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CASE REPORT

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Spontaneous regression of follicular lymphoma on FDG PET/CT; A case report

Peter Choi[1], Alex Newbury[2] and Lacey J McIntosh[2*]

[1]University of Massachusetts Medical School, 55 Lake Avenue, North, Worcester, MA 01655, USA
[2]Department of Radiology, University of Massachusetts Medical School, 55 Lake Avenue, North, Worcester, MA 01655, USA

Abstract

Spontaneous regression of follicular lymphoma (FL) is a rare event without much documentation in the literature. We report the case of a 64-year-old male who was incidentally found to have multiple enlarged retroperitoneal lymph nodes on an abdominal CT. PET-CT revealed increased FDG avidity in a retroperitoneal lymph node with subsequent core-needle biopsy confirming follicular lymphoma. As the patient was asymptomatic, observation and non-medical management was recommended. Repeat PET-CT imaging showed spontaneous regression by seventeen months and the patient remained in remission 3.5 years later.

Keywords: *spontaneous regression; follicular lymphoma; PET-CT*

Case Report

A 64-year-old male with a history of diabetes, hypertension, chronic kidney disease, and coronary artery disease presented to the Emergency Room for abdominal trauma and was incidentally found to have several enlarged retroperitoneal lymph nodes with the largest in the left periaortic region measuring 2.9 cm x 2.4 cm (Figure 1a). These lymph nodes were deemed indeterminate but raised the possibility of lymphoma. At subsequent hematology/oncology consultation, the patient denied any fever, night sweats, or weight loss. He had no family history of hematologic malignancies or blood dyscrasias, and no smoking history. Physical exam was unremarkable without palpable lymphadenopathy or hepatosplenomegaly. Complete blood count was within the normal range, with hemoglobin level of 10.5 g/dL (baseline), platelet level of 160,000/mm3, white blood cell count of 6,000/mm3, and an LDH of 231 U/L.

Due to concerns of a low-grade lymphoma, FDG PET/CT was performed two months later for further characterization and biopsy planning, which demonstrated persistent mildly enlarged retroperitoneal lymph nodes with moderate to intense FDG uptake with an SUVmax = 5.7 and given a classification of Deauville 4 (Figure 1a and b). Targeted core-needle biopsy (Figure 2b) the following month showed B cells of follicular origin and flow cytometry showed a clonal B cell population (6% of total cellularity) positive for CD20, CD19, CD10, BCL2, BCL6 and negative for CD5, TdT, cyclin D1. The proliferative index of the tumor, as quantified with Ki-67, was 50-60% and classified as a low-grade follicular lymphoma. Given incidental diagnosis in an asymptomatic patient, and the typical chronic indolent course of follicular lymphoma, a "watch and wait" course of observation employing surveillance FDG PET/CT ensued.

Follow up FDG PET/CT four months later (Figure 1c and d) showed a resolution in all but the dominant left periaortic lymph node, which had slightly decreased in size measuring 2.6 cm x 1.8 cm but with persistent increased FDG uptake with a SUVmax

