A Patient with Psoriatic Arthritis Imaged with FDG-PET/CT Demonstrated an Unusual Imaging Pattern with Muscle and Fascia Involvement: A Case Report

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Abstract We describe the case of a patient with known history of psoriasis that presented with 1 year of unexplained fever, muscle weakness and marked weight loss, suspicious for B symptoms of a malignant origin. [^{18}F]-Fluorodeoxyglucose positron emission tomography-computed tomography (FDG-PET/CT) scans demonstrated an unusual serpiginous pattern of uptake in the fascia and muscles as well as lymph node activity. Multiple histological samples, including a final PET-probe guided lymph node surgical resection, excluded malignancy and confirmed the diagnosis of reactive inflammatory changes, with a plausible diagnosis of autoimmune lymphoproliferative syndrome with associated lymphadenitis, fasciitis and myositis, possibly mediated by tumor necrosis factor (TNF) inhibitor. To our knowledge, there is no evidence of a previously reported FDG uptake pattern of fascia and muscle involvement in psoriatic arthritis.

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Introduction

[^{18}F]-Fluorodeoxyglucose positron emission tomography-computed tomography (FDG-PET/CT) is widely used to detect increased glucose metabolism in cells such as cancer cells. FDG-PET/CT is widely used clinically in the management of cancer patients. Moreover, FDG can also be taken up by inflammatory cells, and therefore, inflammatory processes such as those of autoimmune origin may be confused for metastases if patterns of uptake and degree of activity are not taken into consideration. Psoriasis, arthritis, and lupus are among several autoimmune disorders that demonstrate such uptake on FDG-PET/CT [1]. Mild FDG uptake in the skin, liver and lymph nodes has been observed on FDG-PET/CT scans of patients with psoriasis; however, FDG uptake within the muscle and fascia has never been seen in such cases [1, 2]. Additionally, there have been no clinical correlations of muscle and fascia involvement in patients with psoriasis.

We describe the case of a young patient with known history of psoriasis and arthritis that underwent two separate FDG-PET/CT scans to rule out malignancy. Both scans persistently demonstrated an unusual pattern of serpiginous patchy heterogeneous FDG activity within the muscles and fascia while also showing widespread inflammatory lymph node activity.

Case Report

We present the case of a 26-year-old man with a known clinical history of autoimmune disease consistent with seborrheic dermatitis, psoriasis and psoriatic arthritis, who had been

on treatment with a tumor necrosis factor (TNF) inhibitor, adalimumab, for approximately 9 months. More recently, the rheumatologist had stopped the TNF inhibitor and placed the patient on anti-inflammatory medication and methotrexate for arthritis pain.

The patient first presented to his primary care clinician with a new onset of unexplained fevers (up to 38.9 °C), night sweats, and unexplained weight loss of 13.6 kg over the course of approximately 1 year, suspicious for B symptoms. On physical exam, the patient presented with psoriatic rash throughout the body, accompanied by pain in the right wrist and fingers. The patient was classified as having grade 3, severe psoriasis with plaques covering 50–69 % of the total body surface area according to the Psoriasis Area and Severity Index (PASI). The patient's blood tests were normal, while testing seropositive for both antinuclear antibodies (ANA) and antiribonuclear proteins (anti-RNP) and negative for double-stranded DNA antibodies. The patient also showed normal complement C3 and C4 values. A dedicated contrast-enhanced CT scan of chest-abdomen-pelvis demonstrated only some borderline enlarged (~1 cm) axillary, pelvic and inguinal lymph nodes. The patient's differential diagnosis included occult malignancy versus chronic infection versus autoimmune disease versus low grade lymphoma.

Within 3 days of examination the patient developed a sore throat, and so a fine-needle aspiration (FNA) biopsy of a palpable right posterior cervical lymph node was performed, which showed polymorphous lymphocyte population, favoring reactive lymphadenopathy.

Eight weeks elapsed while the patient's symptoms persisted. Then, the decision was made to perform a bone marrow core biopsy, which revealed no significant dysplasia, lymphoid aggregate, lymphoma or granuloma. Due to continued high clinical concern for malignancy, a nodal excisional biopsy of a palpable left inguinal lymph was performed and pathology determined it to be negative for malignancy or infection.

