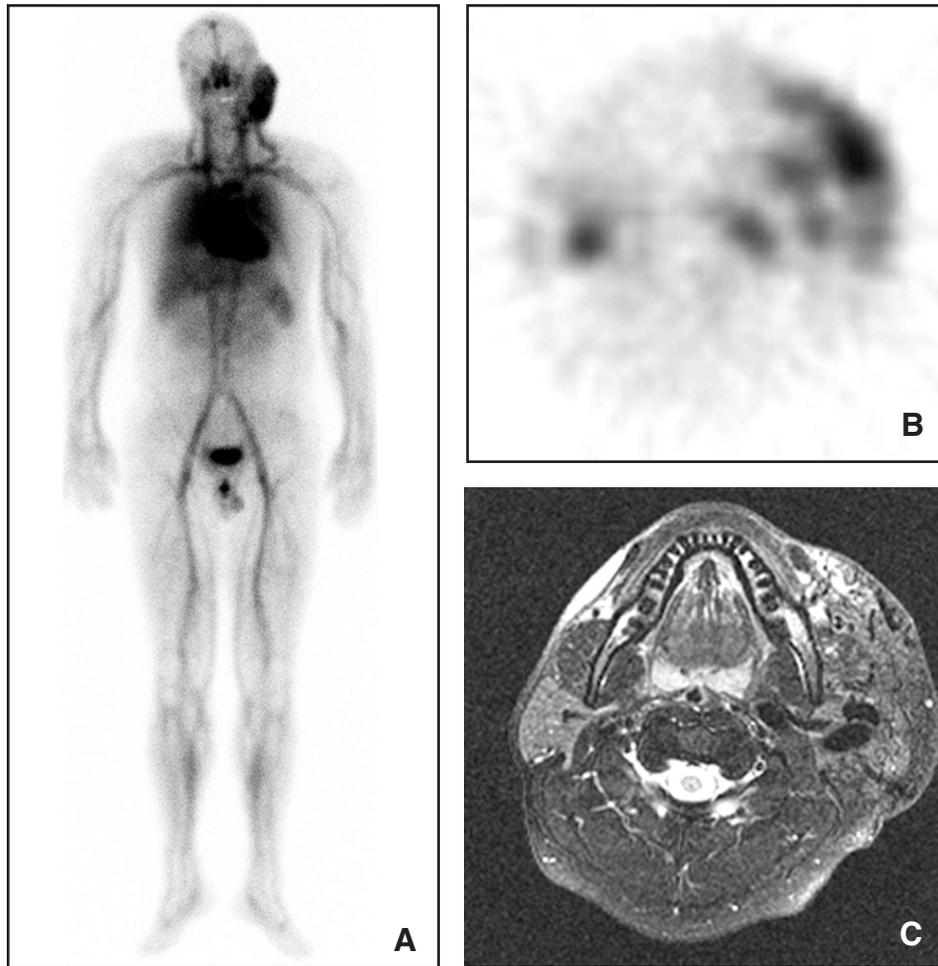


Fig. 2. Anterior image of WBBPS (A), and transaxial images of BP SPECT (B) and T-weighted MRI (C) from a 26-year-old male patient. An abnormal vascular lesion was seen in the left cheek area on MRI. On WBBPS, there was an abnormal blood pooling lesion involving the left cheek with asymmetrically increased left jugular vein (visual grading score = 2), which proved to be AVM by angiography.

economical modalities. Our study showed a relatively high accuracy for head and neck BP SPECT in the classification of CVM patients. Among the classifications, head and neck BP SPECT identified VM and LM with high sensitivities of 91.7% and 100%, respectively. These results are similar to the sensitivity of 93.8% in VM of extremities in previous report (9). Since VM shows distinct abnormal blood pooling, VM is easily differentiated from other types of CVM and was demonstrated by the highest visual

grading score among CVMs. However, there was no typical intense blood pooling uptake in 8 patients with VM. Among these, 3 had no significant uptake suggesting LM, and 4 had mild uptake suggesting VLM, where MRI showed a complication such as thrombosis within the VM lesions. It may be difficult for radiolabeled RBCs to enter into the thrombi. Another possible cause may be a relatively low labeling efficiency by the *in vivo* RBC labeling method due to the young age of the patients (less than 2 years old). MRI may

