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Invited Perspective

Advancing the diagnosis of epithelioid hemangioendothelioma by ^{18}F-FDG PET/CT

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Abstract: Epithelioid hemangioendothelioma (EHE) is a rare vascular tumor originating from endothelial cells. Since ultrasound findings of EHE are nonspecific, computed tomography (CT) and magnetic resonance imaging (MRI) are routinely used for diagnosing the disease. Accumulating evidence indicates that ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) has implemental value in diagnosing EHE. In this *Perspective*, we outline the most recent evidence reporting the diagnostic value of ^{18}F-FDG PET/CT in EHE. The combinational use of CT, MRI, and ^{18}F-FDG PET/CT may help clinicians diagnose the disease in its earlier stages.

Keywords: Epithelioid hemangioendothelioma, ^{18}F-fluorodeoxyglucose, positron emission tomography/computed tomography

Introduction

Epithelioid hemangioendothelioma (EHE) is a rare vascular endothelial neoplasm with characteristic histology and distinctive fusion genes (e.g., *WWTR1-CAMTA1* gene fusion). It is composed of epithelioid endothelial cells and is distinct from epithelioid angiosarcoma [1]. Diagnosis and effective treatment of EHE are still clinical challenges. Novel diagnostic approaches are urgently needed for this rare clinical entity. Meanwhile, summarization of imaging features of EHE on conventional imaging modalities may also help us recognize or at least consider EHE at its first appearance. The establishment of the final diagnosis will initiate the timely treatment, albeit we still lack effective and reproducible treatment options for EHE at the moment.

In this issue of the *American Journal of Nuclear Medicine and Molecular Imaging*, Broski and colleagues reported the value of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) in imaging and characterizing EHE [2]. After retrospectively analyzing the features of ^{18}F-FDG PET/CT images of 35 EHE patients, the authors concluded that EHE is a disease involving multiple organs (e.g., liver, lungs, and bones) with generally low-to-moderate ^{18}F-FDG uptake, which was consistent with that of a previous study [3]. However, rapid progression of pulmonary EHE may have high ^{18}F-FDG uptake in the lesions [4]. Broski *et al.* also emphasized the necessity to perform additional CT and magnetic resonance imaging (MRI) to better depict pulmonary or hepatic lesions, respectively. Dong *et al.* also reported the characteristic MRI features of hepatic epithelioid hemangioendothelioma. More specifically, hepatic lesions showed heterogeneously increased signal intensity on T2-weighted MRI images, hypointensity on T1-weighted MRI images, and peripheral rim-like enhancement on gadolinium-enhanced MRI images [3]. For pulmonary diseases, Broski and colleagues used volume doubling time (VDT) to monitor the progression of the nodules. The reported VDT of ten patients was 1154±772 days (range: 460-2236 days), indicating that VDT is useful in distinguishing EHE from either primary or metastatic lung malignancies. Four patients with supraclavicular vasculature involvement were included

