ESC European Society of Cardiology
European Heart Journal - Case Reports
doi:10.1093/ehjcr/ytab159

CASE REPORT
Cardiac imaging

^{18}F-Fluorodeoxyglucose positron emission tomography/computed tomography as a diagnostic and follow-up tool in *Coxiella burnetii* endocarditis of prosthetic valve and aortic valved tube: a case report

Elisa Ricciardi [1*†], Alessandro Moscatelli [2], Marco Berruti[3], Maria Isabella Donegani[4], Malgorzata Karolina Mikulska[3], and Aldo Pende[1]

[1]Clinic of Emergency Medicine, University of Genoa, IRCCS Ospedale Policlinico San Martino, Genoa, Italy; [2]Division of Gastroenterology and Digestive Endoscopy, Hospital of Lavagna ASL4 Chiavarese, Lavagna, Italy; [3]Clinic of Infective Diseases, University of Genoa, IRCCS Ospedale Policlinico San Martino, Genoa, Italy; and [4]Division of Nuclear Medicine, University of Genoa, IRCCS Ospedale Policlinico San Martino, Genoa, Italy

Received 7 October 2020; first decision 26 October 2020; accepted 9 April 2021

Background European Society of Cardiology 2015 guidelines approved ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) as a useful diagnostic imaging technique in prosthetic valve endocarditis (PVE) and recent evidence seems to suggest a role of nuclear imaging in the follow-up of cardiovascular infections, but nowadays there are no sufficient data available.

Case summary A 67-year-old male presented with fever, weight loss, and fatigue. His medical history included ulcerative colitis and a previous Bentall-De Bono surgical procedure in 2014. A previous recent hospitalization to a small community hospital did not reveal a clear aetiology for the fever: transeosophageal echocardiography showed dubious peri-prosthetic tissue alterations, interpreted as post-surgical fibrosis; consequently, the patient was discharged with steroid therapy. At admission in our ward, we repeated transoesophageal echocardiography that confirmed the peri-prosthetic alterations. Moreover, ^{18}F-FDG PET/CT showed two hypermetabolic areas, one around the prosthetic tube in the aortic bulb and the other in relation with the prosthetic aortic valve. Serological test was positive for *Coxiella burnetii* infection with consequent beginning of a targeted antimicrobial therapy with oral doxicycline and hydroxychloroquine. Echocardiography, serology, and ^{18}F-FDG PET/CT follow-up demonstrated a progressive response to treatment and clinical conditions of the patient gradually improved.

Discussion According to guidelines, ^{18}F-FDG PET/CT can be used in ambiguous PVE to improve diagnostic accuracy of standard techniques. In this case, ^{18}F-FDG PET/CT combined with echocardiography and serological tests is used not only to better define diagnosis but also for treatment response monitoring during follow-up.

Keywords Case report • Infective endocarditis • Q fever • *Coxiella burnetii* • ^{18}F-FDG PET/CT • Aortic valved tube

* Corresponding author. Tel: 0183 537 923, Fax: 0183 536772, Email: ricciardielisa@virgilio.it
† Present address. Division of Cardiology, Hospital of Imperia ASL1, Imperia, Italy
Handling Editor: Harry Klimis
Peer-reviewers: Joseph Moutiris and Annagrazia Cecere
Compliance Editor: Edwina McNaughton
Supplementary Material Editor: Ross Thomas

Learning points

- Identification of the infective process can be sometimes challenging with gold standard imaging for prosthetic valve endocarditis (PVE).
- ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) in combination with specific serological tests is useful for Q fever PVE diagnosis.
- Increasing evidence suggests a possible role of ^{18}F-FDG PET/CT in follow-up, but lack of sufficient data cannot allow a general recommendation.

