**18F-FDG PET/CT imaging of atypical subacute thyroiditis in thyrotoxicosis**

A case report

Katsuya Yoshida, MD, Hitokata Yokoh, MD, Akira Torihara, MD, Hayahiko Fuji, MD, Naoki Harata, MD, Jun Isoi, MD, Ukhide Tateishi, MD

**Abstract**

**Background:** In addition to its established role in oncologic imaging, 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) is useful for the assessment of inflammatory activity. However, subacute thyroiditis (SAT) in thyrotoxicosis is rarely detected during these scans.

**Case:** A 66-year-old man with SAT in thyrotoxicosis demonstrated symptoms of transient fatigue, headache, and fever, without typical neck pain. Using 18F-FDG PET/CT, we found increased 18F-FDG uptake in the thyroid gland, predominantly in the right side due to SAT. We also observed a coexisting decrease in 18F-FDG uptake in the liver and increased 18F-FDG uptake in skeletal muscle due to thyrotoxicosis.

**Conclusion:** Using 18F-FDG PET/CT, the combined observations of increased 18F-FDG uptake in the thyroid and skeletal muscle, and decreased 18F-FDG uptake in the liver, even when the typical symptom of neck pain is subtle or absent, may be helpful for the differential diagnosis of SAT in thyrotoxicosis.

**Abbreviations:** 18F-FDG = 18F-fluorodeoxyglucose, CRP = C-reactive protein, FT3 = free triiodothyronine, FT4 = free thyroxine, PET/CT = positron emission tomography/computed tomography, ROI = region of interest, SAT = subacute thyroiditis, SUVmax = maximum standardized uptake value, SUVmean = mean standardized uptake value, TgAb = antithyroglobulin antibody, TPOAb = anti-TPO antibody, TSH = thyroid-stimulating hormone, US = ultrasonography.

**Keywords:** 18F-FDG PET/CT, case report, subacute thyroiditis, thyrotoxicosis

---

**1. Introduction**

Thyrotoxicosis secondary to subacute thyroiditis (SAT) spontaneously resolves as the thyroid hormone is depleted. This condition is often followed by transient or persistent hypothyroidism. Painful (DeQuervain’s or granulomatous) SAT is a common form characterized by painful swelling of the thyroid gland, which usually follows upper respiratory tract infections, and suggests a viral infection and autoimmune reaction. Painless SAT, including postpartum thyroiditis, which is histologically similar to Hashimoto’s thyroiditis, and drug-related destructive thyroiditis are less common.

To the best of our knowledge, there have been only 4 published cases of SAT in which patients underwent 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT). For 2 of these cases, thyrotoxicosis was reported, and the remaining case report had no data from thyroid function tests. All cases demonstrated increased 18F-FDG uptake in the thyroid; however, 18F-FDG uptake in the skeletal muscle and liver was not reported. Conversely, thyrotoxicosis has been identified in patients with Grave’s disease, for whom increased skeletal muscle 18F-FDG uptake and combined increased skeletal muscle and decreased liver 18F-FDG uptake were reported by Zhang et al and Chen et al respectively.

Here, we reported a case of SAT in concurrence with thyrotoxicosis, without the typical symptom of neck pain. The patient underwent 18F-FDG PET/CT, and we observed increased 18F-FDG uptake in the thyroid and skeletal muscle, and decreased 18F-FDG uptake in the liver.

**2. Patient information**

A 66-year-old man visited the emergency department (ER) of our hospital, complaining of fatigue, headache, and transient fever. There were no symptoms of a recent viral illness, no prior history of taking medications, and no family history of autoimmune thyroid disease.
3. Clinical findings
The patient had no significant abnormalities on physical examination and returned home. Neck pain was not apparent.

4. Timeline
A timeline illustrating the sequence of events, from clinical findings, diagnostic assessment, and therapeutic intervention throughout the patient’s treatment at our hospital is presented in Fig. 1.

5. Diagnostic assessment
Three days later, the patient underwent a complete medical checkup, including 18F-FDG PET/CT, which is mainly used for cancer screening in the health screening center of our hospital. The patient still suffered from mild fatigue on the day of the checkup. Blood tests showed high C-reactive protein (CRP) (4.22 mg/dL; normal range <0.15) and low total cholesterol (117 mg/dL; normal range 120–219) levels. However, the CRP level decreased and total cholesterol level increased (0.29 mg/dL and 182 mg/dL, respectively) 25 days later.

