Case report

Illuminating the nidus: The role of FDG PET/CT in high flow arteriovenous vascular malformations

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The appropriate identification and localization of a nidus of a high flow arteriovenous malformation is crucial to guide targeted interventional therapy. However, the nidus of a complex or previously treated HFAVM can be difficult to non-invasively demonstrate on magnetic resonance imaging alone. We describe a unique case of a 56-year-old female with a complex high flow arteriovenous malformation in which we demonstrated the feasibility of fluorodeoxyglucose positron emission tomography/computed tomography to non-invasively delineate the nidus which subsequently guided successful targeted interventional therapy.

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Introduction

High flow arteriovenous malformations (HFAVMs) shunt blood from a feeding artery into a draining vein via a central collection of dysmorphic, tortuous vessels, referred to as a nidus in the absence of a normal capillary bed [1]. Compared with other vascular malformations, HFAVMs are considered the most symptomatic and also the most difficult to treat [2]. Imaging helps to provide an accurate and early diagnosis which guides appropriate management, with embolosclerotherapy as the primary therapy. In addition, if left untreated, HFAVMs rapidly progress in size and complexity and also have a high rate of recurrence post treatment. Identifying and selectively targeting the nidus of the HFAVMs at an early stage reduces the recurrence rates [3].

Magnetic resonance imaging (MRI) and catheter angiography are the preferred modalities to evaluate HFAVMs in symptomatic patients or in the assessment of vascular anomalies that have equivocal findings at sonographic evaluation [3]. The superior temporal resolution of time-resolved MR angiography assists with nidus localization [4] and 2-dimensional MR...
sequences allow for the evaluation of secondary surrounding soft tissue and bony involvement. However, in large, complex, multifocal or previously-treated HFAVMs, the location of the nidus may be difficult to appreciate on MR imaging alone.

Since the nidus of a HFAVM is a proliferative, highly angiogenic core, it is likely to demonstrate increased radiotracer uptake in on fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT)\(^5\). We describe a unique case in which we non-invasively evaluated a complex HFAVM, using FDG PET/CT to successfully delineate the nidus which subsequently assisted with targeted embolization.

**Case report**

A 56-year-old female presented to the AVM clinic with a 20-year history of increasing swelling of the left shoulder associated with significant pain and disability. Despite multiple previous interventions, her symptoms had progressively worsened over the last 2 years. Clinical examination revealed a large pulsatile swelling involving the left shoulder with visible draining veins and a palpable thrill.

Time resolved MR angiography sequences confirmed the clinical suspicion of a HFAVM with multiple AV fistulations arising from the left subclavian, left axillary and left brachial arteries (Fig. 1). MRI also demonstrated osseous involvement of the left proximal humeral head with severe cortical damage. The nidus was difficult to appreciate on MRI as the speed of AV fistulation flow was beyond the resolution of time-resolved MR angiography (4D Trak, Siemens). A FDG PET/CT scan was requested to help delineate the location of maximum angiogenic proliferation within the AVM; the nidus. The theory behind this was that high metabolic uptake may act as a surrogate marker for angiogenesis, thus assisting with nidus localization. PET/CT showed avid tracer uptake in the head of the left humerus (Fig. 2).

Four weeks following the PET/CT, the patient underwent catheter angiography with a view to image and subsequently treat the complex, large, left shoulder HFAVM. Intraprocedural angiographic findings were directly compared with the PET/CT findings. Particular emphasis was placed on accurately localizing the nidus prior to intervention, which was deemed to be the area seen at the left humeral head since it had an avid, intense FDG uptake (Fig. 3).

The patient then underwent staged treatment by fluoroscopic-guided embolosclerotherapy using both transarterial and percutaneous approaches to access the nidus as demonstrated on both PET/CT and catheter angiography (Fig. 4). The procedure was a technical success with no immediate complications. Following this procedure, the patient reported an improvement in her left shoulder pain and swelling as well as improved perfusion within her left hand.

**Discussion**

Endovascular therapy is the preferred method of treatment in current practice for patients with a HFAVM, since surgical resection is associated with a high recurrence rate and a high rate of morbidity \(^6\). Endovascular treatment is performed us-
ing a percutaneous transcatheter arterial or venous embolization and/or through a direct puncture of the nidus with the injection of sclerosant agents. The principal aim of the aforementioned techniques is selectively obliterate the nidus [7]. Incomplete nidus eradication can stimulate aggressive growth post-procedure and therefore markedly increases the chances of recurrence [8]. Accurate pre-procedural planning and identification of the nidus is thus imperative to reduce these complications.

The nidus in HFAVMs rapidly shunts blood from the arterial to venous circulation in the absence of capillary resistance. This rapid arteriovenous transit creates a narrow enhancement time window [3] which can exceed the resolution of time-resolved MR angiography. Therefore, in the context of large volume HFAVMs, this flow-related time limitation causes difficulties in accurate nidus identification.