Introduction

Prosthetic valve endocarditis (PVE) and aortic graft infections (AGI) are complications of heart surgery accounting for 10–30% of all cases of infective endocarditis (IE).[1] In the European Society of Cardiology (ESC) 2015 guidelines ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) has been approved as diagnostic criterion in PVE.[2]

Recent literature has shown that pathological uptake detected with ^{18}F-FDG PET/CT significantly increases the diagnostic sensitivity of the modified Duke classification for PVE.[3] Positron emission tomography/computed tomography (PET/CT) is mostly important in those cases classified as 'possible IE', and it can also help for detection of peripheral emboli.[2,4] However, ^{18}F-FDG PET/CT can produce some false-positive or false-negative results,[4] and several issues still need to be clarified about its use in PVE. Firstly, other conditions can mimic the pattern of focally increased ^{18}F-FDG uptake that is typically observed in IE, such as vasculitis, cardiac tumours, or post-surgical inflammation.[2] Moreover, interpretation of the images can be both qualitative, with a visual discrimination between normal and pathological findings, and semi-quantitative, measuring metabolic activity of a lesion in the form of the standardized uptake value (SUV). However, current guidelines do not indicate an SUV cut-off level for considering 'pathological' findings. Similarly, the use of no-attenuation-corrected (NAC) images has been proposed as a tool to decide between real and artefactual FDG uptake,[5] but the exact diagnostic value of NAC images is still to be defined.

Herein, we describe a case of Q fever presenting as PVE and AGI using ^{18}F-FDG PET/CT as a relevant tool not only in the diagnostic process but also in the clinical follow-up.

Timeline

Date	Event
October 2018	Onset of symptoms: fever, fatigue, no other signs or symptoms associated Empiric antimicrobial therapy with amoxicillin/clavulanate without benefit
November 2018	Colonoscopy with biopsy excluded ulcerative colitis exacerbation
December 2018	Admission to a small community hospital
	Laboratory tests: only increased C-reactive protein values
	Blood cultures: negative
	Physical examination: no relevant findings, normal vital parameters
	Computed tomography scan: negative for significant findings
	Transoesophageal echocardiography (TEE): hyperechoic material around the aortic valve and the valved tube
	Discharge diagnosis: post-surgical fibrosis, steroid treatment
February 2019	Admission to our hospital
	Laboratory tests: only increased C-reactive protein values
	Blood cultures and common serological tests: negative
	TEE: confirmation of peri-prosthetic tissue alterations of unclear interpretation (10 mm)
	First ^{18}F-FDG PET/CT: two hypermetabolic areas, one around the prosthetic tube in the aortic bulb, and the other in relation with the prosthetic aortic valve Started empiric treatment with daptomycin
March 2019	National Institute for Infective Diseases 'Lazzaro Spallanzani' (Rome, Italy) communicated positive serology for *Coxiella burnetii*; therapy switched to oral doxycycline
April 2019	Second ^{18}F-FDG PET/CT: significant reduction of the standardized uptake value level and the inflammatory extension in comparison to the previous exam
	Cardiac surgery evaluation: continuing oral antimicrobial therapy, unless new clinical exacerbation, therapy failure, or antimicrobial therapy intolerance
	Second TEE: significant reduction of the isoechoic peri-prosthetic material (4 mm). Discharge home and continuing antimicrobial therapy
May 2019	First follow-up visit: improvement in clinical conditions and C-reactive protein values
	Third TEE: new significant reduction of the space between the native vessel and the prosthetic tube (2 mm)
	Third ^{18}F-FDG PET/CT: findings reduced as for extension and metabolic uptake compared to the previous exam in April 2019
June 2019	Second follow-up visit: good general conditions, no fever, increase in bodyweight
June 2020	Stable good general conditions, continuing medical therapy with good tolerance

