Glucose Metabolism in the Vessel Wall Correlates With Mechanical Instability and Inflammatory Changes in a Patient With a Growing Aneurysm of the Abdominal Aorta

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It has been shown by our group and by others\textsuperscript{1,2} that increased glucose metabolism in the aortic wall of patients with aneurysms of the abdominal aorta (AAA) can be visualized in vivo by \textsuperscript{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET). Interestingly, an increased glucose metabolism in AAA wall was strongly associated with rapid progression or acute symptoms and therefore increased rupture risk. Moreover, the PET signal was correlated with histopathological changes such as activation of MMP-9, collagen, and elastic fibers as well as macrophage infiltration in the AAA wall. (It is well documented by preclinical studies that increased activity of MMP-9 facilitates aneurysm rupture). However, the true prognostic value of increased FDG uptake for AAA progression and rupture risk.

Figure 1. Coronal and axial CT sections of the aneurysm in the baseline (A and C) and in the follow-up scans (B and D). Red arrow indicates the area with the maximum glycolytic activity. E, Three-dimensional reconstruction with aneurysm wall displacement of the initially small (right) and later large aneurysm (left). Color scale indicates high (red) or low (blue) wall displacement to stress.

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still remains uncertain. To provide clear evidence, surveillance of small AAA by multiple PET scans would be necessary over a long period. However, PET studies are not routinely performed in patients with AAA for practical and ethical reasons and therefore an increase in glucose metabolism in AAA wall was not directly observed until now. Further, it is not clear whether biomechanical conditions of AAA such as peak wall stress or wall displacement are relevant for FDG uptake.

In this report, we describe a patient with a malignant melanoma with coincident and initially small infrarenal AAA who was examined by PET/computed tomography (CT) for staging and follow-up. During surveillance, the AAA showed rapid progression associated with strongly increased glucose metabolism. The AAA was repaired and histopathological as well as computed biomechanical properties were analyzed.

**Case Presentation**

A 55-year-old patient with a malignant melanoma of the left upper neck, infiltrating the skull base, was referred to PET/CT for exclusion of distant metastases. PET revealed intensive FDG uptake in the primary tumor but not metastases. On diagnostic CT scans, a concomitant small AAA was detected. The maximal diameter of the aneurysm was 46 mm and the length was 70 mm. The renal arteries were not included in the aneurysm. The glycolytic activity in the AAA wall was normal without accentuation (Figure 1B and 1D). The patient was presented to the tumor board and the vascular board of our hospital. It was decided to treat the tumor by radiochemotherapy (Dacarbazine and 60 Gy); regarding the AAA, recommendation for surveillance was given. Six months later, the patient was referred to PET/CT for restaging after radiochemotherapy. PET/CT imaging revealed total local and systemic tumor control by the radiochemotherapy. In contrast, the AAA showed rapid expansion to 60 mm maximum diameter with focally intensified aortic FDG uptake (SUVmax, 6.1; SUVmean, 4.8) at the bottom of the AAA sack on PET but without clinical symptoms (Figure 1B and 1D). The case was discussed again by the vascular board, and prophylactic AAA repair was recommended. During open surgery, samples of AAA wall at areas with low and highly increased FDG uptake were operatively retrieved. Wall samples were immunohistologically processed and evaluated for inflammation, elastin, and collagen fiber degradation and the expression of MMP2 and MMP9 by semiquantitative analyses (Figure 2). In comparison to regions with normal FDG-uptake, areas of AAA wall with strong FDG uptake showed massive inflammatory changes associated with strongly increased glucose metabolism. The AAA was repaired and histopathological as well as computed biomechanical properties were analyzed.

**Figure 2.** Histological slides (×10 magnification) from areas of the AAA wall with strong FDG uptake: Conventional staining and immunostaining reveal massive inflammatory changes of AAA wall with macrophage infiltration (A, CD68 antibody staining; brown, macrophages), increased levels of MMP2 and MMP9 expression (B, MMP2; C, MMP9 antibody staining; brown cells, positive for MMP2 and 9), and reduction of collagen and elastin (D, elastica van Gieson stain; asterisks indicate black elastic fibers; plus signs, red collagen fibers). White arrows in B and D indicate high-density inflammatory infiltrations (blue or black cell infiltrates).

**Discussion**

The patient had rapid progressive infrarenal AAA within 6 months and markedly increased glucose metabolism at the AAA sack in parallel. Moreover, compared with the baseline...
study, increased glycolytic activity correlated well to biomechanical calculated increase of AAA wall displacement. Furthermore, changes in glycolytic activity and AAA wall displacement were associated with inflammation, macrophage infiltration, and MMP2 and MMP9 activity, suggesting a causal relationship of AAA biomechanics with underlying histopathological changes detected by FDG-PET/CT. Further studies about these correlations and their predictive role for AAA progression or AAA rupture risk are needed to establish glycolytic activity as a novel biomarker in risk stratification of such patients.

Disclosures
None.

References
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