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Original Article

^{18}F-FDG PET/CT for the study of primary renal tumors in children

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Abstract: Backgroud: In this study, ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) was used in a series of sixteen patients with primary renal tumors. Methods: The study focused on the observation of clinical and ^{18}F-FDG PET/CT imaging features of sixteen patients diagnosed with primary renal tumors. The diagnosis was based on histopathology. Results: In sixteen patients, ten were Wilms tumor (WT), three were renal cell carcinoma (RCC), one was clear cell sarcoma of the kidney (CCSK), one was malignant rhabdoid tumor of the kidney (MRT) and one was primitive neuroectodermal tumor (PNET). The mean age of patients was 4.4 ± 4.0 years. The mean diameter of tumors was 4.4 ± 3.2 cm. The mean maximum standardized uptake value (SUVmax) of tumors was 5.9 ± 3.7. All renal tumors showed inhomogeneous soft tissue density masses and different level of FDG uptake, frequently with necrosis. Nine patients of WT demonstrated uneven slightly-moderate FDG uptake (SUVmax range: 3.6-8.6) in tumor, with scattered spot radioactive uptake reduced in center and only one patient of WT showed FDG uptake at the rim of tumor (SUVmax: 5.7). RCC demonstrated uneven slight FDG uptake (SUVmax range: 1.8-4.6) at the rim of tumor, presenting a circular distribution with a pole in the center, and the ring wall was relatively thick and irregular. FDG uptake degree of CCSK was similar with WT, while it had significant enhancement on contrast CT. PNET demonstrated highest FDG uptake (SUVmax: 17.9), MRT ranked second (SUVmax: 8.8), and RCC with the smallest size manifested the lowest FDG uptake (SUVmax: 1.8). Conclusion: Primary renal tumors in children are well established in ^{18}F-FDG PET/CT. The tumors commonly appear large, inhomogeneous soft tissue density masses, with necrosis and calcification, and demonstrate evaluated but variable glycolytic activity.

Keywords: FDG PET/CT, Wilms tumor, renal carcinoma, clear cell sarcoma, malignant rhabdoid tumor, primitive neuroectodermal tumor

Backgroud

Wilms tumor (WT) is the most common primary malignant renal tumor of childhood, and non-Wilms tumor (non-WT) forms a small heterogeneous group of renal malignancies in children [1]. Non-WT usually includes renal cell carcinoma (RCC), clear cell sarcoma of the kidney (CCSK), malignant rhabdoid tumor of the kidney (MRT), congenital mesoblastic nephroma (CMN), primitive neuroectodermal tumor (PNET), and renal lymphoma, et al [2].

Clinically, most children have an asymptomatic abdominal mass, and some children have abdominal pain, gross hematuria, or fever. But theses clinical symptoms are not characteristic.

Differential diagnosis of renal tumors in children is important as the treatment and prognosis is different in different types of tumors. Radiological examinations such as ultrasound, computed tomography (CT), and magnetic resonance (MR) are valuable for renal masses before histology. Radiologic features can provide essential information to differentiate different types of renal tumors. ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) imaging has potential advantages over conventional imaging by estimating glucose metabolism. However, as pediatric primary renal tumors are rare, the precise role of ^{18}F-FDG PET/CT imaging in these tumors not yet been well defined. In this study, demographic, clinical characteristics, and performance of ^{18}F-FDG PET/CT imaging in a series of sixteen patients with primary renal tumors was studied to assess the identification and characterization of ^{18}F-FDG PET/CT imaging of renal tumors.

Table 1. Clinical features and CT contrast enhancement of patients

Patient	Diagnosis	Clinical symptoms	CT enhancement
1	WT	Abdominal pain	Slight heterogeneous enhancement
2	WT	Abdominal mass	Slight heterogeneous enhancement
3	WT	Gross hematuria	Slight heterogeneous enhancement
4	WT	Abdominal mass	Not done
5	WT	Abdominal mass	Significantly heterogeneous enhancement
6	WT	Abdominal mass	Moderate heterogeneous enhancement
7	WT	Abdominal mass	Moderate heterogeneous enhancement
8	WT	Abdominal pain with fever	Not done
9	WT	Abdominal mass	Not done
10	WT	Abdominal mass	Moderate heterogeneous enhancement
11	RCC	Gross hematuria	Not done
12	RCC	Abdominal pain	Moderate heterogeneous enhancement
13	RCC	Abdominal pain with fever	Not done
14	CCSK	Abdominal mass	Moderate heterogeneous enhancement
15	MRT	Abdominal mass	Slight heterogeneous enhancement
16	PNET	Fever	Slight heterogeneous enhancement

