Primary Renal Leiomyosarcoma Presenting with Subcutaneous and Osseous Metastases: Staging and Follow-Up with ^{18}F -FDG PET/CT

William Makis¹ · Fadi Brimo² · Stephan Probst³

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Abstract A 60 year old woman who presented with multiple small subcutaneous nodules in the upper back and arms, was referred for an [^{18}F] fluoro-2-deoxy-D-glucose (^{18}F -FDG) positron emission tomography/computed tomography (PET/CT) after histological evaluation revealed metastatic leiomyosarcoma of unknown origin. The PET/CT showed multiple ^{18}F -FDG-avid subcutaneous nodules, bone lesions, as well as a large left renal mass, which was biopsied to confirm a primary renal leiomyosarcoma arising from the renal parenchyma. A post therapy PET/CT showed overall progression of disease. The use of ^{18}F -FDG PET/CT in the staging and evaluation of response to therapy of a renal leiomyosarcoma has not been previously described in the literature.

Keywords ^{18}F -FDG · Fluorodeoxyglucose · Metastases · PET/CT · Renal leiomyosarcoma

Introduction

Primary sarcomas comprise 0.8–2.7% of renal tumors in adults, of which up to 60% are leiomyosarcomas. They

affect women more commonly than men and affect the right kidney more frequently than the left. They often present with a classical triad of signs and symptoms including abdominal mass, flank pain and hematuria, clinically indistinguishable from renal cell carcinoma. They can occur at any age but are more common after the 5th decade of life [1–3].

Primary renal leiomyosarcomas do not have radiological features to distinguish them from more common renal malignancies such as renal cell carcinoma, and although computed tomography (CT) remains the imaging modality of choice, the CT features of this rare tumor are non-specific. Magnetic resonance imaging (MRI) may be helpful in specific situations where venous thrombosis or vessel invasion by tumor are suspected [4–6].

The use of ^{18}F -FDG PET/CT in the staging and follow-up of leiomyosarcomas is becoming well established and supported in the literature [7–11]. Its use in the management of primary renal leiomyosarcomas, however, has not been previously described. Renal leiomyosarcomas are very aggressive with poor long term outcomes. The role of adjuvant chemotherapy or radiotherapy has not been well established [12–14]. It is likely that ^{18}F -FDG PET/CT will play a significant role in guiding the management of these rare tumors in the future.

Case Report

A 60 year old woman was diagnosed with a metastatic high grade leiomyosarcoma of unknown primary, after presenting with multiple small subcutaneous nodules in the upper back and upper arms. Two well circumscribed nodules, measuring 8 mm and 12 mm (excised from the

✉ William Makis
makisw79@yahoo.com

¹ Diagnostic Imaging, Cross Cancer Institute, 11560 University Ave NW, Edmonton, Alberta T6G 1Z2, Canada

² MUHC Glen Site, Pathology, 1001 Decarie Blvd, Montreal, Quebec H4A 3J1, Canada

³ Jewish General Hospital, Nuclear Medicine, 3755 Chemin de la Cote-Sainte-Catherine, Montreal, Quebec H3T 1E2, Canada

Fig. 1 ^{18}F -FDG PET/CT MIP **a** anterior and **b** left lateral images show multiple foci of mild as well as intense ^{18}F -FDG uptake corresponding to subcutaneous soft tissue nodules (*down arrow*), a lobulated left renal mass (*left arrow*) and a sacral bone mass (*right arrow*)

upper back/right arm) showed markedly atypical smooth muscle proliferation, a proliferative index Ki-67 of 30%, and a mitotic score of 5 per 10 high power fields. She was referred for a staging ^{18}F -FDG PET/CT (Discovery ST, GE

Healthcare, Waukesha, WI, USA) to search for the primary and determine the extent of the disease. Maximum intensity projection (MIP) images revealed multiple ^{18}F -FDG-avid subcutaneous nodules, the largest located in the left upper back measuring 2.2 cm with maximum standardized uptake value (SUV_{max}) of 1.9 (Fig. 1), a lobulated 6 cm left renal solid mass with SUV_{max} 9.7 (Fig. 2), and a 3.5 cm sacral mass with SUV_{max} 11.1 (Fig. 3). Additional imaging of the lower limbs was performed and showed a 2.5 cm mass in the right proximal tibia with SUV_{max} 5.1 (Fig. 4). The patient had not complained of any abdominal pain, or bone pain upon presentation.

Following the PET/CT imaging, the 6 cm ^{18}F -FDG avid left renal mass was biopsied, and histopathological evaluation confirmed a high grade primary renal leiomyosarcoma arising from the renal parenchyma (Fig. 5). The patient received chemotherapy (three cycles of doxorubicin, ifosfamide, mesna) and palliative radiation therapy to the sacral and right tibial bone metastases (8 Gy in 1 fraction at each site).

