Fever of Unknown Origin: ^{18}F-Fluorodeoxyglucose Positron Emission Tomography–Computed Tomography Showing Renal Cyst Infection in Autosomal Dominant Polycystic Kidney Disease

Abstract

Fever of unknown origin (FUO) is a convoluted clinical dilemma. It can be caused by infective, inflammatory, malignant, and other pathologies. The identification of etiopathogenesis is essential for instituting definitive management. ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography-computed tomography (PET-CT) is now an integral part of FUO management. We present the case of a 60-year-old female with autosomal dominant polycystic kidney disease (ADPKD), where the infected renal cyst was detected as the cause of FUO on ^{18}F-FDG PET-CT.

Keywords: *^{18}F-fluorodeoxyglucose, autosomal dominant polycystic kidney disease, fever of unknown origin, positron emission tomography-computed tomography*

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Introduction

^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography-computed tomography (PET-CT) is now an integral part of fever of unknown origin (FUO) management because of its ability to demonstrate the etiology in a large proportion of cases.[1] In a patient without potential diagnostic clues, ^{18}F-FDG PET-CT is recommended as first-line imaging.[2] Patients with autosomal dominant polycystic kidney disease (ADPKD) are at increased risk of infection because of the presence of multiple renal cysts as well as often accompanying renal dysfunction.[3] The detection of cyst infection with conventional anatomical imaging such as ultrasonography (USG), CT, and magnetic resonance imaging (MRI) is challenging.[4] ^{18}F-FDG PET-CT has been shown to be a promising technique for the detection of cyst infection in ADPKD.[5]

Case Report

A 60-year-old female presented to the hospital with a history of fever of 2 weeks duration, which was evaluated on an outpatient basis for one more week, with three outpatient visits. It was moderate-to-high grade and associated with no localizing symptoms. There was some abdominal fullness. She was a known case of ADPKD, resulting in end-stage renal disease (ESRD) and was on maintenance hemodialysis (MHD). She also had hypertension and diabetes mellitus. On clinical examination apart from bilateral renal masses, there was no other major finding. There was no flank tenderness. Blood picture showed anemia (hemoglobin: 8.1 g/dL), neutrophilic leukocytosis (total count: 18,900/mL, 93% neutrophils) and raised C-reactive protein (32 mg/L) suggesting infection. Suspecting renal cyst infection, USG of the abdomen was done, which was noncontributory and showed enlarged bilateral kidney with extensive cysts, some of which showed internal debris. Whole-body contrast-enhanced (patient was on MHD) ^{18}F-FDG PET-CT [Figure 1] was made to localize the cause of fever. Maximum intensity projection PET images (A) showed focal areas of increased ^{18}F-FDG uptake in bilateral lumbar regions in the abdomen (*arrows*). Transaxial (B) and coronal (C) contrast-enhanced CT images showed bilateral grossly enlarged kidneys with the renal parenchyma replaced completely with cysts of variable sizes. Fused transaxial (D) and coronal (E) PET-CT images revealed increased peripheral ^{18}F-FDG uptake in two cysts (*arrows*), one in the right kidney mid polar region (maximum standardized uptake value [SUV max] 8.5) and another