Methods

Patients

The records of sixteen patients (10 male, 6 female) from September 2008 to December 2017 were retrospectively reviewed in this study. Contrast material-enhanced CT was performed in eleven patients before ^{18}F-FDG PET/CT imaging. The final diagnosis was confirmed by histopathological findings based on ultrasound-guided biopsies for the renal mass after ^{18}F-FDG PET/CT imaging. All patients were followed up for 32.0 ± 16.0 months. Ten patients received combined chemotherapy, radiotherapy, and operation, five patients received only chemotherapy and one patient received chemotherapy, operation and took targeted drugs. One patient had local recurrence. One patient had recurrence and lung metastasis. Three patients died of severe renal failure.

^{18}F-FDG PET/CT examination

All patients were asked to fast for 6 hours. ^{18}F-FDG (4.07 MBq/kg) with a radiochemical purity of > 95% (Sumitomo Corporation, Japan) was given through intravenous injection and the patients were asked to rest for approximately 60 minutes after injection. Seven patients (< 3 years old) were sedated after injection of ^{18}F-FDG immediately prior to commencement of imaging. The PET/CT scan was performed using a hybrid PET/CT scanner (Biograph 16HR; Siemens, Germany). The scan range was from the mid-thigh to the base of the skull. A low-dose CT protocol (100 mAs, 140 kV, tube rotation time of 0.5 per rotation, pitch of 6, slice thickness of 5 mm, and shallow breathing) was first applied and followed by the PET scan (3- or 5-minutes emission scan per table position, depending on whether the patient could keep the arms above the head during scanning or not). PET imaging data were reconstructed iteratively by adopting CT data for attenuation correction and acquired CT and PET images were displayed on a Xeleris workstation (Siemens, Germany). The maximum standardized uptake value (SUVmax) was calculated by drawing regions of interest within the lesion suspected on the attenuation-corrected PET images. Lesion detection was based on visual observation, and was considered to be positive when FDG uptake was higher than normal renal cortex.

Results

Table 1 summarizes the pathology, clinical symptoms and CT contrast enhancement of patients. **Table 2** summarizes the performance of ^{18}F-FDG PET/CT imaging. The mean age of patients was 4.4 ± 4.0 years. The mean diameter of tumors was 4.4 ± 3.2 cm. The mean SUVmax of tumors was 5.9 ± 3.7.

All renal tumors showed inhomogeneous soft tissue density masses and different level of

Table 2. Performance of ^{18}F-FDG PET/CT imaging

Patient	CT					PET	
	Diameter (cm)	Density	Rim	Necrosis	Calcification	^{18}F-FDG uptake pattern	SUVmax
1	8.6	Uneven	Well-defined	Yes	Yes	FDG uptake in tumor with spot radioactive uptake reduced	8.6
2	8.3	Uneven	Well-defined	Yes	Yes	Uneven FDG uptake in tumor with scattered spot radioactive uptake reduced	3.6
3	9.2	Uneven	Well-defined	Yes	No	Uneven FDG uptake in tumor with scattered spot radioactive uptake reduced	5.5
4	11.0	Uneven	Well-defined	Yes	Yes	Uneven FDG uptake in tumor with scattered spot radioactive uptake reduced	3.8
5	7.0	Uneven	Well-defined	Yes	No	Uneven FDG uptake in tumor with scattered spot radioactive uptake reduced	6.6
6	8.9	Uneven	Well-defined	Yes	Yes	Uneven FDG uptake at the rim of tumor	5.7
7	11.8	Uneven	Well-defined	Yes	Yes	Uneven FDG uptake in tumor with scattered spot radioactive uptake reduced	4.2
8	10.6	Uneven	Ill-defined	Yes	Yes	Uneven FDG uptake in tumor with scattered spot radioactive uptake reduced	4.5
9	5.7	Uneven	Ill-defined	Yes	No	Uneven FDG uptake in tumor with scattered spot radioactive uptake reduced	4.4
10	9.6	Uneven	Well-defined	Yes	Yes	Uneven FDG uptake in tumor with scattered spot radioactive uptake reduced	5.7
11	2.2	Uneven	Well-defined	Yes	No	Uneven FDG uptake at the rim of tumor	1.8
12	15.5	Uneven	Well-defined	Yes	Yes	Uneven FDG uptake at the rim of tumor	4.6
13	6.0	Uneven	Well-defined	Yes	Yes	Uneven FDG uptake at the rim of tumor	4.3
14	10.2	Uneven	Ill-defined	Yes	No	Uneven FDG uptake in tumor with scattered spot radioactive uptake reduced	3.6
15	3.9	Uneven	Ill-defined	Yes	No	FDG uptake in tumor with spot radioactive uptake reduced	8.8
16	6.5	Uneven	Ill-defined	Yes	No	Intense FDG uptake in tumor	17.9

