Clinical note

18F-FDG PET/CT diagnosis of liver cyst infection in a patient with autosomal dominant polycystic kidney disease and fever of unknown origin

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ABSTRACT

The diagnosis, localization and treatment of infected cysts in the kidney or liver of patients with autosomal dominant polycystic kidney disease (ADPKD) remain a clinical challenge. We report the findings of 18F-FDG PET-CT in an ADPKD diagnosed patient who required renal transplantation five years before and in his follow up presented repeated episodes of bacteriemia without known focus on radiological tests performed. The 18F-FDG PET-CT scan showed numerous hypermetabolic images with focal or ring-shaped morphology related to the content and the wall of some hepatic cysts. The increased metabolic activity was localized on segments vi and vii. We proceeded to drainage of one cyst in segment vi, removing 110 cc of purulent fluid which grew Escherichia coli BLEE. The 18F-FDG PET/CT scan should be included in the diagnostic algorithm for detecting infected liver cysts in patients with ADPKD and fever of unknown origin.

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Diagnóstico mediante 18F-FDG PET-TAC de infección quística hepática en paciente con enfermedad poliquística renal autosómica dominante y fiebre de origen desconocido

RESUMEN

El diagnóstico, la localización y el tratamiento de los quistes renales o hepáticos infectados en pacientes con enfermedad poliquística renal autosómica dominante (EPRAD) sigue siendo un reto clínico. Comunicamos los hallazgos de la 18F-FDG PET-TAC en un paciente diagnosticado de EPRAD, trasplantado renal hace 5 años, que presentó episodios repetidos de bacteriemia sin foco conocido en las exploraciones radiológicas practicadas. La exploración con 18F-FDG PET-TAC demostró numerosas imágenes hipermetabólicas de morfología focal o anular relacionadas con el contenido y la pared de alguno de los quistes hepáticos. La mayor actividad metabólica se localizó en los segmentos vi y vii. Se procedió a la punción y drenaje de uno de los quistes del segmento vi extrayendo 110 cc de un líquido purulento en el que creció Escherichia coli BLEE. La exploración de la 18F-FDG PET-TAC debería incluirse en el algoritmo diagnóstico para detectar quistes hepáticos infectados en pacientes con EPRAD y fiebre de origen desconocido.

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Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is the most frequent genetic kidney disease and is characterized by the presence of multiple bilateral renal cysts which cause progressive destruction of the renal parenchyma. The prevalence of this disease in the general population is of 0.5–1/1000 inhabitants and it is responsible for 5–10% of the cases of terminal renal failure. It is a multisystemic disease, with the presence of hepatic cysts being the most frequent extrarenal manifestation. The symptoms usually manifest in adulthood and are related to a progressive increase in kidney size. Other symptoms include pain in the flank, hematuria, renal colic, recurrent urinary tract infection and arterial hypertension. Renal function is maintained until the fourth and sixth decades of life and the incidence of hepatic cysts rises with age while in contrast with renal function, hepatic function is rarely affected. The complications of renal and hepatic cysts are mainly related to infection, cyst hemorrhage or rupture. It has been estimated that up to 30–50% of the patients with ADPKD have some form of kidney infection during their lifetime.1–3

We report the findings of an 18F-FDG PET-CT study in a patient diagnosed with ADPKD requiring kidney transplantation due to terminal renal failure and who presented repeated episodes of bacteremia of unknown origin during the evolving course of the disease.


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In this last study performed according to a standardized protocol, marked hepatomegaly was observed with abundant small and medium sized cysts diffusely distributed in both lobes, with hepatic parenchyma recognized between the two and numerous hypermetabolic images of variable, focal or doughnut-shaped related to the content and wall of some of the cysts (long arrows). The greatest metabolic activity is localized in segments vi and vii (SUVmax = 7.2). No recent hemorrhage was observed in the interior of any of the cystic lesions. Homogeneous splenomegaly. Voluminous polycystic non functioning kidneys. Renal graft in the left iliac fossa (short arrow). Visualization of the vesical catheter. (B) New appearance of increased metabolic activity is seen as an incomplete ring shape on the wall of various hepatic cysts clustered in segment ii (arrows) and complete resolution of the known hypermetabolic hepatic lesions.

