

PET/CT role in the diagnosis of infective endocarditis in patients with congenital heart disease[☆]



Papel de la PET/TC en el diagnóstico de endocarditis infecciosa en pacientes con cardiopatía congénita

Dear Editor:

Infectious endocarditis (IE) is a serious disease with a poor prognosis.¹ In developed countries, it occurs mainly in patients with congenital heart disease (CHD) requiring complex surgical procedures and placement of prostheses, among other factors.^{2,3}

The main challenge in the management of IE in patients with CHD is its detection, due to its nonspecific manifestations, the limitations of the modified Duke criteria, the high frequency of negative blood culture results and the low sensitivity of echocardiography, both transthoracic (TTE) and transoesophageal (TOE).^{2,4}

Recently, there has been an increase in the use of 18F-fluorodeoxyglucose (18F-FDG) positron-emission tomography/computed tomography (PET/CT) for diagnosis and follow-up of certain infectious diseases, including IE in patients with CHD.⁵

The aim of this article is to describe our experience in a department of paediatric cardiology with the use of PET/CT in the diagnosis and follow-up of IE in children with surgically corrected CHD.

Case 1. Girl aged 4 years that had underwent the Rastelli procedure and implantation of a bovine jugular vein (BJV) graft. She developed sepsis caused by *Staphylococcus aureus* with evidence of a pulmonary lesion in the conventional CT scan, which was interpreted as necrotic pneumonia. The PET/CT scan detected hypermetabolic activity in the pulmonary artery graft (Fig. 1). After treatment, the patient developed symptoms again; the blood culture results were negative, but since the follow-up PET/CT scan revealed abnormalities, the final diagnosis was IE relapse, and stepwise treatment proved effective.

Case 2. Boy aged 5 years treated with the Rastelli procedure and a BJV graft. The patient presented with persistent fever, with no features of IE in the echocardiogram. The PET/CT scan detected hypermetabolic activity in the BJV graft, which worsened despite adequate treatment and required surgical replacement of the conduit.

Case 3. Boy aged 8 years operated of tetralogy of Fallot who required percutaneous stent implantation. The patient developed febrile episodes with negative blood cultures and inconclusive findings in the echocardiogram; the PET/CT scan evinced accumulation of 18F-FDG in the stent area. The patient had an optimal outcome after antibiotherapy.

Case 4. Patient operated of truncus arteriosus type 1. He had episodes of high fever and positive blood culture results and a pedunculated lesion in the conventional CT scan in the area of the BJV graft. The PET/CT scan found tracer uptake in the area, but also a peripheral pulmonary lesion secondary to embolism that had not been detected in the conventional CT scan. After appropriate antibiotherapy, the imaging features of inflammatory activity disappeared (Table 1).

Since PET/CT offers a high sensitivity (91%) and specificity (97%) in the diagnosis of IE in valve prostheses and intracardiac devices, it is particularly useful in paediatric patients with CHDs in who both anatomical complexity and the presence of cardiac grafts complicate and often delay the diagnosis of IE.¹

It is particularly important to interpret PET/CT findings cautiously in patients that have recently undergone heart surgery, as postoperative inflammation at the surgical site can result in nonspecific uptake of 18F-FDG. Other pathological conditions that may mimic the pattern of focal increased 18F-FDG uptake are active thrombi, soft plaque atherosclerosis, vasculitis, primary cardiac tumours, cardiac metastases and foreign body reactions.²

Although the number of patients in the case series was limited, the use of PET/CT in these cases was essential for diagnosis, making evident its value by decreasing the frequency of missed diagnosis of IE: 3 of the 4 cases, initially classified as "possible" applying the Duke criteria, were reclassified to "definite", and the fourth one, in which IE was initially "rejected", was reclassified as "possible".⁴ In addition, the PET/CT scan detected septic pulmonary emboli in 2 of the patients, something that was only possible thanks to the use of this technique. Although the prognosis of IE is poor, its early detection with the use of PET/CT identification allowed correct management that achieved favourable outcomes in every patient. We ought to highlight that in these 4 patients with right-sided IE, the infection was found in the BJV conduit, an aspect that was consistent with the previous literature.³ The mechanisms involved in the increased incidence of endocarditis in these grafts could be related to late tissue degeneration, turbulent flow, increased thrombogenicity or an intrinsic increased susceptibility of these conduits to infection.³

In this article, we share evidence that supports the importance of this imaging technique in the diagnosis of IE in patients with CHD. We believe that in the field of paediatric cardiology, PET/CT is a reliable technique to rule out or confirm IE, detect foci of septic embolism and assess the response to antibiotherapy.