Over the course of the following 2 weeks the patient continued to have low-grade fevers and joint pain. On developing a new onset of tachycardia, increased weakness and a non-productive cough, the patient was admitted to the emergency room with a main complaint of severe dizziness, weakness and leg pain. His vitals and laboratory tests were normal. A whole-body FDG-PET/CT scan was then requested to assess for occult malignancy, and identification of metabolically active lymph nodes for a possible additional biopsy. The scan, which was performed about 4 months from the patient's initial fever, showed multiregional, mildly hypermetabolic lymph nodes (Fig. 1), and more interestingly, an abnormal pattern of FDG activity in the muscles of the upper extremities, chest wall, and lower extremities, more prominent in the thighs, where there was clear uptake of FDG along the fascias. The findings were considered to be more consistent with a systemic inflammatory process.

The patient's clinical differential diagnosis at this point was still contemplating Hodgkin's lymphoma, indolent B cell NHL, T cell lymphoma, post-transplant lymphoproliferative disorder (PTLD) or Castleman's disease. The patient's myalgias were questioned to be inflammatory (possibly autoimmune) versus paraneoplastic related to lymphoma, especially likely if the patient had Hodgkin's disease. Muscle strength testing was normal and creatine kinase levels were within the normal range. The decision was made to perform a second excisional biopsy, this time of a left axillary lymph node that had mild FDG activity on FDG-PET/CT. Histology once again demonstrated a reactive lymph node with no signs of malignancy.

The patient was discharged and although the patient's psoriatic plaques were improving, as he now had grade 2, moderate psoriasis with 30–49 % area coverage according to the PASI, a punch biopsy of a psoriatic plaque on the patient's right elbow was performed 7 days later to further address the possibility of bacterial infection. Pathology showed no bacterial infection and diagnosed it as psoriasiform spongiotic dermatitis.

The decision was then made to perform a second FDG-PET/CT scan (2 months following the initial PET/CT scan), which showed a pattern similar to the prior scan (Fig. 2). At this point, it was decided to perform a final excisional biopsy of a left cervical lymph node with FDG activity. To confirm that the surgical specimen was a cervical lymph node visualized with FDG, a PET probe was used for assistance in the operating room. A left 2.5-cm cervical level II lymph node with high emission of positrons was surgically removed in the operating room. The final histological report of the lymph node was again negative for malignancy and reported as reactive.

The patient was subsequently followed-up by rheumatology, where he was kept off the TNF inhibitor and put on aggressive anti-inflammatory medication with a slow response. The patient was also placed on methotrexate for management of his psoriatic arthritis and he has since been generally feeling better. The patient's B symptoms have resolved, while he has continued to gain weight, skin plaques have improved, and his strength returned. The patient has been diagnosed with autoimmune lymphoproliferative syndrome, likely mediated by the TNF inhibitor, adalimumab.

FDG-PET/CT Imaging Methods

The FDG-PET/CT studies were acquired at the San Francisco Veterans Affairs Medical Center using a Discovery 64 slice PET/CT scanner GE 690 with LYSO crystals and time of flight.

On the day of the FDG-PET/CT scans, the patient had a random blood glucose level of 84 mg/dl for scan 1 and 89 for scan 2, after fasting for >6 h. The patient was intravenously

Fig. 1 The FDG-PET/CT scan demonstrated multiple hypermetabolic anterior cervical lymph nodes (right more than left) at levels II, III, and V. The most prominent lymph node was a 2-cm in the short axis left level II lymph node with a SUVmax of 6.9. Several hypermetabolic lymph nodes were also noted in the axillae, subpectoral space and mediastinum. For example, a left axillary node measured 7×14 mm with a SUVmax of 2.7, a right axillary node cluster measured 13×26 mm with a SUVmax of 4.3, and multiple left axillary and left subpectoral nodes measured up to 1.5 cm with SUVmax values up to 4.7. The lungs were clear. Also, multiple hypermetabolic iliac lymph nodes were seen (whole-body MIP image shown in **a**). Interestingly,