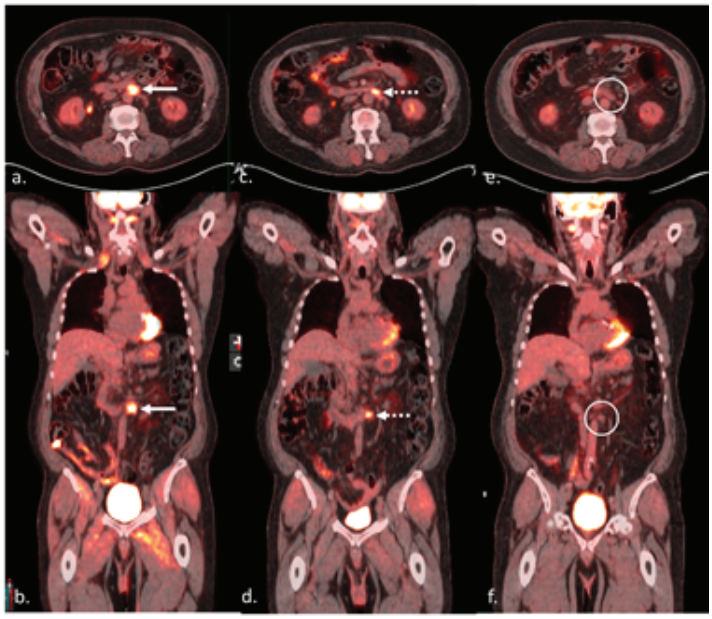

Figure 1. *Serial FDG PET/CT showing complete spontaneous regression of follicular lymphoma in a 64-year-old male. Baseline axial (a) and coronal (b) fusion images demonstrate a moderately to intensely FDG avid mildly enlarged retroperitoneal lymph node (white arrows) with an SUVmax of 5.7. As this patient was asymptomatic, he was managed with observation and a follow up FDG PET/CT performed 4 months later (c and d) showed slight decrease in size of the lymph node which continued to demonstrate intense FDG uptake (dashed white arrows). FDG PET/CT obtained approximately one year later (e and f) demonstrates complete resolution of FDG uptake and normalization of the lymph node (white circles) in the absence of any treatment or intervention, consistent with a complete spontaneous regression. At present, the patient remains symptom and disease free on FDG PET/CT and by laboratory and clinical evaluation.*

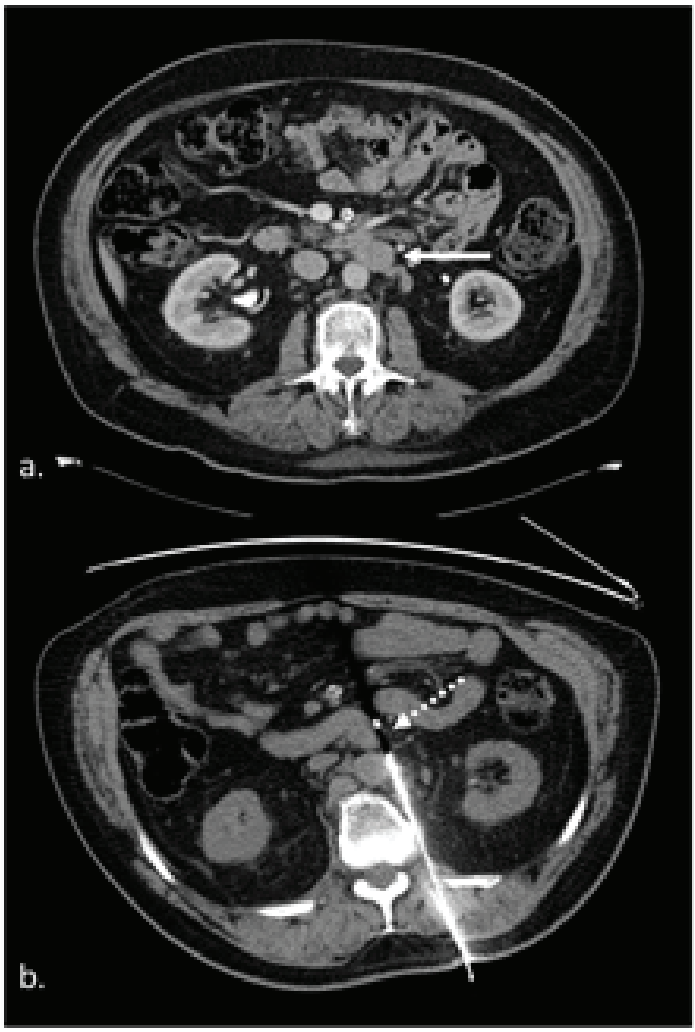

Figure 2. *Diagnostic and biopsy CT images in a 64-year-old male with enlarged retroperitoneal lymph nodes, suspicious for lymphoma. Axial contrast enhanced (a) and axial noncontrast (b) images demonstrate the dominant enlarged left periaortic lymph node measuring 2.9 cm x 2.4 cm (white arrow). Biopsy images demonstrate the sampling needle traversing the periphery of the abnormal lymph node with open sample trough (white dashed arrow). Pathology revealed follicular lymphoma.*

= 6.4, and classified as Deauville 4, slightly improved. As such, observation continued. Subsequent FDG PET/CT at seven months showed slight further regression of the retroperitoneal lymph node measuring 1.8 x 0.9 cm with a SUVmax = 2.5 and classified as Deauville 3. FDG PET/CT one and a half years after initial detection demonstrated normalization of the lymph node and complete resolution of FDG uptake. Durable resolution continues to be seen on serial FDG PET/CT, currently 3.5 years after diagnosis, and the patient has remained asymptomatic without palpable lymphadenopathy or laboratory abnormalities, apart from chronic anemia secondary to known chronic kidney disease.