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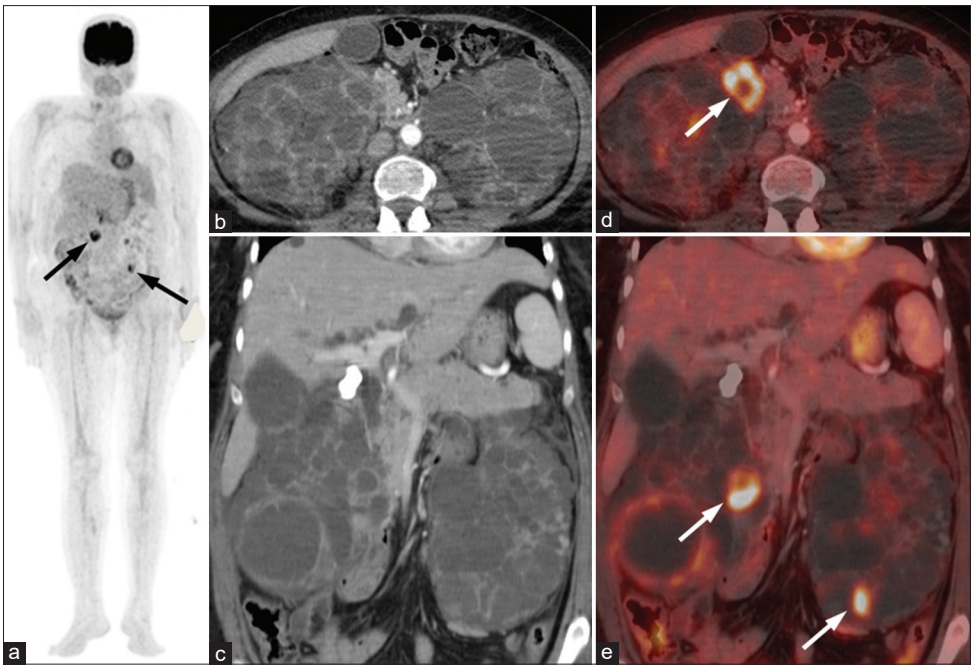

Figure 1: Maximum intensity projection positron emission tomography images (a) showed focal areas of increased ^{8}F-fluorodeoxyglucose uptake in bilateral lumbar regions in abdomen (arrows). Transaxial (b) and coronal (c) contrast-enhanced computed tomography images showed bilateral enlarged kidneys with the renal parenchyma replaced completely with cysts of variable sizes. Fused transaxial (d) and coronal (e) positron emission tomography-computed tomography images revealed increased peripheral fluorodeoxyglucose uptake in two cysts (arrows), one in the right kidney mid polar region (maximum standardized uptake value 8.5) and another in the left kidney lower pole region (maximum standardized uptake value 5.1)

in the left kidney lower pole region (SUV max 5.1). Findings were suggestive of cyst infection. No other significant abnormality was seen in the rest of the body. The patient was treated with intravenous broad-spectrum antibiotics but failed to respond. Aspiration of the right renal mid-pole cyst under guidance showed turbid fluid, which grew *Klebsiella pneumoniae* on culture, resistant to many antibiotics. She was started on sensitive antibiotics but achieved no response. Considering the risk of septicemia and the inability of systemically administered antibiotics to reach the cysts, the patient underwent bilateral nephrectomy. Postnephrectomy gross examination showed bilateral multiple subcapsular cysts with purulent collection in three cysts and clear to brown fluid in others. Microscopic examination showed cysts (dilated tubules and collector ducts) lined by cuboidal or flattened epithelium containing an eosinophilic fluid. The parenchyma between cysts was represented by very few atrophic/compressed but still functional nephrons, along with interstitial fibrosis and chronic inflammation. There was no evidence of renal cell carcinoma in either kidney. The fever subsided a few days after surgery. She is awaiting transplantation.

Discussion

ADPKD is a hereditary condition caused due to mutation in PKD-1 or PKD-2 gene, which leads to the development of multiple renal cysts.[3] While it is usually asymptomatic in childhood, symptoms begin to appear with increasing age. Patients can present with flank pain and hematuria, or nonspecific gastrointestinal symptoms. Hypertension due to activation of the renin-angiotensin system is common. ESRD develops over the course of time. Cyst infection is a common but sinister complication and can present with fever and flank pain. However, these symptoms can also be seen in cyst hemorrhage, pyelonephritis, and nephrolithiasis; hence, further evaluation is needed to reach the correct diagnosis.[6] The reference standard is the analysis of the cyst fluid, but aspiration is fraught with the risk of complications such as bleeding, rupture, and contamination of adjacent cysts, and is therefore rarely performed. It was performed in this case to check the antibiotic sensitivity as the patient was not responding even to high-end antibiotics.