administered with 10 mCi (370 MBq) of F18-FDG in the antecubital region in both occasions using a MEDRAD INTEGO robot and 60 min later taken to the scanner for imaging. A transmission scan (5 mm contiguous axial cuts) was obtained using an integrated multi-slice helical non-enhanced CT from vertex to toes for attenuation correction and anatomic localization. The acquisition was obtained with a one-slice overlap at the borders of the field of view to avoid artifacts, using 120 kV, 75 mAs, and a 512×512 matrix size. Immediately after, and without moving the patient, an emission scan was obtained in 3D mode with time of flight in 11 beds at 3 min per bed over the same anatomical regions. The PET

the scan also showed an abnormal, heterogeneous, patchy pattern of FDG activity in the muscles of the upper extremities, chest wall, and lower extremities, with a serpiginous appearance more prominent in the thighs, where the patient experienced his main area of weakness and pain. This was a very atypical pattern of FDG uptake different from the typical pattern observed in normal up-regulation of metabolism in the muscle groups due to exercise, muscle strain or as frequently observed in the postprandial state. This pattern was also different from prior case reports of lymphoma in the muscles and local myositis. In fact, in the thighs the FDG activity seemed to clearly favor localization in the intermuscular fascia consistent with fasciitis (**b**)

emission scan was corrected using segmented attenuation data of the conventional transmission scan. A Gaussian filtering (6.4 mm) was performed for smoothing of images. The PET images were reconstructed with a standard iterative algorithm (OSEM, two iterative steps, 24 subsets) using GE software release 5.0 VUE Point FX intelligent reconstruction.

Discussion and Review of Literature

Psoriasis is an inflammatory disease of the skin and joints affecting 2–3 % of the adult population in the USA and a

Fig. 2 The second whole-body FDG-PET/CT scan showed similar findings when compared with the prior one. Again seen was cervical lymphadenopathy at levels II, III, and V, bilateral axillary and right subpectoral hypermetabolic lymph nodes. There was new hypermetabolic right paratracheal, prevascular, bilateral hilar, and subcarinal hypermetabolic lymph nodes. Again seen were multiple hypermetabolic iliac lymph nodes. A right external iliac lymph node had slightly increased in size from prior scan and a new hypermetabolic common iliac lymph node was seen. Furthermore, the heterogeneous patchy pattern of increased FDG activity throughout different muscular groups was once again observed and again noted in the thighs where FDG activity within the intermuscular fascias was seen

little over 3 % worldwide [3]. Studies have tried to grade the severity of psoriasis in patients using the Psoriasis Severity and Area Index (PSAI) and have evaluated it on psoriatic plaque intensity and coverage of total body surface area. The intensity describes the redness, thickness, and scaling of the individual plaques on a grading scale of 0–4, corresponding to absent-very severe, whereas the body surface area coverage is determined on a scale of 0–6, corresponding to the percent of body surface area covered by plaques [1]. According to this criterion, our patient had grade 3, severe psoriasis with 50–69 % body surface-area coverage and therefore other complications associated with this autoimmune disease were expected in this patient; in fact, the patient had known psoriatic arthritis.

Our patient developed “B-symptoms” and severe weakness. Psoriatic arthritis is not known to be associated with the development of “B-symptoms” or weakness and therefore the patient’s onset of symptoms and clinical examination raised suspicions of malignancy, mainly lymphoma. However, from a thorough workup, including positron-guided lymph node surgical biopsies and bone marrow biopsies, malignancy

was excluded. Imaging was also negative for occult malignancy. Primary extranodal lymphoma was a possibility, as it can occur either with or without any lymph node involvement [4]. Involvement of muscle is extremely rare in lymphomas, although not unheard of, Broski et al. [5] reported the case of a 65-year-old man with newly diagnosed primary muscular non-Hodgkin’s lymphoma, who presented with a 2-month history of fever, night sweats, severe lower-back pain, and a 20-pound weight loss. He had muscle enlargement and an FDG-PET scan that showed diffuse elevated FDG activity in multiple skeletal muscle groups. In lymphoma, FDG seems to be taken up by the enlarged muscle in a diffuse way, providing a more fusiform shape pattern following the muscle fibers. The pattern of FDG activity in the muscle presented by our patient was completely different. The pattern of FDG activity in the muscle was patchier and serpiginous, the muscles were not enlarged, and did not seem to follow the muscle fibers or have a typical fusiform shape.