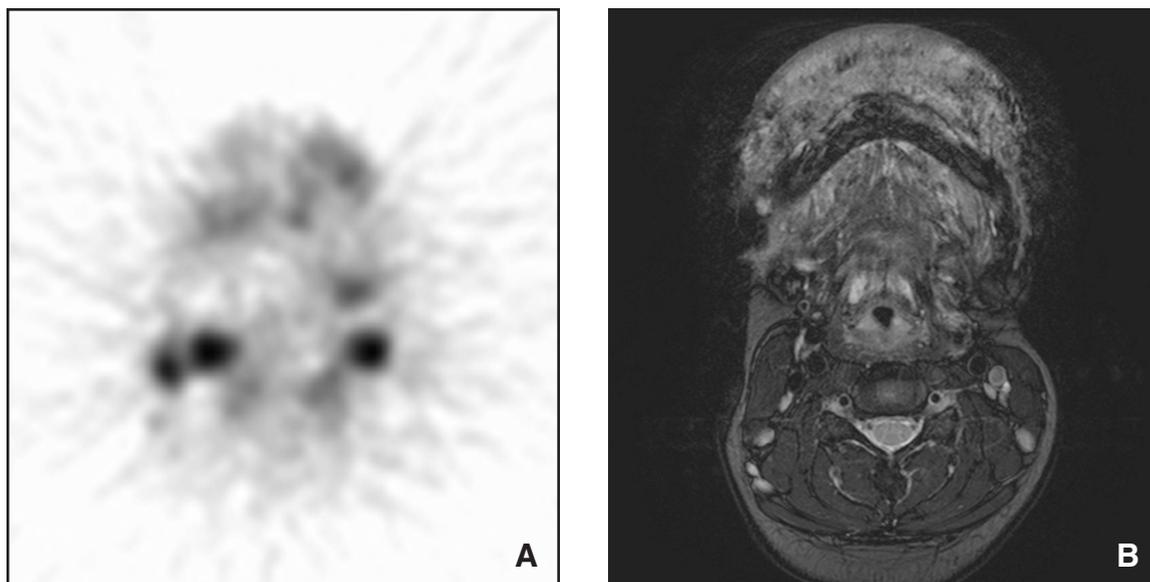


Fig. 3. Transaxial images of BP SPECT (A) and MRI (B) of a 6-year-old female patient. On MRI, an infiltrating mass was seen in the chin area, suggesting a low flow type lesion. On BP SPECT, there was mild uptake in the chin area (visual grading score = 1), which proved to be VLM.

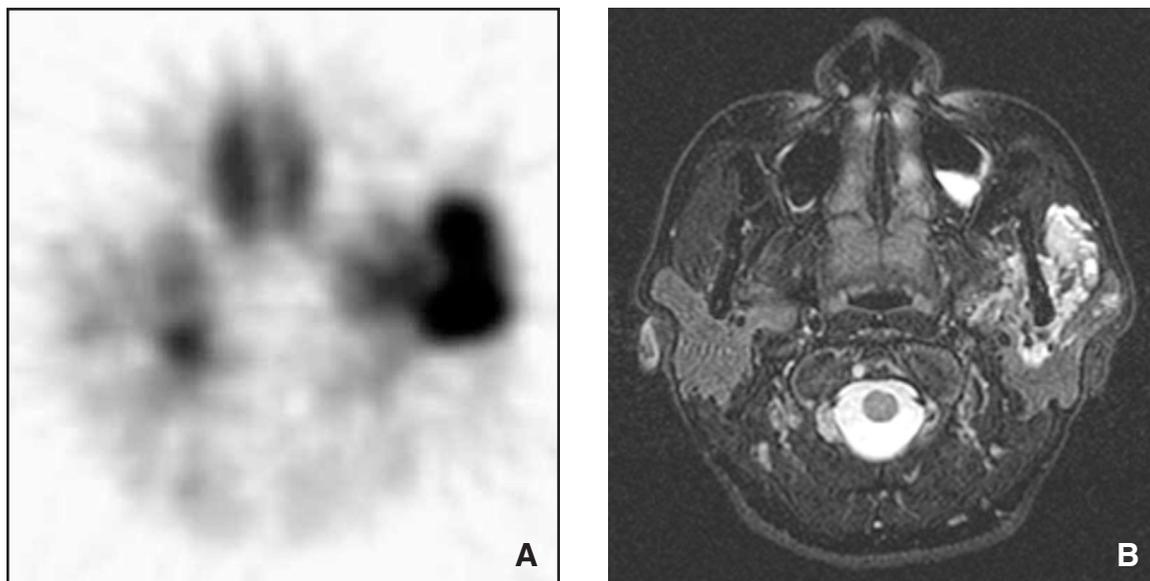


Fig. 4. Abnormal blood pooling lesion in the left cheek area on transaxial image of BP SPECT (visual grading score = 3) (A) and high signal intensity in the same area on MRI image (B) of a 55-year-old female patient. Final diagnosis was VM.

complement these weak points of head and neck BP SPECT by providing information on the combined complication. However, MRI is

limited in its ability to differentially diagnose LM from VM, whereas BP SPECT showed an excellent result (sensitivity 100%, specificity

TABLE 2
Uptake Score of BP SPECT According to the Final Diagnosis

Uptake Score	0	1	2	3
VM (n = 96)	3 (3.1%)	13 (13.5%)	26 (27.1%)	54 (56.3%)
AVM (n =36)	0	10 (27.8%)	20 (55.6%)	6 (16.6%)
VLM (n = 9)	1 (11.1%)	5 (55.6%)	1 (11.1%)	2 (22.2%)
LM/NVD (n = 13)	13 (100%)	0	0	0