The 18F-FDG PET/CT scans were performed in accordance with the Japanese Society of Nuclear Medicine’s 2012 guidelines for 18F-FDG PET cancer screening. Data were collected using a PET/CT scanner (Siemens Biograph LSO DUO, Knoxville, TN) at 100 minutes after the intravenous injection of 18F-FDG (3 MBq/kg body weight), following overnight fasting, as described previously.[8] In order to compare liver and muscle 18F-FDG uptake to that of healthy controls, we analyzed 11 consecutive control subjects (7 men, 4 women; age 54–75 years), who underwent 18F-FDG PET/CT as a part of their regular medical checkups, using the same imaging protocol and during the same time period as patient imaging (August 18 to 27, 2015). The patient’s blood glucose level was 116 mg/dL, while that of the controls ranged from 78 to 119 mg/dL.

On the 18F-FDG PET/CT images (Figs. 2 and 3), we observed increased 18F-FDG uptake in the thyroid gland, predominantly on the right side, with a maximum standardized uptake value (SUVmax) of 8.8 by drawing a region of interest (ROI) surrounding the region of thyroid FDG uptake. Additionally, we measured 18F-FDG uptake in the liver and skeletal muscle by drawing spherical ROIs (15–20 mm radius for the liver and 12–15 mm radius for skeletal muscle). The mean standardized uptake value (SUVmean) was higher for the skeletal muscle of the patient with SAT (averaged for the bilateral deltoid muscles, psoas muscles, and quadriceps muscles), than for skeletal muscle in the 11 control subjects (Table 1). Furthermore, the SUVmean of the patient’s liver was lower compared to that of the controls (Table 1). A symmetrical and diffuse increase in 18F-FDG uptake in the patient’s skeletal muscle was also demonstrated visually as shown in Fig. 1.

Ten days after visiting the ER, the patient was referred to the otolaryngology department after complaining of hoarseness and underwent rhino-laryngo fiberscopy. However, there were no abnormal findings.

Figure 1. Timeline of patient information, clinical findings, diagnostic assessment, and therapeutic intervention.

Figure 2. Maximum intensity projection image of 18F-FDG PET/CT (18F-fluorodeoxyglucose positron emission tomography/computed tomography) revealing an increase in diffuse and symmetrical 18F-FDG uptake in skeletal muscle, in addition to high 18F-FDG uptake in the relatively enlarged right thyroid lobe. 18F-FDG = 18F-fluorodeoxyglucose, PET/CT = positron emission tomography/computed tomography.
The patient was referred to the endocrinology department 11 days after visiting the ER, with no remaining clinical symptoms other than fatigue. Thyroid tests revealed low thyroid stimulating hormone (TSH) (<0.01 mIU/L; normal range 0.35–4.94), high free triiodothyronine (FT3) (7.42 pg/mL; normal range 1.71–3.71), high free thyroxine (FT4) (1.95 ng/dL; normal range 0.7–1.48), and high thyroglobulin (265 ng/mL; normal range, <32.7). Antithyroglobulin antibody (TgAb) (<6.00 IU/mL; normal value, <13.6), anti-TPO antibody (TPOAb) (<3.00; normal value, <3.2), and TSH receptor antibody (0.4%; normal value, <15) were not elevated. The thyroid stimulating antibody titer was slightly higher than normal (147%; normal range, <120), but returned to normal (102%) 9 months later. Three days later, thyroid ultrasonography (US) was performed, identifying a relatively enlarged right lobe (right lobe 20×14×41 mm, left lobe 11×11×32 mm), with a heterogeneous hypoechoic pattern. SAT in thyrotoxicosis was diagnosed based on the combined clinical observations, laboratory data, US findings, and 18F-FDG PET/CT images.

Table 1

| Organs                  | Patient | Controls |
|-------------------------|---------|----------|
| Liver                   | 1.54    | 1.70–2.42|
| Deltoid muscle          | 1.04    | 0.58–0.96|
| Psoas muscle            | 1.14    | 0.58–0.93|
| Quadriceps muscle       | 1.41    | 0.59–0.80|

18F-FDG = 18F-fluorodeoxyglucose, PET/CT = positron emission tomography/computed tomography.