On conventional anatomical imaging with USG, CT, or MRI, it is difficult to differentiate infected and noninfected renal cysts.[4] Diffusion-weighted MRI has shown some promise, but results are still mixed.[7] ^{18}F-FDG PET-CT is now an integral part of FUO management. Because of the nonspecific nature of ^{18}F-FDG, it is taken up by leukocytes as well as malignant cells, thereby allowing detection of a wide range of malignant, infective and inflammatory diseases which could present with FUO.[1,2] It has shown promising results for the detection of infection in renal cysts associated with ADPKD. Pijl *et al*. showed a sensitivity of 88.9%, a specificity of 75.0%, a positive predictive value (PPV) of 84.2%, and a negative predictive value (NPV) of 81.8% for the diagnosis of cyst infection in ADPKD.[8] In another study, Kwon *et al*.

showed a sensitivity of 85.7%, specificity of 87.5%, PPV of 85.7%, and NPV of 87.5% for the same purpose.[9] More recently, Neuville *et al*. suggested a 4-point visual scoring system (with respect to blood pool and liver) for the diagnosis of cyst infection in ADPKD.[10] The visual assessment of PET-CT images reached a sensitivity of 73.1% and a specificity of 70.6%. Using the 4-point scale, an^{18}F-FDG score ≥3 (i.e., cyst uptake >liver) improved the specificity to 85.3%.

Conclusion

^{18}F-FDG PET-CT is an important imaging modality in the management of patients with FUO. In patients with ADPKD, it can demonstrate cyst infection with higher sensitivity and specificity than conventional anatomical imaging, thereby providing a reliable noninvasive tool in this setting, as demonstrated in the case presented above.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Nazar AH, Naswa N, Sharma P, Soundararajan R, Bal C, Malhotra A, *et al*. Spectrum of 18F-FDG PET/CT findings in patients presenting with fever of unknown origin. AJR Am J Roentgenol 2012;199:175-85.
2. Kouijzer IJ, Mulders-Manders CM, Bleeker-Rovers CP, Oyen WJ. Fever of unknown origin: The value of FDG-PET/CT. Semin Nucl Med 2018;48:100-7.
3. Chebib FT, Torres VE. Autosomal dominant polycystic kidney disease: Core curriculum 2016. Am J Kidney Dis 2016;67:792-810.
4. Jouret F, Lhommel R, Devuyst O, Annet L, Pirson Y, Hassoun Z, *et al*. Diagnosis of cyst infection in patients with autosomal dominant polycystic kidney disease: Attributes and limitations of the current modalities. Nephrol Dial Transplant 2012;27:3746-51.
5. Pijl JP, Kwee TC, Slart RH, Glaudemans AW. FDG-PET/CT for diagnosis of cyst infection in autosomal dominant polycystic kidney disease. Clin Transl Imaging 2018;6:61-7.
6. Hogan MC, Norby SM. Evaluation and management of pain in autosomal dominant polycystic kidney disease. Adv Chronic Kidney Dis 2010;17:e1-6.
7. Suwabe T, Ubara Y, Ueno T, Hayami N, Hoshino J, Imafuku A, *et al*. Intracystic magnetic resonance imaging in patients with autosomal dominant polycystic kidney disease: Features of severe cyst infection in a case-control study. BMC Nephrol 2016;17:170.
8. Pijl JP, Glaudemans AW, Slart RH, Kwee TC. $^{(18)}$F-FDG PET/CT in autosomal dominant polycystic kidney disease patients with suspected cyst infection. J Nucl Med 2018;59:1734-41.
9. Kwon HW, Lee HY, Hwang YH, Park HC, Ahn C, Kang KW. Diagnostic performance of 18F-FDG-labeled white blood cell PET/CT for cyst infection in patients with autosomal dominant polycystic kidney disease: A prospective study. Nucl Med Commun 2016;37:493-8.
10. Neuville MF, Lovinfosse P, Jadoul A, Thys M, Seidel L, Hustinx R, *et al*. The use of a visual 4-point scoring scale improves the yield of (18) F-FDG PET-CT imaging in the diagnosis of renal and hepatic cyst infection in patients with autosomal dominant polycystic kidney disease. Eur J Nucl Med Mol Imaging 2020. (Online ahead of print).[doi: 10.1007/s00259-020-04903-x.].