Clinical Case Report

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Hemolymphangioma involving bones and bladder detected on ^{68}Ga-NEB PET/CT

A rare case report

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Abstract

Rationale: Hemolymphangioma is a rare developmental defect of combined vasal and lymphatic vasculature. It is very rare that hemolymphangioma affects the bones and bladder simultaneously, and this condition has never been reported in PubMed.

Patient concerns: A 12-year-old male has a history of hospitalization for recurrent episodes of chyluria of 8 years duration and progressively worsening gross hematuria with right hip pain for 6 months.

Diagnosis: Chylous test of urine fluid was positive. There was no organic disease in the kidneys. ^{68}Ga-NOTA-Evans Blue (NEB) positron emission tomography/computed tomography (PET/CT) images demonstrated clearly several round and strip-shaped low-density shadows with mildly increased radioactive uptake in both bladder wall and pelvis, including sacral, pubic, and ischial bones. Histopathological analysis of biopsy on pubic and ischial bones confirmed the diagnosis of hemolymphangioma.

Interventions: The patient received treatment with traditional Chinese medicine.

Outcomes: At the 6-month follow-up visit, the patient's symptoms of chyluria, hematuria, and pain were all mitigated.

Lessons: Hemolymphangioma is a rare benign disease. ^{68}Ga-NEB PET/CT is a specific method for the lymphatic system, and it might provide more accurate and comprehensive information about the disorder of the lymphatic system compared with CT and magnetic resonance imaging. When patients suffer from suspected lesions of the lymphatic system, ^{68}Ga-NEB PET/CT might be recommended.

Abbreviations: MIP = maximum intensity projection, MRI = magnetic resonance imaging, NEB = NOTA-Evans Blue, PET/CT = positron emission tomography/computed tomography.

Keywords: ^{68}Ga-NOTA-Evans Blue, bladder, bone, hemolymphangioma, positron emission tomography/computed tomography

1. Introduction

Hemolymphangioma is a congenital and benign malformation of both lymphatic and blood vessel.[1] It is preferentially situated in the head and neck, seldom in the spleen, small intestine, orbit, pancreas, vermiform appendix, or omentum.[2,3] Hemolymphangioma rarely involves bones and bladder simultaneously. At present, there are about 70 cases of lymphangioma that have been reported. This is the first case of lymphangioma involving both bladder and bones simultaneously. ^{68}Ga-NOTA-Evans Blue (NEB) positron emission tomography/computed tomography (PET/CT) is a new lymphoscintigraphy technique,[4] which could detect the anatomy and function of the lymphatic system. ^{68}Ga-NEB PET/CT might evaluate lymphatic disorders more accurately than ^{99m}Tc-SC lymphoscintigraphy.[4]

In this report, we present a very rare case of a 12-year-old male hospitalized in our hospital for recurrent episodes of chyluria for 8 years and progressively worsening gross hematuria with right hip pain for 6 months. Finally, this patient was diagnosed hemolymphangioma by histopathological analysis of biopsy on pubic and ischial bones.

2. Case report

A 12-year-old male was hospitalized for recurrent episodes of chyluria for 8 years and progressively worsening gross hematuria with right hip pain for 6 months. ^{68}Ga-NEB is a new PET tracer to evaluate the disorder of the lymphatic system.[4] Several studies have reported the utilization of ^{68}Ga-NEB in lymphatic related

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GH and YJ contributed equally to this work.

The study was registered with ClinicalTrials.gov (NCT02496013). This study was approved by the Ethics Committee of the Peking Union Medical College Hospital. The subject wrote informed consent, who was notified of the potential benefits and risks in this study. Patient has provided informed consent for publication of the case.