4. 18F-FDG uptake in the liver and skeletal muscle.

6. Therapeutic intervention

Two months after visiting the ER, thyroid tests revealed high levels of TSH (14.47 mIU/L), normal FT3 (3.16 pg/mL), and low FT4 (0.67 ng/dL), which suggested hypothyroidism; therefore, hormone replacement therapy was commenced. The patient has continued to maintain an euthyroid state 15 months after commencing therapy.

7. Discussion

In the present case of SAT, a prior history of viral infection was unclear and the typical symptom of neck pain was absent. However, the following characteristics were concordant with painful SAT: TPOAb and TgAb titers were not elevated, CRP level was transiently elevated, US and PET findings suggested an asymmetrical thyroid disorder, and the patient had no prior history of taking medications, such as amiodarone. Previously, Daniels[9] reported 9 cases of atypical SAT, in which patients also had minimal or no complaints of thyroid pain. Furthermore, TPOAb tests yielded negative results in 8 of these patients. The clinical findings in our case study were consistent with these observations.

There has been only 1 community-based epidemiologic study on painful SAT, which was performed in Olmsted County, Minnesota, and reported an incidence of 4.9 cases per 100,000 persons per year.[10] However, this low incidence rate could be an underestimate, which does not include misdiagnosed cases of SAT, in which patients presented with subtle or no neck pain. Neck pain is one of the key diagnostic criteria for painful SAT. If this symptom is subtle or absent in patients with thyrotoxicosis, SAT may be missed during initial examinations. Likewise, in the present case study, we attribute our patient’s SAT going undetected during our initial examinations to the absence of neck pain.

Painful SAT can involve one or both lobes of the thyroid, either diffusely or focally. Nishihara et al[11] reported that 581/852 (68%) patients developed unilateral neck pain at the onset of painful SAT. Using the US examination, they also found a unilateral hypoechoic area in the thyroid of 19/42 (45%) patients within 7 days after onset. Park et al[12] also reported notable US features in painful SAT, showing unilateral thyroid involvement in 23/27 (85%) patients. In addition to its established role in oncological imaging, 18F-FDG PET/CT has clinical utility for identifying infection and inflammation, because 18F-FDG uptake reflects inflammatory activity.[21] In the existing literature, 3 of 4 reported cases of SAT demonstrated asymmetrical 18F-FDG uptake in the thyroid.[3–5] In agreement with these reports, our patient demonstrated increased 18F-FDG uptake in the thyroid, predominantly on the right side of the gland.

In the present case study, 18F-FDG uptake was decreased in the liver and increased in skeletal muscle. These findings suggest that the changes in our patient’s glucose metabolism mimic those observed in patients with hyperthyroidism caused by Graves’ disease.[6–7] Hyperthyroidism is associated with increased glucose production, absorption, and utilization through a variety of actions of thyroid hormones on many organs, particularly the liver, muscle, pancreas, and adipose tissue.[13–15] Specifically, gluconeogenesis and glycogenolysis are induced in the liver, hepatic glucose output is increased, and skeletal muscle glucose uptake is increased to maintain euglycemia and overcome a depletion in glycogen stores. Although the molecular and
intracellular mechanisms of thyroid hormone regulation are complex and still under investigation, there are direct effects of thyroid hormones that regulate glucose metabolism at the liver and peripheral tissues. The expression of glucose-6-phosphatase and GLUT-2 are increased at the liver, resulting in increased gluconeogenesis, glycogenolysis, and glucose output at the liver. The expression of GLUT-1 and GLUT-4 are increased at peripheral tissues, resulting in increased basal and insulin-induced glucose transport at peripheral tissues. Thyroid hormones also have indirect effects of on the liver via a sympathetic pathway, which connects the paraventricular hypothalamus.

Focal FDG uptake in the thyroid gland is one of the incidental findings encountered during the routine clinical use of FDG PET/CT. It is not only caused by malignancy, but also by a variety of benign lesions such as nodular hyperplasia, Hurthle cell and follicular neoplasms, and even chronic lymphocytic thyroiditis. Barrio et al. demonstrated that 845/6212 (13.6%) patients with nonthyroidal cancers had a thyroid incidentaloma, and 21 of the 98 patients who underwent fine-needle aspiration biopsy or thyroidectomy had malignant disease (21.4%), whereas the others (78.6%) had benign tumors. Increased FDG uptake in skeletal muscle and decreased uptake in the liver are also observed in a variety of pathological and physiological conditions. In other words, the individual findings were insufficient on their own, and a combination of clinical observations, laboratory data, and US and PET findings was needed to reach the final diagnosis of SAT. Furthermore, radioiodine uptake measurement and thyroid scintigraphy are useful for the evaluation of hyperthyroidism and thyrotoxicosis, although those were not performed in this case.