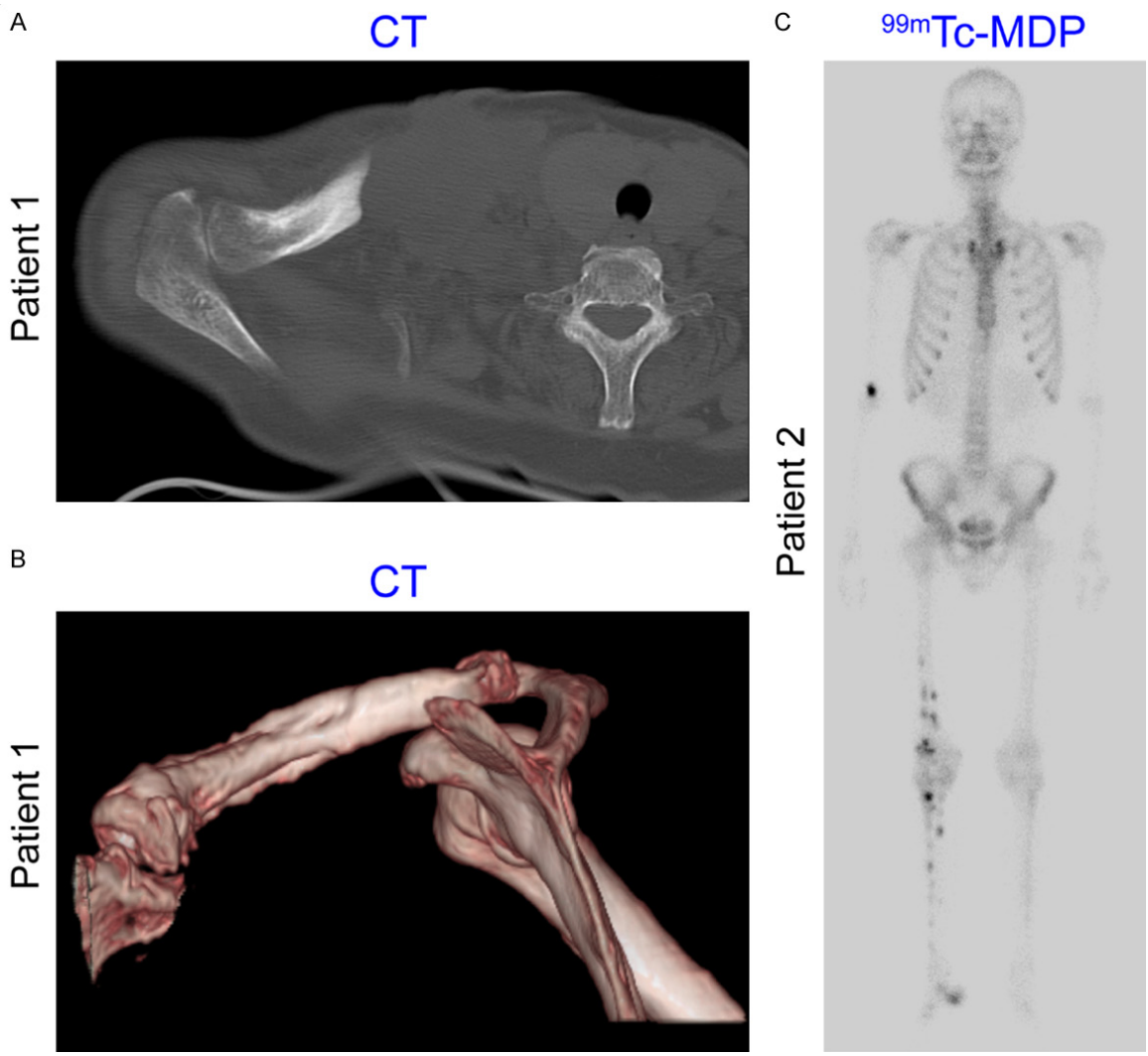

Figure 1. Features of EHE on CT and ^{99m}Tc-MDP images. A, B. A 57-year-old patient with pathologically confirmed right clavicle EHE. The soft tissue mass infiltrated the cortex of the right clavicle. C. A 24-year-old patient with right calcaneal bone EHE underwent ^{99m}Tc-MDP whole-body bone scan. The results indicated multiple metastases from EHE in the right lower limb. The patient refused amputation and lost follow-up after being discharged from our hospital.

in the patient cohort. EHE may involve supraclavicular vasculature, claviculate, and adjacent soft tissues without involving other organs. Although presenting with low uptake on ^{18}F-FDG PET/CT images, EHE may have intense uptake on ^{68}Ga[Ga]-DOTATATE PET/CT images [5]. With the accumulation of diagnostic information, the use of multimodal imaging is helpful in diagnostic dilemmas [6]. We have encountered three pathologically confirmed EHE cases in the past five years. These three patients received CT and bone scans but not ^{18}F-FDG PET/CT scans. CT features of EHE are not typical (**Figure 1A**, **1B**). ^{99m}Tc-methylene diphosphonate (MDP) whole-body bone scan may find metastases from EHE (**Figure 1C**). In general, radiological and nuclear medicine imaging may provide valuable clues in diagnosing EHE, but establishment of the final diagnosis relies on pathological findings.

Timely diagnosis of EHE is quite difficult because most patients with EHE are asymptomatic. Early diagnosis of EHE may facilitate the onset of treatments, including surgery, radiotherapy, chemotherapy, and even hepatic transplantation in the case of localized liver involvement. Surgery is the treatment option

of choice for the localized disease. EHE is derived from vascular endothelial or preendothelial cells, it is rational that targeting vascular endothelial growth factor (VEGF)-vascular endothelial growth factor receptor 2 (VEGFR2) pathway may serve as a viable treatment approach [7]. However, the efficacy of anti-angiogenic agents is not confirmatory [8, 9]. It has been reported that the mTOR inhibitor sirolimus was effective in EHE patients without serosal effusions [10, 11]. Systemic therapies effective for patients with serosal effusions remain to be explored.

To conclude, EHE is a rare disease with varying radiological and nuclear medicine imaging features. The final diagnosis relies on comprehensive consideration of the symptoms, medical imaging findings, and pathological findings. Bearing the already-known knowledge in mind, radiologists and nuclear medicine physicians may avoid misdiagnosis of the disease and advance the treatments for the patients.

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Disclosure of conflict of interest

None.

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