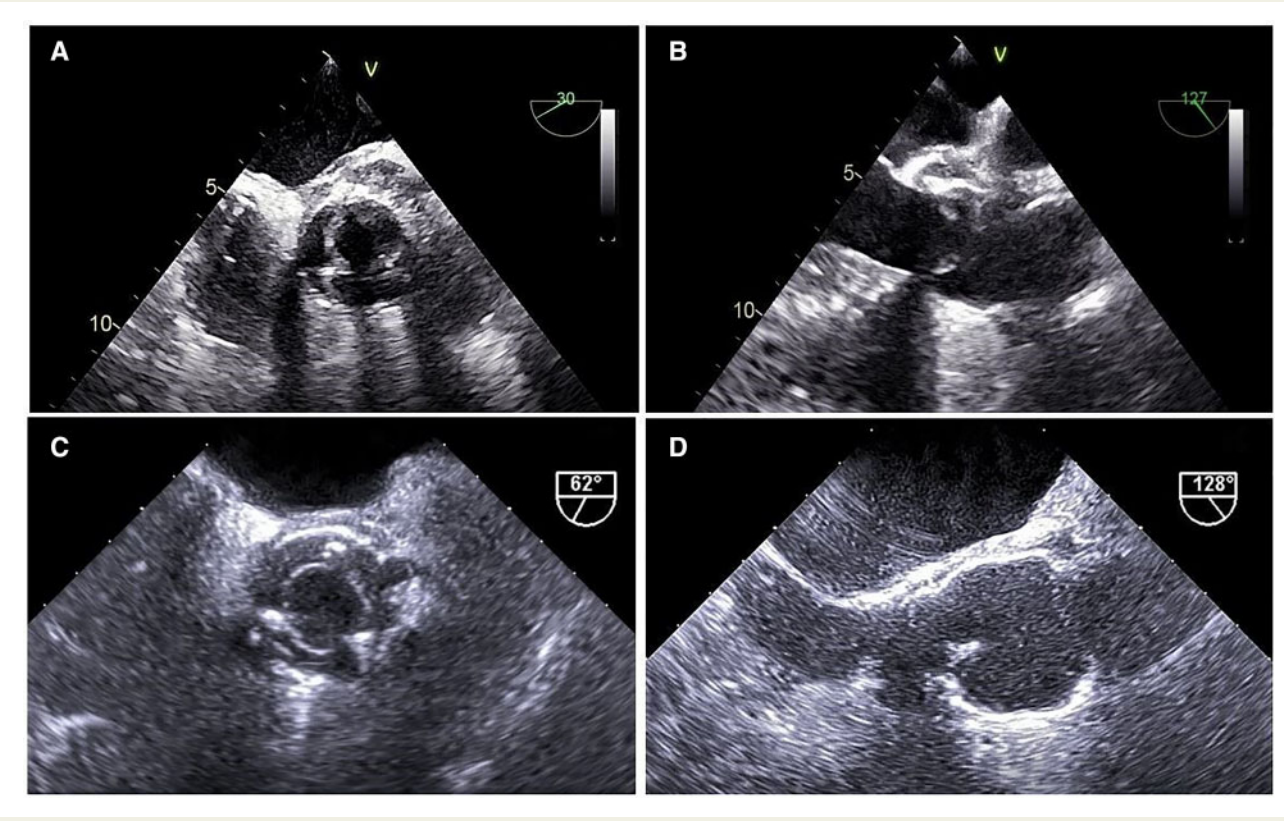

Figure 1 Transoesophageal echocardiography images. (*A*) and (*B*) show first exam performed in February 2019: echoic irregular material occupy the space between the native vessel, the prosthetic valve, and the aortic tube; (*C*) and (*D*) are images from follow-up exam on May 2019.

Case presentation

A 67-year-old Caucasian male presented with a 4-month history of fever, weight loss, and fatigue. The patient had a history of ulcerative colitis (UC) on azathioprine (100 mg q.d.) and previous Bentall–De Bono surgical procedure in 2014; he also had cardiac resynchronization therapy defibrillator.

The onset of fever was in October 2018 and antibiotic therapy with amoxicillin/clavulanate did not improve the clinical condition; a colonoscopy excluded UC exacerbation.