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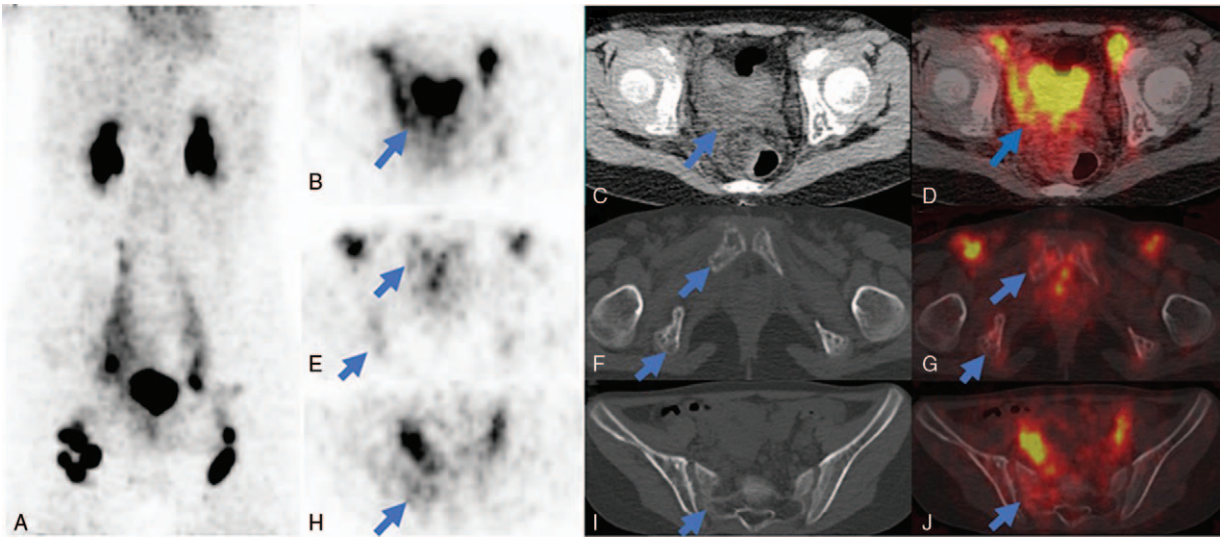

Figure 1. The ^{68}Ga-NEB PET/CT images (A, MIP; B–D, transaxial PET, CT, and fusion; E–G, transaxial PET, CT, and fusion; H–J, transaxial PET, CT, and fusion). ^{68}Ga-NEB PET/CT results show several round and strip-shaped low-density shadows with mildly increased radioactive uptake in both bladder (B–D, blue arrows) wall and pelvis, including sacral, pubic, and ischial bones (E–J, blue arrows). CT = computed tomography, MIP = maximum intensity projection, NEB = NOTA-Evans Blue, PET = positron emission tomography.

diseases, such as lymphedema, lymphangioma, and chyloperitoneum.[4–6]^{68}Ga-NEB PET/CT lymphoscintigraphy was performed to identify the cause of chyluria and suspicious lymphatic abnormity 20 minutes after subcutaneous injection of ^{68}Ga-NEB at the web space between the first and second toes of both feet (0.5 mL, 37 MBq/foot). The patient was asked to walk after the injection. ^{68}Ga-NEB PET/CT (PoleStar m660, Sinounion Healthcare Inc., Beijing, China) images demonstrated several round and strip-shaped low-density shadows with mildly increased radioactive uptake in both bladder wall and pelvis, including sacral, pubic, and ischial bones (Fig. 1A–J, blue arrows). Histopathological analysis of biopsy on pubic and ischial bones revealed abundant dilated vessels among the broken trabeculae and immunohistochemical staining demonstrated cells positive for CD31, CD34, and D2–40 (Fig. 2). Based on pathology and clinical appearance, the patient was diagnosed as hemolymphangioma involving bladder and bones. The patient received the therapy of traditional Chinese medicine, and the symptoms, such as chyluria, hematuria, and pain were all mitigated at the 6-month follow-up.