A follow-up ^{18}F -FDG PET/CT was performed 1 year after the staging PET/CT to assess the response to chemotherapy and radiation therapy. PET/CT MIP images showed that the left upper back lesion seen in Fig. 3 responded completely to chemotherapy. The left renal mass SUV_{max} increased from 9.7 to 11.6, while the sacral lesion metabolism did not change significantly (SUV_{max}

Fig. 2 **a** Contrast enhanced CT, **b** PET, **c** CT, and **d** PET/CT fusion images showing a lobulated 6 cm ^{18}F -FDG left renal mass (*left arrow*) which was histologically confirmed to be a primary renal leiomyosarcoma

Fig. 3 **a** CT, **b** PET, and **c** PET/CT fusion images showing a 2.2 cm subcutaneous metastasis in the left upper back (*up arrows*) with SUV_{max} of 1.9 and **d** CT, **e** PET, and **f** PET/CT fusion images showing a 3.5 cm

sacral bone metastasis with SUV_{max} 11.1 (*right arrows*), which was subsequently treated with palliative radiation therapy (8 Gy in 1 fraction)

10.4, from previous SUV_{max} 11.1). The right proximal tibial lesion was slightly larger in size but showed no change in SUV_{max} (4.6 from previously 5.1). There was a new bone metastasis in the right proximal humerus with SUV_{max} 3.1 as well as multiple new subcutaneous metastases in both thighs, consistent with progression of metastatic disease (Fig. 6).

Discussion

Primary sarcomas of the kidney account for 1–2% of all malignant renal tumors in adults, and leiomyosarcoma accounts for 50–60% of these. Primary renal leiomyosarcoma may arise from the smooth muscle fibers of the renal parenchyma (as in this case), renal capsule, renal pelvis or renal vessels. The

Fig. 4 Additional PET/CT views of the limbs were obtained. **a** Anterior MIP, **b** lateral MIP, **c** lateral CT, and **d** lateral PET/CT fusion images showing a 2.5 cm bone metastasis in the right proximal tibia with SUV_{max} 5.1 (*right arrows*), which was subsequently treated with palliative radiation therapy (8 Gy in 1 fraction)

Fig. 5 Hypercellular spindle tumor invading the renal parenchyma. *Inset:* the cells which grow in a fascicular growth pattern are spindle in shape, show severe hyperchromasia and abundant mitotic activity. These features are consistent with a high grade leiomyosarcoma

mean patient age at diagnosis is 58.5 years and it affects women more commonly with a ratio of 3:2. Patients usually present with flank pain and an abdominal mass, with or without hematuria, and occasionally spontaneous rupture and severe peri-renal haemorrhage. The right kidney is affected approximately 60% of the time [1, 2].

Renal leiomyosarcoma presents a diagnostic challenge, because there are no reliable clinical or radiological features to distinguish it from more common renal malignancies such as renal cell carcinoma, and histological evaluation is the only way to truly establish the diagnosis. These tumors can present as solid or cystic masses and neither ultrasonography, CT, nor MRI are able to differentiate renal leiomyosarcomas from renal cell carcinomas or other more common renal tumors [3–5]. MRI may be useful in very specific cases to assess for inferior vena cava thrombosis or tumor invasion of vessels [6].

^{18}F -FDG PET/CT is routinely used in the staging and follow-up of therapy of leiomyosarcomas, although it cannot differentiate low grade leiomyosarcomas from benign soft tissue tumors [7–11]. The use of ^{18}F -FDG PET/CT in the evaluation of primary leiomyosarcoma of the kidney has not been previously described in the literature. Renal leiomyosarcomas are considered to be very aggressive due to their rapid growth rate, frequent metastases, and high rate of tumor recurrence. Five year survival is less than 25% and median survival ranges from 1.5 to 2 years [1]. Radical nephrectomy offers the best chance for cure and the role of adjuvant chemotherapy or radiotherapy has not yet been established [12–14]. In this rare case, ^{18}F -FDG PET/CT was useful in identifying the location of the

Fig. 6 A post therapy ^{18}F -FDG PET/CT was performed 1 year after the staging PET/CT to assess response to chemotherapy and radiotherapy. **a** Anterior MIP, and **b** lateral MIP views showed that the left upper back lesion seen in Fig. 3 responded completely to therapy. The left renal mass SUV_{max} increased from 9.7 to 11.6, while the sacral metastasis ^{18}F -FDG uptake did not change significantly (SUV_{max} 10.4 from SUV_{max} 11.1). The right proximal tibial lesion was slightly larger but showed no change in SUV_{max} (4.6 from previous 5.1). There was a new ^{18}F -FDG avid bone metastasis in the right proximal humerus with SUV_{max} 3.1 (*right arrow*), as well as multiple new subcutaneous metastases in both thighs (*left arrow*), consistent with progression of metastatic disease

primary metastatic leiomyosarcoma of unknown origin and a post therapy PET/CT was able to assess response to chemotherapy and radiation therapy, and confirm overall progression of metastatic disease.

Compliance with Ethical Standards

Conflict of Interest William Makis, Fadi Brimo and Stephan Probst declare that they have no conflict of interest.

Ethical Statement The study was approved by an institutional review board or equivalent and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All subjects in the study gave written informed consent or the institutional review board waived the need to obtain informed consent.

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