Two months later, the patient was admitted to a small hospital; a transoesophageal echocardiography (TEE) was performed, showing hyperechoic material around the aortic valve and the valved tube, findings interpreted as post-surgical fibrosis.

Upon arrival at our ward (February 2019), the patient presented with the same symptoms; on physical examination, he had a mild systolic murmur on auscultation, no significant thoracic or abdominal signs; blood pressure was 125/75 mmHg, oxygen saturation was 98%, heart rate was 86 b.p.m.

Laboratory tests revealed only mild inflammation, all the collected blood cultures or markers of infections were negative (toxoplasmosis, syphilis, brucellosis, Mycobacterium Tubercolosis, β-D-glucan, gactomannan, urinary pneumococcical, and legionella antigens); we also ruled out viral infections (human immunodeficency test, Herpes Simplex virus, Cytomegalovirus, Epstein Barr Virus) or autoimmune diseases.

Transoesophageal echocardiography confirmed peri-prosthetic tissue changes: the space between the native vessel and the prosthetic valve and the aortic tube was occupied by echoic irregular material (10 mm of thickness), but ultrasound could not discriminate between septic or post-surgery material (*Figure 1A* and *B*).

According to Duke's criteria, the patient had one minor criteria in keeping with possible IE, so we performed an ^{18}F-FDG PET/CT scan, which showed two hypermetabolic areas, one around the prosthetic tube in the aortic bulb, 8 SUV, and the other in relation with the prosthetic aortic valve, 6.9 SUV (*Figure 2*).

Empirical treatment was commenced with daptomycin (750 mg q.d.). After several weeks, a serological test performed was positive for *Coxiella burnetii* (IgM phase I 1:1024, IgM phase II > 1:256, IgG phase I > 1024, IgG phase II > 1:1024), and consequently, the diagnosis of Q fever endocarditis was made.

The patient was moved to the Clinic of Infective Diseases to continue treatment with doxycycline (100 mg b.i.d.), and hydroxychloroquine (200 mg q.d.): rapid resolution of the fever was observed.

Two months later on TEE, the space between the native vessel and the prosthetic valve and aortic tube was occupied by isoechoic material, 4 mm of thickness, significantly reduced compared to the previous exam. ^{18}F-FDG PET/CT showed persistence of the infectious process around the prosthetic valve and the valved tube, but SUV (4.8) and inflammatory extension were reduced (*Figure 3*).