FDG uptake, frequently with necrosis. Nine patients of WT demonstrated uneven slightly-moderate FDG uptake (SUVmax range: 3.6-8.6) in tumor, with scattered spot radioactive uptake reduced in the center and only one patient of WT showed FDG uptake at the rim of tumor (SUVmax: 5.7). RCC demonstrated uneven slightly FDG uptake (SUVmax range: 1.8-4.6) at the rim of tumor, presenting circular distribution with a pole in the center, and the ring wall was relatively thick and irregular. FDG uptake degree of CCSK was similar with WT, while it had significant enhancement on contrast CT. PNET demonstrated highest FDG uptake (SUVmax: 17.9), MRT ranked secondly (SUVmax: 8.8), and RCC with the smallest size manifested lowest FDG uptake (SUVmax: 1.8).

In sixteen patients, five patients (case 1, case 2, case 5, case 6 and case 11) of WT, all patients (case 10, 11, 12) of RCC and one patient (case 15) of PNET showed perirenal, abdominal, and around the aortic lymph nodes enlargement on CT, lymph nodes in case 2 and 10 had no FDG uptake, lymph nodes in case 15 had intense FDG uptake (SUVmax: 9.7). Case 16 also showed FDG uptake in lumbago (SUVmax: 13.2) and skull, vertebrae, iliac bone, pubic bone, femur (SUVmax: 14.3) on PET, but there was no density changes on CT.

Discussion

Primary renal tumors are rare in the pediatric population. Radiology, together with clinical and epidemiological data, enables the diagnostic work-up of pediatric renal tumors [3]. In this study, sixteen patients with renal masses from our institution were analyzed using ^{18}F-FDG PET/CT imaging, including eleven cases of WT, three cases of RCC, one case of CCSK, one case of MRT and one case of PNET. Clinical symptoms of pediatric renal tumors are not characteristic, which is not easy for early diagnosis. However, it commonly appears as a large mass at the time of diagnosis. The mean diameter in our study was 4.4 ± 3.2 cm.

WT is the most common malignant renal tumor in young children. In our study, among sixteen patients, ten patients (6 boys and 4 girls) were confirmed as WT. Median age of the patients with WT is significantly lower than non-WT [2]. On CT, WT usually appears as a bulky, spherical intrarenal mass with well-defined rim of compressed renal parenchyma or pseudocapsule surrounding it [4]. Most WT concentrate FDG slightly and contain FDG uptake reduced areas which are corresponded to necrosis. Regrading to WT, Olukayode AA [4] showed that half of his subjects were involved in lymph nodes metastasis. In this study, four patients presented lymph nodes metastasis under ^{18}F-FDG PET/CT imaging. Moinul Hossain AK [5] demonstrated that FDG PET was not sensitive for lung nodules less than 10 mm in diameter, but lung nodules were better visualized by CT.

RCC accounts for > 5% of all malignant renal tumors after 12 year and the odds of having an RCC diagnosis are increased by 50% for every of increasing age [6]. Xp11.2 translocation RCC is the most common subtype of RCC in children and adolescents. Xp11.2 translocation RCC is often sized < 4-7 cm in diameter and located in one pole [7]. It is distinguished by hyper-attenuation at non-enhanced CT, a defined capsule, and associated retroperitoneal lymphadenopathy [8]. ^{18}F-FDG PET/CT imaging of Xp11.2 translocation RCC is quite different from other subtypes of RCC. Xp11.2 translocation RCC commonly shows FDG uptake at the rim of the tumor, presenting circular distribution, and FDG deficiency in the center of the tumor. The ring is relatively thick and irregular. This representation is in concordance with performance of CT enhancement. The SUVmax of Xp11.2 translocation RCC in our study was much lower than the SUVmax of high-grade clear cell RCC and papillary RCC which were reported in the study of Takahashi M [9].