3. Discussion

Hemolymphangioma is a rare developmental defect of vasculature including vasal and lymphatic.[7] The lesions might be local or diffused.[8] It is preferentially situated in the head and neck, seldom in the spleen, small intestine, orbit, pancreas, vermiform appendix, or omentum.[2,3] Hemolymphangioma was first reported by Couinaud et al[9] in 1966, and the lesion was located in the pancreas. It is very rare that hemolymphangioma invades bones and bladder simultaneously, which has never been reported before in PubMed. The codependence of lymphatic and vascular endothelial cells in this lesion confirms that lymph and blood endothelial cells derive from a mutual stem cell.[10] The expression of D2–40 is specific in lymphatic endothelial cells, and the expressions of CD34 and CD31 are specific in vascular endothelium.[11,12] This patient's histopathologic immunostaining is positive for D2–40, CD34, and CD31, confirming the diagnosis of hemolymphangioma.

The application of traditional radiological examinations, such as CT and magnetic resonance imaging (MRI), alone can be a challenge in making the diagnosis of hemolymphangioma. The radiological appearance of the hemolymphangioma on CT or MRI is not specific, because it is a mixture of multiple tissues. For those lesions mainly composed of water-based substance, such as hemolymphangioma, cyst, and abscess, CT and MRI provide only limited information instead of the origin of the fluid.[13,14] The cyst component of the hemolymphangioma will not show enhancement on contrast-enhanced CT, and the capsule wall might demonstrate no, mild, or uneven enhancement.[13,15,16] The presentations of hemolymphangioma in enhanced CT were variable, thus making the diagnosis difficult. Hemolymphangioma might present low or high signal intensity on MRI, which mainly depends on the proportion of lymphatic and vascular vessels.[14] Nevertheless, ^{68}Ga-NEB PET/CT is a specific modality for assessing the lymphatic system because it could provide comprehensive information about lymphangial positions[5] and accurate guidance for biopsy. Hemolymphangioma invading bladder should be taken into consideration in those patients with chyluria after ruling out kidney disease. According to the literature, it might take patients less time for ^{68}Ga-NEB PET/CT lymphoscintigraphy than ^{99m}Tc-SC lymphoscintigraphy, and ^{68}Ga-NEB PET/CT lymphoscintigraphy could provide more information about the anatomy and disorder of lymphatic system than ^{99m}Tc-SC lymphoscintigraphy, and the images of ^{68}Ga-NEB PET/CT lymphoscintigraphy are more revealing than ^{99m}Tc-SC lymphoscintigraphy.[4] Besides the lymphatic system, ^{68}Ga-NEB PET/CT lymphoscintigraphy also reveals distributions of radioactivity in the liver, kidneys, spleen, and cardiac blood pool.[4] Some lymphatic drainage diseases have been reported to be detected by ^{68}Ga-NEB PET, such as lymphedema, lymphangioma, lymphangioleiomyomatosis, lymphatic cyst, chylothorax, and chyloperitoneum.[4–6]

Some limitations of ^{68}Ga-NEB PET/CT lymphoscintigraphy must be illuminated in the case. The CT utilized in PET/CT is low-