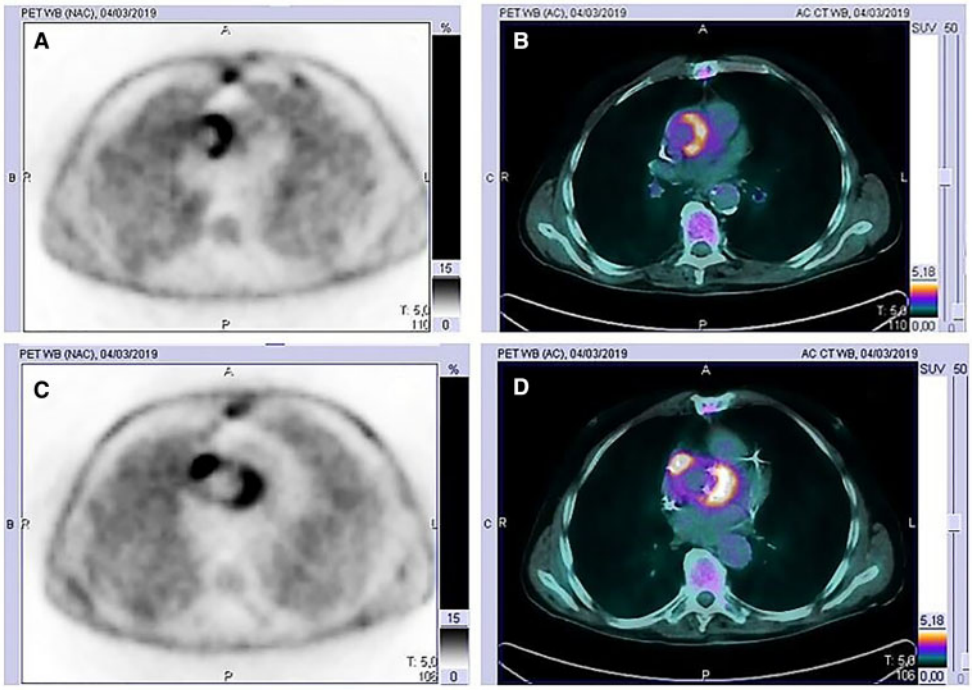

Figure 2 Basal ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography scan with corresponding no-attenuation-corrected images; (*A*) and (*B*) show the hypermetabolic area around the prosthetic tube in the aortic bulb (8 standardized uptake value); (*C*) and (*D*) show the hypermetabolic area in relation with the prosthetic aortic valve (6.9 standardized uptake value).

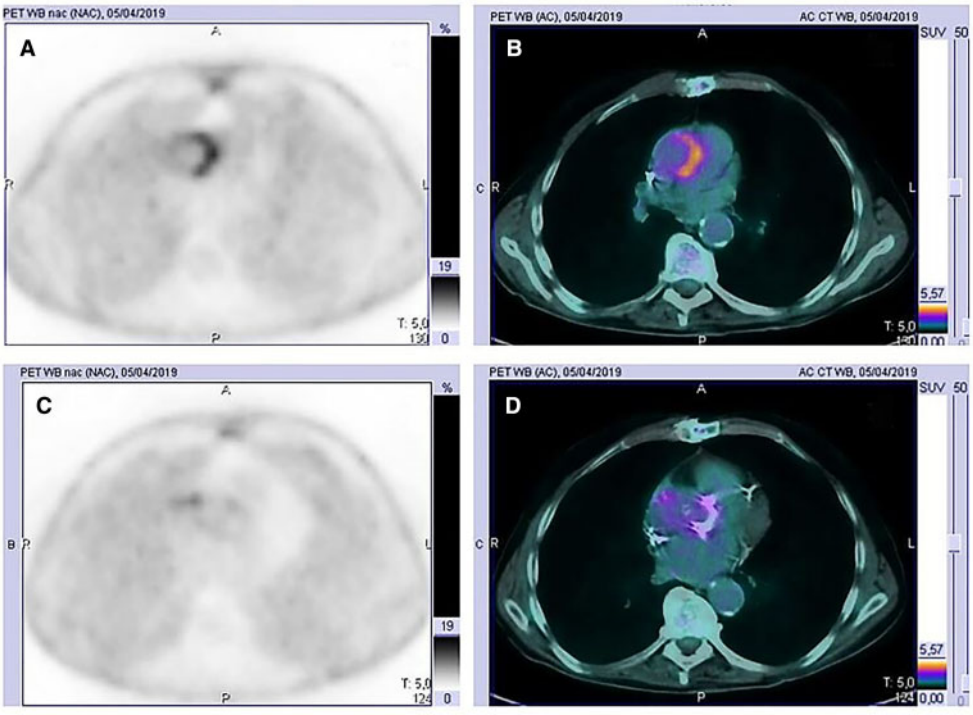

Figure 3 Second ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography scan with no-attenuation-corrected images (April 2019) showing a significant decrease of the inflammatory process. (*A*) and (*B*) are related to the prosthetic valved tube, (*C*) and (*D*) to the prosthetic aortic valve.