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Table 1 Main clinical data.

Case	Sex	CC	Age at surgical correction	Procedure	Stents/age	Blood culture	TTE/TOE	Initial diagnosis of IE	IE after PET/CT
1	F	D-TGA, VSD, PS	20m	Rastelli, pulmonary BJV graft	Ductal/1 m	<i>S. aureus</i>	Negative	Possible: BC major criterion + fever	Definite
2	M	LVOTO, HAA, CoA	9m	Rastelli, pulmonary BJV graft	Aortic/3 m LPAB/8 m RPAB /14 m	<i>S. con-</i> <i>stellatus</i>	Thickened BJV graft	Possible: BC minor criterion + fever	Definite
3	M	Tetralogy of Fallot	8m	VSD closure, transannular patch	LPAB /4 y 8 m	Negative	Negative	Rejected but strongly suspected: fever	Possible
4	M	CAT 1	4m	VSD closure, pulmonary BJV graft	RPAB /7 y 11 m None	<i>S. epi-</i> <i>dermidis</i>	Thickened BJV graft	Possible: BC minor criterion + fever	Definite

BC, blood culture; BJV, bovine jugular vein; CAT 1, common arterial trunk type 1; CHD, congenital heart disease; CoA, coarctation of the aorta; D-TGA, dextro-transposition of the great arteries; F, female; HAA, hypoplastic aortic arch; IE, infectious endocarditis; LPAB, left pulmonary artery branch; LVOTO, left ventricular outflow tract obstruction; m, months; M, male; PS, pulmonary stenosis; RPAB, right pulmonary artery branch; TTE/TOE, transthoracic/transoesophageal echocardiography; VSD, ventricular septal defect; y, years.