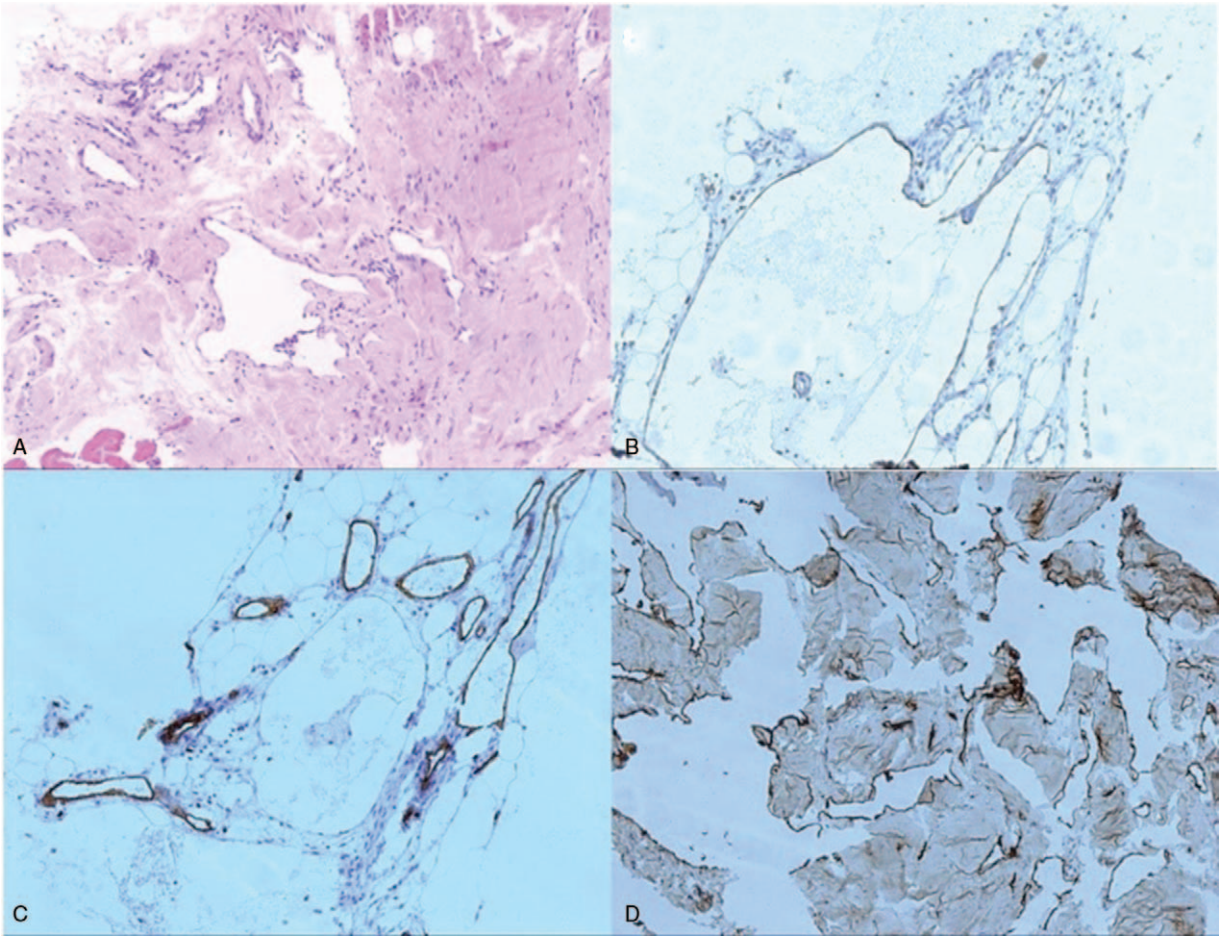

Figure 2. Hematoxylin and eosin (A, ×100), staining revealed abundant dilated vessels among the broken trabeculae and positive immunostaining for CD31 (B), CD34 (C), and D2–40 (D).

dose CT, which has relatively lower spatial resolution and definition in soft tissue compared with high-resolution CT or enhanced CT. Compared with MRI, CT could only provide limited information about soft tissue. The symptoms of chyluria and hematuria disappeared and pain mitigated after the treatment of Chinese traditional medicine 6 months ago, but the specific mechanism of Chinese traditional medicine mitigating the disease is still not clear.

Although hemangiolymphangioma is a benign tumor, it still has the potential to invade the ambient organs and relapse after therapy.[17] The surgery therapy was considered the most effective treatment for hemangiolymphangioma, and the excision extension should contain the surrounding tissue suspected of being invaded.[18] It was reported that the lesions would recur after complete excision in the percentage of 10% to 27%, while the recurrence rate was 50% to 100% for part resection.[7] The nonsurgical therapy was less effective than operation, such as radiotherapy, laser treatment, the injection of curing agent, and cryotherapy.[19] Hemolymphangioma presents a developmental defect of combined vasal and lymphatic vasculature. ^{68}Ga-NEB PET/CT is a specific method for the lymphatic system, which might provide more accurate and comprehensive information about the disorder of the lymphatic system compared to CT and MRI. When patients suffering from lymphatic related disease are suspected, ^{68}Ga-NEB PET/CT should be recommended.

Author contributions

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