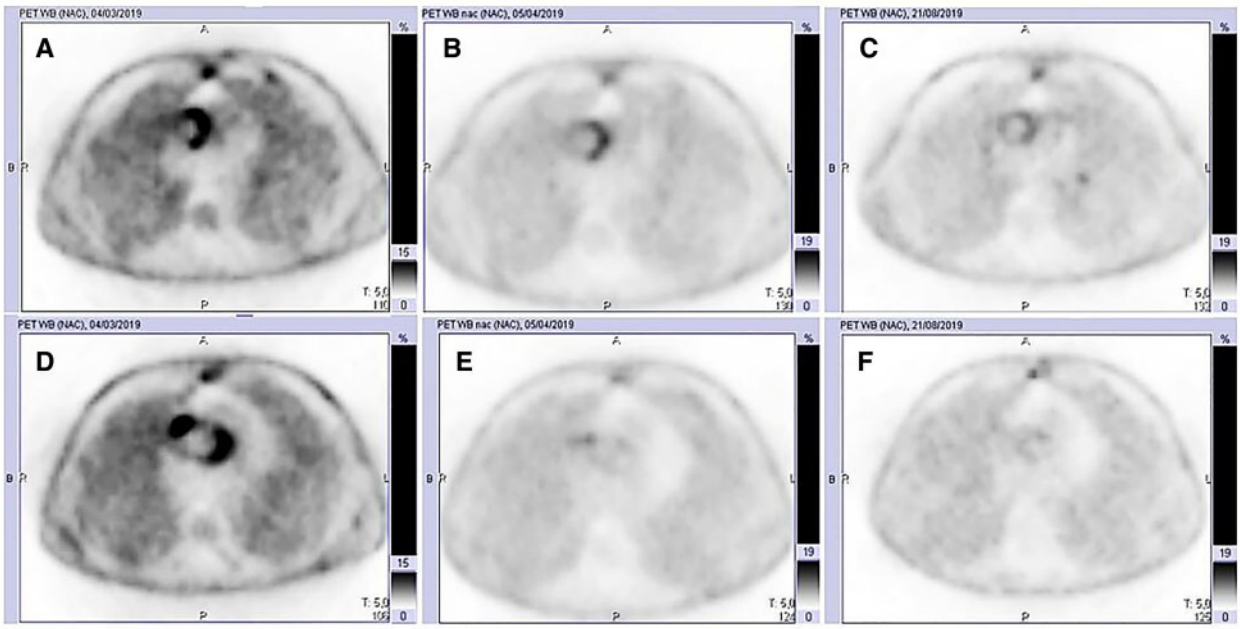

Figure 4 No-attenuation-corrected images in sequence, showing the good response to treatment from the basal scan—(*A*) and (*D*)—to an intermediate one—(*B*) and (*E*)—and to the last one—(*C*) and (*F*). (*A*), (*B*), and (*C*) are related to the valved aortic tube; (*D*), (*E*), and (*F*) refer to the aortic prosthetic valve.

After 1 month of therapy, in agreement with heart surgeons, the patient was discharged in good general conditions. We opted for a follow-up strategy based on clinical/laboratory response, using TEE and ^{18}F-FDG PET/CT for imaging control.

In the first visit one month later, he reported good general condition and therapy was well tolerated. On TEE, the space between the native vessel and the prosthetic tube was 2 mm, a further significant reduction (*Figure 1C* and *D*). ^{18}F-FDG PET/CT demonstrated persistence of non-homogeneous uptake at the aortic bulb (SUV 3) and at the proximal portion of the aortic arch (SUV 2). At the prosthetic aortic valve plane, radiotracer accumulation persisted below the diagnostic significance level (*Figure 4*).

Stable health conditions were maintained until today.

Discussion

Coxiella burnetii infection is very rare in Italy, with only three cases of confirmed Q fever from 2012 to 2016.[6] The most common form of chronic Q fever is endocarditis, which represents 60–70% of cases, and typically develops in patients with predisposing conditions, such as heart valve disease and immunosuppression.[7] Patients with prosthetic valves or intracardiac devices account for around 20% of all cases of IE, and in this special population, echocardiography imaging can be a real challenge.