The pathogenesis of HFAVM is attributable to abnormal, uncontrolled angiogenesis driven by the action of vascular growth factors [9]. Elevated levels of vascular endothelial growth factor (VEGF) have been demonstrated in the nidus and adjacent cells in cerebral arteriovenous malformations [10]. PET imaging with F-18 labelled 2-flouro 2-deoxy-D glucose (F-18DG) is a functional imaging modality that has evolved as an important role in the diagnosis and management of malignancies [11]. The premise for this is the increased utilization of glucose by malignant cells which are hypermetabolic in nature with a high mitotic activity [12]. Angiogenesis also plays a central role both in tumor growth and nidus formation. Although no prior studies have shown a correlation between non-invasive nidus localization and avid uptake on FDG PET/CT imaging, several studies have shown a correlation between angiogenic activity in tumors and FDG PET uptake both in vitro and in vivo [13]. Furthermore, a recent feasibility study by Lobeek et al. demonstrated increased uptake in AVMs with angiogenic activity compared with the surrounding tissues with absent angiogenic activity on 68 Ga-labeled arginine-glycine-aspartate tripeptide sequence (RGD) PET/CT imaging [5].
In our case report, we have demonstrated that in a large complex HAVM, FDG PET/CT can be used to non-invasively identify and locate the nidus by utilizing inherent properties of high metabolic activity secondary to increased angiogenesis. As demonstrated, this therefore has the potential to guide targeted interventional therapy.

**Patient consent**

The authors of this manuscript have obtained written, informed consent from the patient to write up the case report and for the use of images pertinent to the case. We have ensured anonymity of all clinical and graphical data used.

**References**

1. Donnelly LF, Adams DM, Bisset GS 3rd. Vascular malformations and hemangiomas: a practical approach in a multidisciplinary clinic. AJR Am J Roentgenol 2000;174(3):597–608.
2. Cahill AM, Nijs ELF. Pediatric vascular malformations: pathophysiology, diagnosis, and the role of interventional radiology. Cardiovasc Intervent Radiol 2011;34(4):691–704.
3. Dunham GM, Ingraham CR, Maki JH, Vaidya SS. Finding the nidus: detection and workup of non-central nervous system arteriovenous malformations. Radiographics 2016;36(3):891–903. doi:10.1148/rg.2016150177.
4. Mulligan PR, Prajapati HJS, Martin LG, Patel TH. Vascular anomalies: classification, imaging characteristics and implications for interventional radiology treatment approaches. Br J Radiol 2014;87 1035):20130392.
5. Lobeek D, Bouwman FCM, Aarnitzen EHJG, Molkenboer-Kuenen JDM, Flucke UE, Nguyen HL, et al. A clinical feasibility study to image angiogenesis in patients with arteriovenous malformations using 68Ga-RGD PET/CT. J Nucl Med 2020;61(2):270–5. doi:10.2967/jnumed.119.231167.
6. Calligaro KD, Sedlacek TV, Savarese RP, Carneval P, DeLaurentis DA. Congenital pelvic arteriovenous malformations: long-term follow-up in two cases and a review of the literature. J Vasc Surg 1992;16(1):100–8.
7. Conway AM, Qato K, Drury J, Rosen RJ. Embolization techniques for high-flow arteriovenous malformations with a dominant outflow vein. J Vasc Surg Venous Lymphat Disord 2015;3(2):178–92.
8. Ernemann U, Kramer U, Miller S, Bisdas S, Rebmann H, Brueninger H, et al. Current concepts in the classification, diagnosis and treatment of vascular anomalies. Eur J Radiol 2010;75(1):2–11.
9. Neto CASF, Durans M. Arteriovenous malformation: concepts on physiopathology and treatment. J Vasc Endovasc Ther 2019;4(1):6.
10. Sandalciglu IE, Wende D, Eggert A, Müller D, Roggenbuck U, Gasser T, et al. Vascular endothelial growth factor plasma levels are significantly elevated in patients with cerebral arteriovenous malformations. Cerebrovasc Dis 2006;21(3):154–8.
11. Hillner BE, Siegel BA, Liu D, Shields AF, Gareen IF, Hanna L, et al. Impact of positron emission tomography/computed tomography and positron emission tomography (PET) alone on expected management of patients with cancer: initial results from the National Oncologic PET Registry. J Clin Oncol 2008;26:2155–61.
12. Lawal I, Sathekghe M. F-18 FDG PET/CT imaging of cardiac and vascular inflammation and infection. Br Med Bull 2016;120(1):55–74.
13. Niccoli Asabella A, Di Palo A, Altini C, Ferrari C, Rubini G. Multimodality imaging in tumor angiogenesis: present status and perspectives. Int J Mol Sci 2017;18(9):1864.