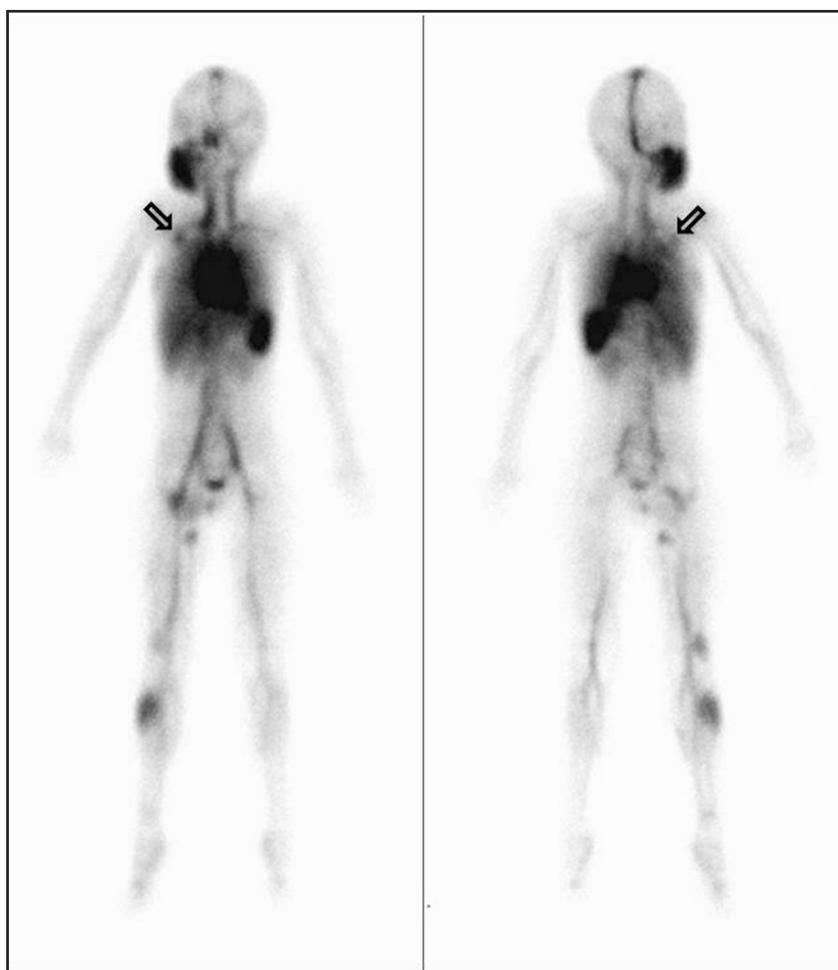


Fig. 5. Anterior and posterior images of WBBPS of an 11-year-old female patient with VM in the right cheek. Clinician in charge noticed that the patient also had CVM in the right lower extremity. On WBBPS, another clinically unexpected abnormal blood pooling lesion suggesting CVM was found in the right infraclavicular area (open arrow).

97.1%) in the differentiation of LM/NVD from other types of CVM.

BP SPECT showed relatively low sensitivities for diagnosing AVM and VLM. Nine patients with AVM were misdiagnosed as VM according to our diagnostic criteria of BP SPECT, since there was an absence of increased jugular vein uptake on the ipsilateral side. In contrast, MRI diagnosed AVMs by showing anomalous signal void vessels in 2 patients. Another 3 patients with VLM were also classified incorrectly as VM. Due to intense blood pooling, these lesions may have more VM component than LM component. Transarterial lung perfusion scintigraphy (TLPS) and lymphoscintigraphy are helpful in characterizing the AVM and VLM, as previously reported. However, these modalities are not available for evaluating head and neck lesions due to a lack of appropriate sites for radiopharmaceutical administration (13,14). Since BP SPECT alone was not always able to provide all the necessary information for the CVM classification, it is important to include not only clinical correlation but also other modalities such as MRI. Since BP SPECT and MRI are complementary in classifying CVMs of the head and neck, both modalities are necessary for initial non-invasive assessment.

Our study showed that the grading score of VM was significantly the highest, followed by AVM, VLM, and LM (*Table 2*). These results suggest that the grading score for classifying CVMs has a high predictive value. In other words, a typical finding of LM/NVD on BP SPECT was no uptake, mild uptake corresponded to VLM, moderate uptake corresponded to AVM and intense uptake indicated VM. Therefore, the grading score system was helpful for CVM classification as well as jugular vein uptake evaluation.

In our study, WBBPS found additional, clinically unexpected CVMs in 2.6% of subjects, which were not identified by BP SPECT. Therefore, WBBPS, along with BP SPECT, may be necessary to fully evaluate head and neck CVMs.

Our study was limited given that only patients with CVM undergoing WBBPS and BP SPECT were included based on clinicians' decisions and the retrospective design; this may have resulted in a selection bias.

In conclusion, BP SPECT is a useful method for classifying CVMs in the head and neck area due to its high diagnostic efficacy. Therefore, BP SPECT may be a suitable initial routine diagnostic imaging modality for head and neck CVM. The relatively low sensitivity of BP SPECT for diagnosing AVM and VLM suggests that BP SPECT should complement other diagnostic modalities such as MRI.

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