Both American Heart Association and ESC guidelines for IE management proposed new diagnostic imaging techniques, such as ^{18}F-FDG PET/CT, to improve diagnostic accuracy in complicated cases of IE.[8]

The role of this method in the follow-up of IE has not been well defined yet. Some authors tried to use ^{18}F-FDG PET/CT not only for the diagnostic process but also in the management of the follow-up, for example as a tool to decide on antibiotic suspension.[9] However, the risk of false-positive findings should be carefully considered. In particular, in recently operated patients, structural and metabolic changes attributable to postoperative inflammation might generate false-positive results. A recent study tried to prospectively define the anatomic changes and metabolic patterns associated with postoperative reactive inflammation and their evolution over time, based on the serial cardiac PET/CT scans performed on postoperative patients without suspected infections.[10] In this study, FDG uptake in the prosthetic/periprosthetic area was visually detected in 79.3% of the performed scans and, more importantly, its uptake intensity and distribution pattern remained stable during the 1st year after surgery. Although a clear SUV cut-off value providing a differential diagnosis between PVE and postoperative aseptic inflammation is currently lacking, this study showed that the most detectable pattern was a diffuse and homogeneous distribution with mild uptake values that seems to be the characteristic pattern of postoperative reactive inflammation. In contrast, PVE showed much higher SUV levels and a focal uptake pattern. The present case report is in line with these findings and suggests that the FDG signal might guide the clinical monitoring and the antibiotic therapy discontinuation in the follow-up.

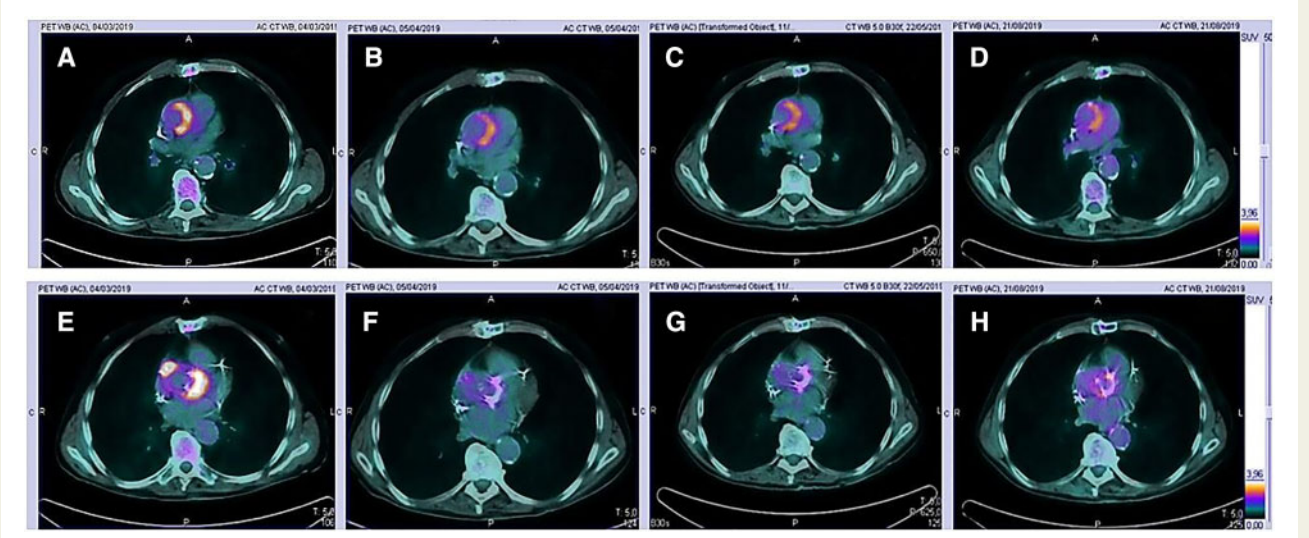

Figure 5 Sequence of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography scan images, summarizing follow-up controls and showing progressive resolution of infective endocarditis. Images from (*A*) to (*D*) are related to the valved aortic tube, images from (*E*) to (*H*) show the aortic prosthetic valve.

