

Unused Arteriovenous Grafts as a Source of Chronic Infection in Haemodialysed Patients with Relevance to Diagnosis of Fluorodeoxyglucose PET/CT Examination

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Abstract

Introduction: Clotted arteriovenous grafts (AVG) for haemodialysis which are not used (silent grafts) can serve as a potential source of chronic bacterial infection in patients on dialysis programs. In some cases, the local finding is unclear. The patient only suffers from repeated metastatic infection and the detection of AVG infection is difficult. Nuclear medicine methods have the potential to uncover AVG infection. In this study, we correlated the positron emission tomography (PET)/ computed tomography (CT) findings of the AVG examination with the microbiological findings from removed grafts. The aim was to evaluate the relevance of the Fluorodeoxyglucose (FDG) PET/CT method in detecting clotted graft infection. **Material and Methods:** A cohort of 13 patients with clotted grafts were followed-up. Four patients had overall symptoms of infection and 9 patients were asymptomatic. In all cases, the PET CT examination and microbiological examination of the removed graft were provided. **Results:** Only one mismatch—negative PET CT finding and positive microbiological culture was recorded in the 13 followed-up patients. **Conclusion:** In patients with silent grafts and recurrent infection of equivocal aetiology, PET CT examination can contribute to the diagnosis of AVG infection and, subsequently, to prevent further infectious complications, if the AVG infection is treated appropriately and the graft is removed.

Ann Acad Med Singapore 2012;41:335-8

Key words: ePTFE prosthesis, Nuclear medicine imaging, *Staphylococcus aureus*, Vascular access infection

Introduction

As a primary dialysis access, autologous, arteriovenous fistulas (AVF) is recommended in Europe and in North America.¹⁻³ In patients who lack a suitable autologous subcutaneous venous circulation for AVF creation, an arteriovenous graft (AVG) is inserted between arterial and venous bed and serves as a cannulation segment. There are a variety of AVG modifications in terms of localisation, width and quality of wall. The ePTFE prosthesis is considered a golden standard in term of material.^{2,4} Its use however is associated with complications: stenotic and thrombotic complications on the venous anastomoses and on the cannulation side are the most common.⁵ Another serious complication is AVG infection which can lead not only to graft loss but also to metastatic infectious complications and sepsis.^{6,7}

If graft patency is lost due to stenotic or thrombotic complication that cannot be resolved with surgical or

endovascular treatment, the graft is usually left in the subcutis and a new dialysis access is created: an AVG in another localisation, or central venous cannulation. Many haemodialysis patients thus, have one or more old clotted grafts in their extremities. The clotted graft, even if not used, can serve as a source of bacterial infection that can lead to further infectious complications.⁸

The clinical finding of infected graft is apparent particularly if still used: redness above the graft, skin warmth and infiltration, fluctuation or secretion from cannulation side can occur. The local finding is accompanied by overall symptoms of infection.

The clotted graft is overlooked as a potential source of infection when the local finding is unclear. The patient is merely subfebrile and often suffers only from repeated metastatic infection. Since it is not simple to prove AVG infection, the decision to remove the prosthesis is difficult. Elevated CRP and leucocyte level can be present but

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haemocultures are often negative. Ultrasound examination of the graft is not significant. The following nuclear medicine methods are recommended for diagnosis statement—Indium labelled leucocyte scanning or FDG PET/CT.^{9,10}

In the current literature, we found one publication that evaluated the correlation between PET CT and microbiological findings from removed graft in one patient who had clinical symptomatology of infection.¹⁰

The aim of our study was to evaluate the relevance of the FDG PET/CT method in clotted graft examination. AVG with symptoms of infection as well as AVG with negative clinical findings were evaluated.

Materials and Methods

Between 2001 and 2010, we had created 214 AVG for haemodialysis. In our clinic, AVG creation is indicated after autologous venous bed exhaustion. Thirteen clotted AVG were followed up. AVGs were non-functional for at least 6 months. In the follow-up, 6 patients underwent renal transplantation, 5 patients were dialysed through central venous catheter and in 6 patients, AVG on the contralateral extremity or colar arteriovenous fistula was created. In all cases, the new haemodialysis access was apparently uninfected. All patients were examined for C-reactive protein (CRP) and leucocyte level, and haemocultures were also done. Four patients were suspected of AVG infection due to subfebrile body temperature, recurrent pneumonia and joint inflammation. These patients had positive haemoculture. In the remaining 9 patients, there was no clinical symptomatology of AVG infection. In 2 patients, CRP was elevated to 20 mg/L. Haemoculture was not done or was negative. No explanation for the CRP elevation was found from clinical examination. In all cases, ultrasound examination was performed without any pathological finding. Leucocyte level evaluation either was not significant due to immunosuppression in transplant patients or was not elevated.