Clinical case

This 62-year-old patient had a personal history of ADPKD and terminal renal failure and received the first kidney transplant in August 2005, undergoing transplantectomy during the immediate postoperative period due to thrombosis of the renal vein. The patient was retransplanted in March 2006, having remained on immunosuppressive treatment with prednisone, mycophenolate and tacrolimus since then.

The patient was admitted to our center between May and June 2011 for recurrent septic episodes due to multiresistant *Escherichia coli* (extended-spectrum betalactamase (ESBL)-producing *E. coli*), which were resolved with intravenous antibiotic treatment determined by the antibiogram. The patient was readmitted at the end of July of the same year for a new febrile syndrome with no apparent foci and with a positive blood culture for ESBL with a leukocyte count of 5100/mm$^3$ with deviation to the left, Hb: 9.8 g/dL, platelets: 142,000/mm$^3$, VSG: 120 mm (Wintrobe), creatinine: 1.48 mg/dL, glomerular filtrate (MDRD-4-IDMS): 48.5 mL/min and normal urine sediment. Seriated sputum, urine and stool cultures for parasite and rotavirus study were repeatedly negative. Serology for *Brucella, Leishmania*, HIV, hepatitis A and C, toxoplasmosis, varicella zoster, *Borreia*, viral load and antigenemia for cytomegalovirus were also negative. Anti-HBc and anti-HBs were positive. For identifying the origin of the recurrent infection, abdominal ultrasound, thoracoabdominal CT, scintigraphy with $^{67}$Ga citrate, transthoracic and transesophageal echocardiogram and abdominal magnetic resonance (MR) were performed, which only depicted chronic basal alterations (hepatorenal polycystosis, splenomegaly and kidney graft in the left iliac fossa) and did not demonstrate the origin of the infection for which the $^{18}$F-FDG PET/CT study was requested (Fig. 1A). In this last study performed according to a standardized procedure, marked hepatomegaly was observed with abundant small and medium sized cysts diffusely distributed throughout both lobes, with hepatic parenchyma recognized between the two and numerous hypermetabolic images of variable, focal or doughnut-shaped related to the content and wall of some of the cysts. The greatest metabolic activity was localized in segments vi and vii (SUVmax = 7.2). No recent hemorrhage was observed in the interior of any of the cystic lesions. Puncture and drainage of one of the cysts in segment vi was performed oriented by the PET-CT results, extracting 110 cc of purulent fluid in which the growth of ESBL-producing *E. coli* was detected. Intravenous antibiotic treatment with tigecycline was prolonged for 3 more weeks. The patient remained afebrile with rapid improvement in the general status and the analytical parameters and was discharged with oral treatment with sulfamethoxazole trimethoprim and controlled in the outpatient clinic.

The patient returned 3 months later for a new febrile episode due to infectious, tumoral or inflammatory processes. The $^{18}$F-FDG PET-CT (Fig. 1B) was repeated, showing complete resolution of the known hepatic lesions and the appearance of a new incomplete ring-shaped hypermetabolic lesion on the wall of several hepatic cysts clustered in segment ii (arrows). The patient satisfactorily responded to wide spectrum empiric antibiotic treatment, remaining without fever and with a good general status at 6 months.

Discussion

The diagnosis, localization and treatment of infected renal and hepatic cysts in patients with ADPKD continue to be, at present, an important clinical challenge. The symptoms are usually unspecific and there is no diagnostic imaging method considered as the reference standard. The most common form of presentation is with fever and abdominal pain with a more or less marked elevation of inflammatory markers leading to a wide spectrum of differential diagnoses, particularly in immunosuppressed patients with kidney transplantation and including infectious processes related to the transplanted kidney, cysts of the non extracted native kidneys or the liver, and even, with an intraabdominal process not related to the ADPKD.\textsuperscript{1,2} The symptoms of infection of the renal or hepatic cysts are usually similar and simultaneous infection of both is not rare. It is difficult to determine the precise origin of the infection with ultrasonography, CT and MR, and these techniques do not always allow the differentiation of cyst infection from hemorrhage with an organized hematoma or pyelonephritis.\textsuperscript{3,4} Some anecdotal cases of an infected renal cyst with high signal intensity in diffusion-weighted MR imaging (DWI) have been described.\textsuperscript{5}