Conclusion

We reported a case of IE caused by *C. burnetii* infection in which a definite diagnosis was reached only using ^{18}F-FDG PET/CT as a support for TEE findings.

One of the most interesting aspects of this case is the role that 18 85 F-FDG PET/CT played during follow-up (*Figure 5*). Therefore, there is an increasing need for further clinical studies and evidence to better define recommendations about ^{18}F-FDG PET/CT use in IE.

Lead author biography

Elisa Ricciardi graduated in 2013 at University of Genoa (Italy). She was a resident physician at the University of Genoa until 2019. Her particular areas of interest are heart failure and arrhythmias. Recently, she carried out an observational study about clinical characteristics and differences among heart failure patients with a collaboration between Cardiologists and Internal Medicine physicians. At present, she works as Cardiologist at the Cardiology Division of Imperia's Hospital (Italy) and is an ordinary member of Italian Society of Cardiology.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

Funding: Work performed at IRCCS Ospedale Policlinico San Martino, Genoa, Italy.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

References

1. Habib G, Thuny F, Avierinos JF. Prosthetic valve endocarditis: current approach and therapeutic options. *Prog Cardiovasc Dis* 2008;**50**:274–281.
2. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F *et al.* 2015 ESC guidelines for the management of infective endocarditis. *Eur Heart J* 2015;**36**:3075–3128.
3. Saby L, Laas O, Habib G, Cammilleri S, Mancini J, Tessonnier L *et al.* Positron emission tomography/computed tomography for diagnosis of prosthetic valve endocarditis: increased valvular ^{18}F-fluorodeoxyglucose uptake as a novel major criterion. *J Am Coll Cardiol* 2013;**61**:2374–2382.
4. Nuvoli S, Fiore V, Babudieri S, Galassi S, Bagella P, Solinas P *et al.* The additional role of ^{18}F-FDG PET/CT in prosthetic valve endocarditis. *Eur Rev Med Pharmacol*

Sci 2018;**22**:1744–1751.
5. Joshi U, Raijmakers PG, Riphagen II, Teule GJ, Van Lingen A, Hoekstra OS. Attenuation-corrected vs. nonattenuation-corrected 2-deoxy-2-[F-18] fluoro-D-glucose-positron emission tomography in oncology: a systematic review. *Mol Imaging Biol* 2007;**9**:99–105.
6. European Centre for Disease Prevention and Control. Q fever. In: ECDC. *Annual Epidemiological Report for 2016*. Stockholm: ECDC; 2019; 6.
7. Parker NR, Barralet JH, Morton Bell A. Q fever. *Lancet* 2006;**367**: 679–688.
8. Hohmann C, Michels G, Schmidt M, Pfister R, Mader N, Ohler M *et al.* Diagnostic challenges in infective endocarditis: is PET/CT the solution? *Infection* 2019;**47**:579–587.
9. Kouijzer IJE, Kampschreur LM, Wever PC, Hoekstra C, Van Kasteren MEE, De Jager-Leclercq MGL *et al.* The value of ^{18}F-FDG PET/CT in diagnosis and during follow-up in 273 patients with chronic Q Fever. *J Nucl Med* 2018;**59**:127–133.
10. Roque A, Pizzi MN, Fernández-Hidalgo N, Permanyer E, Cuellar-Calabria H, Romero-Farina G *et al.* Morpho-metabolic post-surgical patterns of non-infected prosthetic heart valves by [^{18}F]FDG PET/CTA: "normality" is a possible diagnosis. *Eur Heart J Cardiovasc Imaging* 2020;**21**:24–33.