Discussion and conclusion

Follicular lymphoma (FL) is the second most common lymphoma diagnosed in the United States and Western Europe [1], accounting for approximately 35% of all non-Hodgkin lymphomas and 70% of indolent lymphomas [2]. Patients with FL generally present with asymptomatic lymphadenopathy, which may wax and wane for years. Less than 20% of patients present with B symptoms, and similarly, less than 20% of patients present with increased serum lactate. FL cells typically express monoclonal immunoglobulin light chain, CD19, CD20, CD10, and BCL-6 protein due to a t(14:18) translocation [2]. Transformation to diffuse large B cell lymphoma occurs in 10-70% of patients over time, with a risk of 2% per year [3]. Medical treatment depends on histologic grade, presence of symptoms or organ dysfunction, and disease tempo.

Spontaneous regression is defined as the complete or partial resolution of a tumor without administration of immunochemotherapy. Patients with indolent lymphoma have higher rates of spontaneous regression compared to high-grade Non-Hodgkin's Lymphoma (NHL) such as diffuse large B-cell lymphoma with one study citing a spontaneous regression rate of 10-20% [4]. However, spontaneous regression of follicular lymphoma is still considered to be uncommon with few cases followed by serial FDG PET/CT as a part of surveillance found in the literature.

Here, we describe a case of spontaneous regression of asymptomatic follicular lymphoma that was followed with serial FDG PET/CT on a "watch and wait" management strategy. In this report enlarged paraaortic lymph nodes were detected incidentally on imaging performed for trauma and was ultimately found to be FL on biopsy. Without intervention, local, or systemic therapy, the patient achieved a complete spontaneous regression over approximately one and half years after the initial CT scan and remained free from any new or residual FDG avid disease at 3.5 years in follow-up. Several groups have reported similar cases of spontaneous regression of low-grade NHL, including FL, in the literature. In a retrospective review, Gattiker et al. identified 18 patients who demonstrated spontaneous regression of FL out of 140 cases, six of which demonstrated complete remission [5]. Similarly, Horning identified 19 cases of spontaneous regression out of a group of 83 patients with low-grade NHL [4,5].

Spontaneous regression is not unique to lymphoma and the initial immunomodulatory stimulation theory proposed by Cole and Everson in 1956 continues to provide the foundation for contemporary hypotheses. Specifically, they reported significant spontaneous tumor regression of myosarcoma of the thigh and papillary bladder cancer after diagnostic biopsy [6]. While the precise mechanism continues to be unclear, some groups have posited that tumors are a means of evading the immune surveillance and that trauma to the tumor bed exposes tumor-specific antigens to the host immune system, also known as the so-called "danger model [7]." Still others have proposed spontaneous regression may be initiated by modulation of the immune system secondary to concurrent bacterial or viral infection or in the setting of acute inflammation [8].

Despite the mechanism remaining elusive, our case highlights the importance of how FDG PET/CT plays an important role in diagnosis, staging, and monitoring treatment response in lymphoma, and as illustrated in this case, is often used to guide biopsy planning. This imaging modality was the mainstay in monitoring disease course in this asymptomatic patient without significant laboratory abnormalities or palpable disease. FDG PET/CT continues to play a role for this patient for careful monitoring for disease relapse. Fortunately, this case demonstrated the uncommon disease course of a complete spontaneous regression of follicular lymphoma.

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***Correspondence:** Lacey J. McIntosh, Department of Radiology, University of Massachusetts Medical School, 55 Lake Avenue, North, Worcester, MA 01655, USA, E-mail: lacey.mcintosh@umassmemorial.org

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