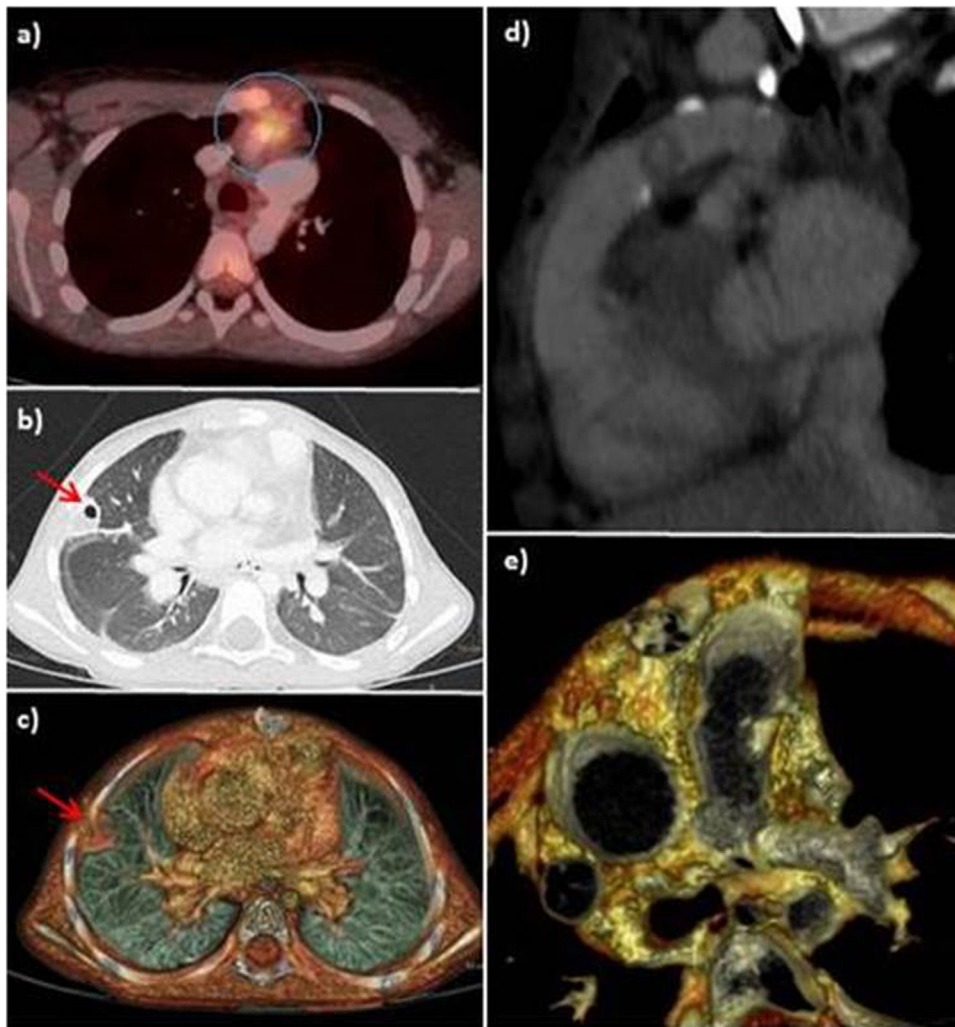


Figure 1 (a) Axial PET/CT image showing focal FDG uptake in the pulmonary graft (circle). (b) Chest CT, lung window. (c) 3D volume rendering image showing a peripheral cavitory lesion (red arrow) in the upper right lobe. (d) and (e) The retrospective interpretation of the CT scan revealed a nodular lesion suggestive of a thrombus/vegetation in the lumen of the pulmonary conduit.

References

1. Aguadé Bruix S, Roque Pérez A, Cuéllar Calabria H, Pizzi MN. Cardiac-18/F-FDG PET/CT procedure for the diagnosis of prosthetic endocarditis and intracardiac devices. *Rev Esp Med Nucl Imagen Mol.* 2018;37:163–71, <http://dx.doi.org/10.1016/j.remnm.2018.01.002>. English, Spanish. Epub 2018 February 26. PMID: 29496402.
2. Chau A, Renella P, Arrieta A. Multimodality cardiovascular imaging in the diagnosis and management of prosthetic valve infective endocarditis in children: report of two cases and brief review of the literature. *Cardiol Young.* 2019;29:1526–9, <http://dx.doi.org/10.1017/S1047951119002233>. Epub Oct 8 October 2019. PMID: 31590699.
3. Mery CM, Guzmán-Pruneda FA, De León LE, Zhang W, Terwelp MD, Bocchini CE, et al. Risk factors for development of endocarditis and reintervention in patients undergoing right ventricle to pulmonary artery valved conduit placement. *J Thorac Cardiovasc Surg.* 2016;151:432–9, <http://dx.doi.org/10.1016/j.jtcvs.2015.10.069>, 441.e1-2 Epub 2015 October 27. PMID: 26670191.
4. Pizzi MN, Dos-Subirà L, Roque A, Fernández-Hidalgo N, Cuéllar-Calabria H, Pijuan Domènech A, et al. 18/F-FDG-PET/CT angiography in the diagnosis of infective endocarditis and cardiac device infection in adult patients with congenital heart disease and prosthetic material. *Int J Cardiol.* 2017;248:396–402, <http://dx.doi.org/10.1016/j.ijcard.2017.08.008>. Epub 2017 August 9. PMID: 28807509.
5. Meyer Z, Fischer M, Koerfer J, Laser KT, Kececioglu D, Burchert W, et al. The role of FDG-PET-CT in pediatric cardiac patients and patients with congenital heart defects. *Int J Cardiol.* 2016;220:656–60, <http://dx.doi.org/10.1016/j.ijcard.2016.06.109>. Epub 2016 June 23. PMID: 27393845.