With malignancy excluded, the other possible etiologies of the patient’s findings became very unclear. One possibility was that the “B symptoms”, muscle weakness and abnormalities

identified in the FDG-PET/CT images were related to the patient's underlying psoriasis. Psoriasis has been shown to be associated with metabolic disease, high mortality and often obesity; however, it is unclear as per the literature that psoriasis can be associated with fasciitis and/or myositis (considering symptoms of weakness and imaging findings) [6, 7]. Another possibility was the treatment that the patient was receiving for his psoriasis. TNF inhibitor (adalimumab) was the medication the patient was initially placed on for 9 months while the symptoms were progressing. Adalimumab has previously been associated with the development of drug-induced lupus and even non-Hodgkin's lymphoma [8, 9]. In this respect, our patient developed a positive antinuclear antibody, although he did not meet the criteria for systemic lupus erythematosus. Also, and to our knowledge, adalimumab has not been associated either with the development of myositis or fasciitis. However, since his myalgias, fevers, lymphadenopathy, and night sweats improved following the discontinuation of adalimumab and his psoriatic arthritis is currently being well managed with methotrexate and non-steroidal anti-inflammatory drugs with further improvement, it is a plausible hypothesis that the initiation of tumor necrosis alpha inhibition may have played a key role in the development of these systemic symptoms. In this patient, it likely led to an immune deregulation with the development of an autoimmune lymphoproliferative syndrome.

Whatever the etiology of the patient's symptoms was, psoriasis versus TNF inhibitor-induced, it is clear that the patient developed "B symptoms" and muscle weakness which translated into findings in the FDG-PET/CT imaging studies. The serial FDG-PET/CT scans showed mild FDG activity throughout multiple lymph nodal stations within the body, with large- and small-sized lymph nodes, more consistent with an inflammatory systemic disease such as autoimmune lymphoproliferative syndrome (also confirmed by multiple negative biopsies). The FDG-PET/CT scans also showed an abnormal pattern of activity in the muscles, more noted in the thighs, where the patient localized his worse muscle weakness and aches. Interestingly enough, the FDG activity in the thighs seem to localize in the muscular fascia more than in the muscle itself. The patient having normal muscle strength testing and normal creatinine kinase levels favors the idea of the patient suffering more from fasciitis than myositis (or at least a more significant component). In fact, prior reports of FDG-PET imaging of myositis have shown a completely different pattern of FDG activity in the muscle. To our knowledge, there are only two cases in the literature that report patients with myositis imaged with FDG-PET. In both cases the myositis was localized and focal (and neither had any association to psoriasis). Mulier et al. [10] described the case of a 14 year-old boy imaged with FDG-PET, which showed a single intense focus of FDG activity in an affected left paraspinal muscle. Clarencon et al. [11] discusses the other case, this time myositis ossificans

circumscribed in the longus supinatus muscle, which again demonstrated focal hypermetabolism on FDG-PET exam. The pattern of FDG activity in our patient is completely different. Rather than focal uptake, our patient shows a more heterogeneous and patchy, somehow serpiginous pattern of high FDG uptake throughout the musculature of the upper extremities, chest wall and lower extremities, and in the hybrid PET/CT images, it clearly localizes in the intermuscular fascia in the thighs.

There are several cases in the literature reporting on FDG for visualization of psoriasis; however, neither case has shown any related findings of FDG activity in the muscles or fascias. In 2011, Mehta et al. [1] presented a case of a patient with severe psoriasis that showed FDG activity in regions of the skin, tendons, liver and aorta. Another case also showed a correlation between psoriasis and focal FDG uptake in the skin [2].

Whatever the origin of our patient's symptoms and his imaging findings (psoriasis-related or psoriasis-treatment-related), to our knowledge, this is the first reported case to show an FDG pattern of widespread reactive lymphadenopathy, likely autoimmune lymphoproliferative syndrome, with associated fasciitis and myositis in a patient under treatment for severe psoriasis. We consider it important for nuclear molecular imagers to become familiar with this unusual pattern in patients imaged with FDG-PET/CT and suffering from severe autoimmune diseases or being treated with TNF inhibitors.

Conflicts of Interest None.

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