Most of the diseases causing fever of unknown origin (FUO) are due to infectious, tumoral or inflammatory processes. The $^{18}$F-FDG not only accumulates in the neoplastic tissue but also deposits in the foci of infection and inflammation as well as in the lesions related to autoimmune and granulomatous diseases. The mecha-
nisms of $^{18}\text{F}-\text{FDG}$ uptake in these non tumoral processes is due to the overexpression of GLUT transporters, mainly GLUT 1 and GLUT 3, and the overproduction of glycolytic enzyme by the inflammatory cells. In an cost-effective analysis, about the use of $^{18}\text{F}-\text{FDG}$ PET/CT in the diagnosis of FUO Becerra Nakayo et al\textsuperscript{6} state than PET-CT may be cost-effective in the diagnostic process of FUO, particularly if used early since it shortens the time to establish a diagnosis, reduces the days of hospitalization due to delays in the diagnostic tests and avoids other types of studies. Kaim et al.\textsuperscript{7} were the first to describe the diagnosis and localization of an infected renal cyst by $^{18}\text{F}-\text{FDG}$ PET-CT in a patient with ADPKD, thereby allowing percutaneous puncture of the cyst. In the last years clinical cases or short series have been published on patients with ADPKD and infection of some of the hepatic or renal cysts diagnosed with $^{18}\text{F}-\text{FDG}$ PET-CT\textsuperscript{8–10} All the authors coincide in the superiority of $^{18}\text{F}-\text{FDG}$ PET-CT versus conventional imaging techniques and even studies with $^{67}\text{Ga}$ citrate\textsuperscript{8} or labeled leukocytes. $^{18}\text{F}-\text{FDG}$ PET-CT study allows identification of the infected cyst, the precise anatomical hepatic or renal localization and, on occasion, diagnosis of the abdominal tumoral process causing the symptoms of the patient.

Sallée et al.\textsuperscript{3} described the episodes related to cyst infection in 398 patients with ADPKD over a period of 11 years. According to these authors, cyst infections are relatively infrequent, with an incidence of 0.01 episodes per patient and year and are the cause of 10% of hospital admissions. Renal cyst infection is most frequent than liver cyst infection and radiological studies are frequently of scarce diagnostic aid. Based on the results obtained, $^{18}\text{F}-\text{FDG}$ PET-CT is considered a first line tool for the diagnosis of cyst infections. The antibiotic association is the treatment of choice and infected cysts of more than 5 cm in diameter, particularly those localized in the liver, requiring drainage together with antibiotic treatment.

In our patient with ADPKD with repeated bacteremias of unknown origin and inconclusive radiologic results, the $^{18}\text{F}-\text{FDG}$ PET-CT study allowed confirmation of clinical suspicion of infection, determination of the precise anatomical site of the infected hepatic cysts and oriented the percutaneous drainage. The PET-CT performed upon readmission for the reappearance of a febrile picture demonstrated normalization of the previous metabolic alterations detected in the liver, although a new infected cyst was located in the left hepatic lobe. In contrast with what occurs in the field of oncology, which has well defined criteria for the evaluation of tumoral response to chemotherapy and/or radiotherapy with $^{18}\text{F}-\text{FDG}$ PET-CT, in infectious processes there are no established standardized criteria of metabolic response to treatment. Piccoli et al.\textsuperscript{9} have suggested the use of $^{18}\text{F}-\text{FDG}$ PET-CT to modulate the duration of antibiotic treatment in patients with ADPKD and infected renal cysts.

In conclusion, we consider that, in view of the literature reviewed and the results obtained in the present case, $^{18}\text{F}-\text{FDG}$ PET-CT studies should be included in the diagnostic algorithm for the detection of infected hepatic cysts in patients with ADPKD and FUO. Metabolic imaging may contribute to the resolution of old problems and provide answers to new questions which arise in both the diagnosis and specific treatment of infected cysts.

References