All AVG were examined with PET/CT. Contrast-enhanced 18F-FDG PET/CT images were acquired using a scanner Biograph 16 HI-REZ (Siemens Medical Systems). Patients fasted at least 6 hours before the PET/CT examination, and the blood glucose level was less than 10 mmol/L in all patients. 18F-FDG (400 MBq/70 kg of body weight) was injected intravenously, and subjects rested in a quiet room for 60 minutes. PET acquisition was then performed over 30 minutes (3D mode, bed positions of 4 minutes each). Attenuation weighted ordered-subset maximisation expectation reconstruction (8 subsets, 4 iterations, 5 mm Gauss filter, zoom 1, scatter correction, matrix 168x168) was performed using CT for localisation and attenuation correction of PET data. The acquisition parameters for contrast-enhanced CT were 120 kV, quality reference

mAs 130 (controlled by CARE Dose 4D), slice thickness 16 x 1.5 mm). The contrast media (Ultravist 370, Bayer Schering Pharma AG) was injected with an automatic injector (Stellant, MedRAD), with an injection rate of 3 mL/s. Transaxial CT slices with a 3-mm slice thickness and 1.5 mm reconstruction increments were reconstructed. Images were simultaneously evaluated by an experienced nuclear medicine specialist and a radiologist. Scans were visually and semiquantitatively assessed for X-ray morphology and distribution of 18F-FDG uptake. Increased pathologic 18F-FDG uptake was classified as a diffuse, non-homogenous or focal accumulation. Areas with the maximal focal 18F-FDG uptake were detected, and the maximum standardised uptake value (SUVmax) in the prosthesis was obtained. SUV values were normalised to blood 18F-FDG activity by dividing the SUVmax by SUV of blood in abdominal aorta to produce a blood-corrected prosthesis SUVmax.

Results

Among these 13 patients, 4 patients had overall symptoms of infection, recurrent pneumonia or arthritis without any suspect local finding on the side of AVG. In 2 of them, there was positive haemoculture (*Staphylococcus aureus*) while there was negative haemoculture in the other 2. All 4 patients had CRP elevation. The remaining 9 patients were asymptomatic without any signs of local or overall infection of AVG. Laboratory parameters were within normal limits but CRP was slightly increased in 2 patients.

Surgical Treatment

In all patients, the graft was removed under general anaesthesia and the anastomoses were treated. Prior to procedure, all patients without any local finding on AVG have been informed in details about all aspects of the procedure and have signed an informed consent. The original venous anastomosis was oversewn with continuous prolene sutures. Arterial anastomosis was primarily treated in 8 cases, autologous venous patch for arterial closure was used in 2 cases, in 3 cases resection of artery and venous interposition was performed. There were no surgical complications associated with graft removal. Wounds healed per primam intentionem.

Microbiological Examination

All removed grafts were microbiologically examined (cultures and bacterial sensitivity tests). Four patients with positive clinical findings and positive PET CT finding also had positive microbiological findings (*Staphylococcus aureus* in 3 cases, *Staphylococcus epidermidis* in 1 case). Microbiological findings from removed graft and

haemoculture were identical. Patients with negative clinical findings, CRP elevation and positive PET CT findings (2 cases) also had positive microbiological findings (*Staphylococcus aureus*). Among the 7 patients with negative clinical findings, there were also positive microbiological findings (*Staphylococcus aureus*) in one case and negative microbiological findings in the remaining 6 patients. In the case of positive microbiological findings, antibiotics sensitivity tests were performed and patients were treated with adequate antibiotics. In the following 6 months of follow-up, we found no evidence of any other infectious complication.

The correlation between clinical finding, PET CT examination result and microbiological finding in followed-up patients is shown in Table 1.

Table 1. Correlation Between Clinical Finding, PET CT Finding and Microbiological Finding in Followed-up Patients

Number of patients	Clinical finding, CRP	PET CT finding	Microbiological finding
4	positive, elevation	positive	positive
2	negative, elevation	positive	positive
7	negative, normal value	negative	positive (1) negative (6)

Discussion

AVG infection is a known complication with a typical clinical picture and in our experience is associated with partial or total AVG removal.^{7,11} Non-functional clotted AVG with symptoms of infection is also indicated for removal. Another issue is the management of non-functional clotted AVGs that create no complications. These should be removed but are commonly kept in situ and a new AVG is created.^{8,9} This so-called silent AVG is not monitored but obviously can be a potential source of chronic infection. Infection is usually demonstrated as overall symptoms such as a subfebrile condition and/or metastatic infectious complications such as endocarditis, arthritis, pulmonary embolism or osteomyelitis.¹² This potential source of infection must be kept in mind while the patient is examined. The only suitable method for infected AVG treatment is complete AVG removal.¹¹ This procedure can burden the patient with end-stage renal failure remarkably. It is performed under general anaesthesia, the surgical treatment of vascular anastomoses can substantially prolong the procedure and an extensive surgical wound is inevitable.¹³ The procedure must be indicated only if evidence of AVG infection is provided.

Beside traditional markers of infection, the following methods can be used in the assessment; in the presence of infectious complications of unknown aetiology, we should

be aware of this potential source of infection and the patient should undergo labelled leukocyte scintigraphy^{14,15} and/or positron emission tomography scanning (FDG-PET).¹⁰ The PET CT is considered an easier and more accurate diagnostic method than Indium 111-leukocyte imaging.^{10,14,15}

Conclusion

Our experience with the cohort of patients with silent AVG suggests ultrasound examination is not beneficial in terms of diagnosing AVG infection. The clinical findings do not indicate the infection, CRP elevation and haemocultures have interpretative value. FDG PET/CT examination confirmed a high correlation between PET CT and the microbiological findings obtained from the removed prosthesis. In 13 patients there was only one mismatch – a negative PET CT finding and positive microbiological culture.

Especially in patients with silent grafts and recurrent infection of equivocal etiology, PET CT examination can contribute to the diagnosis of AVG infection. The graft should be removed if infection is confirmed. On the other hand, it remains clear that in patients with silent AVG and without any signs of local or overall infection, the PET CT examination is not beneficial.

Acknowledgments

We would like to acknowledge that we have received support from grant IGA NT 11062-5/2010.

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