Title: Benign uterine uptake of FDG: a case report and review of literature

Authors: D Vriens, MD*, LF de Geus-Oei, MD, PhD*, UE Flucke, MD, PhD†, AJ van der Kogel, PhD§, WJG Oyen, MD, PhD*, ME Vierhout, MD, PhD ‖, JWM van der Meer, MD, PhD‡

*Depts. of Nuclear Medicine, †Pathology, §Radiation Oncology, ‖Obstetrics and Gynaecology and ‡General Internal Medicine

All authors contributed equally in writing of the manuscript. The PET/CT scan was reviewed by LFdGO and WO, the histopathology by UEF, the clinical picture and treatment by MEV and JWMvdM. AJvdK helped in analysis of potential pathways of increased FDG-uptake.

Institution: Radboud University Nijmegen Medical Centre.

P.O. Box 9101, 6500 HB Nijmegen, the Netherlands

Correspondence: D. Vriens, MD

Department of Nuclear Medicine (internal postal code 444)
Radboud University Nijmegen Medical Centre
P.O. Box 9101, 6500 HB Nijmegen, the Netherlands
Phone: +31-24-3614048, Fax: +31-24-3618942
E-mail: D.Vriens@nucmed.umcn.nl

Grant support: This study was entirely funded by internal resources.

Word count: 495
Dear Editor,

We observed very high uterine $[^{18}F]$/fluorodeoxyglucose (FDG) uptake on positron emission tomography (PET) in what proved to be a benign uterine leiomyoma. Although clinically apparent in 25% of women (1) and prevalent in up to 77% (2), only incidentally this phenomenon is described. Here we present a case of a 49-year old woman.

Our patient underwent an FDG-PET/CT for follow-up of an infectious focus on the lower back. Apart from a metabolically active lymph node and bone marrow, it revealed a ~9.6cm large, inhomogeneous but sharply demarcated FDG-avid lesion in the posterior uterine wall (figure 1). The lesion was ultrasonographically a typical large leiomyoma.

An abdominal hysterectomy was performed for lumbago and anaemia due to meno-metrorrhagia. Histopathological examination revealed an enlarged uterus with an intramural leiomyoma of 7.8 cm in diameter and multiple small subserosal leiomyomas the size below the resolution of the PET/CT scanner. Microscopy showed the typical image of a leiomyoma, without signs of necrosis, haemorrhage, atypia or inflammation. There was no cervical atypia and the endometrium was thin (<1mm) and showed some changes corresponding to progestagen suppletion.

In search of an explanation for the high FDG-uptake, sections of the anterior - on PET normal - uterine myometrium, were compared to sections of the leiomyoma. Immunohistochemical staining of markers for proliferation, inflammation, hypoxia, apoptosis, vascularity, glucose metabolism and glycogen content was quantified. This quantification demonstrated a slight increase in proliferation and glycogen content.

Incidently found leiomyomas are occasionally reported to have elevated FDG-uptake (SUV 6.0-16) (3, 4). Retrospective analysis of screening FDG-PET in 589 healthy women found increased FDG-uptake due to leiomyomas in 22 females of which only 14% showed FDG-uptake higher than the liver (5). A screening FDG-PET in 1357 healthy women found an standardized uptake value (SUV) larger than 3.0 in 10% of the leiomyomas in premenopausal women and in only 1.2% in postmenopausal women (6).
A prospective study of 61 proven leiomyomas showed that 17% have an SUV$_{\text{max}}$ higher than 2.5, but only one had an SUV larger than 5.0 (7).

The differential diagnosis of increased uterine FDG-uptake should include the menstrual and ovulation phase of the menstrual cycle, menorrhagia, postpartum changes, atypical polypoid adenomyomas and IUDs. The SUV in leiomyosarcoma is significantly higher than in leiomyomas but the overlap limits its ability to distinguish these in individual patients (8).

The reason for enhanced FDG-uptake in leiomyomas is suggested to be related to the high levels of cervical and endometrial tissue glycogen in a myomatous uterus, the increased blood fraction and the proliferation of the smooth muscle cells due to increased metabolic need. Finally, it is measured that leiomyomas have severe hypoxia, even though no stress-reaction could be quantified by HIF-1α, CAIX or GLUT1 expression (9).

To clinicians and nuclear medicine specialists it is important to be aware of the fact that benign leiomyomas of the uterus may rarely show high FDG-uptake. Although leiomyosarcomas show higher FDG-uptake than leiomyomas, it does not distinguish benign and malignant disease.
Acknowledgements

Immunohistochemical staining was performed by W.J.M. Peeters (hexokinase isoenzymes), C. Frielink (HIF-1α, CAIX and GLUT1) and C.N. Maass (CD3, CD31 and caspase-3).

This study was funded by internal resources only.

All authors declare not to have any conflicts of interest.
Figures

Figure 1: [18F]-fluorodeoxyglucose (FDG) positron emission tomography with non-diagnostic, low-dose x-ray computed tomography performed in a 49-year-old woman with a history of soft tissue infection of the lower back. Arrow: intense FDG-uptake (max SUV: 12.7, mean SUV: 8.4) in the enlarged uterus, posterior wall. Arrowhead: urinary bladder. SUV: standardized uptake value, parameter representing the relative increase of the regional uptake of the tracer above expected from homogenous distribution over the body.