CCSK is a rare tumor that is diagnosed most often in children between 2- and 4-years-old of age [10]. Clinical features and radiological performance of CCSK is similar to WK. Uncomplicated cysts are a well-established feature of CCSK [11]. Cysts are common but are small and few in number. Necrosis is also often seen in tumors. However, sometimes it is hard to distinguish cysts from necrosis based on low doses CT. Kato M [12] revealed irregular circular calcification around the necrosis in a case. ^{18}F-FDG PET/CT imaging on CCSK has not reported as far. In this case, the patient showed bulky tumor on right kidney with nodular calcification in the center, strip calcification under the capsule, small cysts and patchy necrosis in tumor and show uneven slightly FDG uptake,

which was misdiagnosed as WT on PET/CT in our center. Contrast enhancement CT is helpful for differential diagnosis of CCSK and WT. CCSK show significant enhancement in tumor [13], whereas WT show slight enhancement in tumor.

MRT is an aggressive embryonal tumor arising from renal medullary cells [14]. It accounts for an estimated 0.9-2% of renal tumor [15] in infants and young children, with a median age of 10.6 months (mean 15 month) [16]. MRT is located deep within the renal pelvis and sinus in contradistinction to WT and RCC which are usually located in the renal cortex [17]. CT is a good tool for diagnosis of MRT [18]. Typical finding on CT is subcapsular renal hemorrhage or peripheral tumor necrosis and calcification. As per the existing literature, ^{18}F-FDG PET/CT imaging on extra renal MRT has been reported. But there are some controversial points on FDG uptake of lesions. Some cases of extra renal MRT demonstrated intense FDG uptake at the primary and metastatic sites [19]. But some cases showed low-grade FDG uptake [19, 20]. ^{18}F-FDG PET/CT imaging on a suspected renal MRT recurrence showed intense, multiple, and inhomogeneous FDG uptakes in the left renal fossa [21]. In this study, renal MRT showed intense FDG uptake and the SUVmax of MRT ranked second in all tumors. This kind of tumor is likely to infiltrate the adjacent parenchyma and extend into the renal vein or inferior vena cava [22].

Renal PNET is extremely rare entity and considered as Ewing's sarcoma family-related group [23]. It is an aggressive tumor with a relatively short overall survival [24]. Median age of presentation is 27 years and it is extremely uncommon in < 15 years. On CT, renal PNET shows a large heterogeneous mass with areas of hemorrhage or necrosis [25]. In the study of Sun Q [26], the tumors ranged from 4 cm to 22 cm in size and few showed calcified areas. PNET is aggressive and diagnosed as advanced stage at presentation with extra renal spread and metastasis. The tumors commonly invade the renal sinus or perinephric fat, renal vein, adrenal gland and metastasize into the lungs and bone [27, 28]. PNET has high glucose metabolism and it is easily recognized on ^{18}F-FDG PET/CT imaging [29]. Here, both the primary tumor and metastatic lesions showed intense FDG uptake.

An advantage of ^{18}F-FDG PET/CT is that is a whole-body scan, allowing all tissues and organs to be evaluated in a single-step examination. PET/CT is also possible for identification of high-activity tumor cells without any anatomic alteration. PET/CT is used as detection for lymph nodes metastasis and distant metastasis in many tumors. Five patients of WT, all patients of RCC, and one patient of PNET had lymph nodes metastasis, distributed in perirenal, abdominal, and around the aortic. PNET patients showed lumbago infiltration and bone metastasis, including the skull, vertebrae, iliac bone, pubic bone, femur bone on PET, whereas there was no any changes on CT.

When the tumors are large, pediatric renal tumors should be distinguished the retroperitoneal tumors such as neuroblastoma, malignant teratoma, and giant hepatoblastoma. Primary renal tumors often lost the normal kidney outline and boundary between cortex and medullary. Renal cortex, renal calyx, and renal pelvis are likely destroyed in primary renal tumors, which is quite different from compressions from extra renal tumors.

Diagnosis of renal tumors is challenging. The imaging characteristics of renal tumors in children are often non-specific and overlap with each other. As the number of patients was limited, more cases are required for analysis of the common points and differences of ^{18}F-FDG PET/CT imaging on pediatric renal tumors in order to achieve even better results.

Conclusions

Primary renal tumors in children are well established in ^{18}F-FDG PET/CT imaging. These tumors usually demonstrate elevated but variable glycolytic activity.

Acknowledgements

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Disclosure of conflict of interest

None.

Abbreviations

^{18}F-FDG, ^{18}F-fluorodeoxyglucose; PET/CT, Positron Emission Tomography/Computed Tomography; WT, Wimls tumor; RCC, renal cell carci-

noma; CCSK, clear cell sarcom of the kidney; MRT, malignant rhabdoid tumor of the kidney; PNET, primitive neuroectodermal tumor; CMN, congenital mesoblastic nephroma; MR, magnetic resonance; SUVmax, maximum standardized uptake value.

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