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Asymptomatic hyperkalemia as a form of presentation of pseudohypoaldosteronism☆☆☆



Hiperpotasemia asintomática como forma de presentación de pseudohipoaldosteronismo

Dear Editor:

In the paediatric age group, hyperkalaemia tends to be asymptomatic, so serum potassium levels greater than 5.5 mEq/L should be verified and investigated, as they may be indicative of potentially severe diseases, as occurred in the case presented here.¹

The patient was a boy aged 5 years with a personal history of obesity and type 1 diabetes in whom a blood chemistry panel ordered during a check up revealed a serum potassium level of 6.8 mEq/L in absence of other electrolyte abnormalities. A second test confirmed the finding of hyperkalaemia. Previous blood tests have not found abnormal levels of this ion, and the patient had been asymptomatic at all times.

The assessment was completed with measurement of the arterial blood pressure, which yielded values in the normal range for age and sex. The patient underwent an electrocardiogram that did not evince any abnormalities, as well as venous blood gas analysis that revealed mild metabolic acidosis with a pH of 7.29, a carbon dioxide pressure (pCO₂) of 39.3 mmHg, a serum bicarbonate level of 18.2 mEq/L and an excess base of -2.3 mmol/L. We measured basal levels of aldosterone, renin, cortisol and adrenocorticotropic hormone (ACTH), which were normal. We expanded the work up with analysis of a urine sample to calculate the transtubular potassium gradient, which was of 1.8 (normal range, 4–7), which suggested deficient renal secretion of this ion with preserved renal function and a

high calcium/creatinine ratio of 0.4 mg/mg (normal range, <0.2 mg/mg).

Retaking the family history revealed that the father had a history of long-term high blood pressure, muscle weakness, calcium renal lithiasis and episodes of atrial fibrillation in the past decade. Both the father and the paternal grandfather (who had died of cancer) had elevated potassium levels in multiple blood tests.

Since the family history and tests performed to date suggested a hereditary aetiology of hyperkalaemia, we approached the illness as a possible case of pseudohypoaldosteronism type II and ordered genetic testing for this syndrome, which confirmed the suspected diagnosis with the detection of a heterozygous change in the *KLHL3* gene in both the patient and his father.

Following the diagnosis of pseudohypoaldosteronism type II, despite remaining completely asymptomatic, the patient started treatment with oral hydrochlorothiazide at a dose of 1 mg/kg/day, which achieved normalization of serum levels of potassium and renal calcium excretion, with a favourable outcome thereafter.

In conclusion, if a paediatric patient has elevated potassium levels in 2 or more consecutive blood tests without an apparent cause, the clinician should initiate an aetiological diagnosis.

As Fig. 1 shows, to determine the aetiology of the hyperkalaemia, that the work up of these patients should include a urine test to calculate the transtubular potassium gradient and blood tests to measure the glomerular filtration rate and levels of renin, aldosterone, cortisol and ACTH.² If the transtubular potassium gradient is low (<4) and the glomerular filtration rate is normal, the decreased excretion of this ion by the kidney suggests a mineralocorticoid deficiency or resistance,^{2,3} and therefore, the presence of normal or slightly elevated levels of renin and aldosterone guides the diagnosis toward unresponsiveness or resistance to the action of aldosterone in target cells.⁴

Pseudohypoaldosteronism type II, also known as Gordon syndrome, is a rare disease characterised by hyperkalaemia, hypercalciuria and high blood pressure with preserved renal function and normal or slightly elevated levels of aldosterone and renin.^{2,3} More than 180 families affected by this disease have been reported to date, with a mean age at diagnosis of 26 ± 14 years.² It is produced by changes in the *WNK1*, *WNK4*, *CUL3* or *KLHL3* gene that affect the renal excretion of sodium and potassium.^{3,4} In most cases, the pattern of inheritance is autosomal dominant, although cases of autosomal recessive changes in the *KLHL3* gene have

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