The SUV is widely used in clinical FDG PET/CT as a relative measure of glucose metabolism, and many factors can affect it. Busing et al. analyzed FDG uptake (SUV) in normal organ tissues including skeletal muscle in 90 patients with blood glucose levels ranging from 30 to 372 mg/dL, and showed that increased blood glucose levels were associated with increased skeletal muscle FDG uptake. However, the SUV_max of skeletal muscle did not differ significantly between patients with blood glucose levels ranging from 80 to 100 mg/dL and those with levels from 100 to 120 mg/dL. There was also no significant association between blood glucose levels and the SUV_max of the liver. In the present report, the blood glucose levels of the patient and controls ranged from 78 to 119 mg/dL, implying that the influence of blood glucose levels on FDG uptake in the liver and skeletal muscle could be negligible.

In conclusion, this case study highlights the utilization of 18F-FDG PET/CT for the differential diagnosis of SAT. We have demonstrated that the combined observations of increased 18F-FDG uptake in the thyroid and skeletal muscle, and decreased liver 18F-FDG uptake, may be useful for the differential diagnosis of SAT in thyrotoxicosis. These findings are particularly significant, given that atypical SAT may be accompanied with little or no neck pain, and therefore can be difficult to identify using standard diagnostic procedures.

References

[1] Hennessey JV, De Groot LJ, Chrousos G, Dungan K, et al. Subacute Thyroiditis. Endotext MDText.com, Inc, South Dartmouth, MA:2000.
[2] Meller J, Sahlmann CO, Scheel AK. 18F-FDG PET and PET/CT in fever of unknown origin. J Nucl Med 2007;48:35–45.
[3] Lambert M, Jourret F, Lonneux M, et al. Mismatch of F-18 fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) and Tc-99m pertechnetate thyroid scan in subacute thyroiditis. Acta Clin Belg 2008;63:209–10.
[4] Song YS, Jiang SJ, Chung JK, et al. F-18 fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) and Tc-99m pertechnetate scan findings of a patient with unilateral subacute thyroiditis. Clin Nucl Med 2009;34:456–8.
[5] Yeo SH, Lee SK, Hwang I, et al. Subacute thyroiditis presenting as a focal lesion on [18F] fluoro-2-deoxyglucose whole-body positron emission tomography/CT. Am J Neuroradiol 2011;32:E58–60.
[6] Zhang Q, Miao Q, Ye H, et al. The effects of thyroid hormones on brown adipose tissue in humans: a PET-CT study. Diabetes Metab Res Rev 2014;30:513–20.
[7] Chen YL, Chen YK, Tsui CC, et al. The significance of alteration 2-[fluorine-18]fluoro-2-deoxy-(D)-glucose uptake in the liver and skeletal muscles of patients with hyperthyroidism. Acad Radiol 2013;20:1218–23.
[8] Ryu Y, Yoshioka K, Suzuki Y, et al. Long-term changes of aortic 18F-FDG uptake and calcification in health-screening subjects. Ann Nucl Med 2013;27:239–46.
[9] Daniels GH. Atypical subacute thyroiditis: preliminary observations. Thyroid 2001;11:691–5.
[10] Fatourechi V, Aniszewski JP, Fatourechi GZ, et al. Clinical features and outcome of subacute thyroiditis in an incidence cohort: Olmsted County, Minnesota, study. J Clin Endocrinol Metab 2003;88:2100–5.
[11] Nishihara E, Ohye H, Amino N, et al. Clinical characteristics of 852 patients with subacute thyroids before treatment. Intern Med 2008;47:725–9.
[12] Park SY, Kim EK, Kim MJ, et al. Ultrasonographic characteristics of subacute granulomatous thyroiditis. Korean J Radiol 2006;7:229–34.
[13] Brenta G. Why can insulin resistance be a natural consequence of thyroid dysfunction? Journal of Thyroid Research 2011;2011:152850.
[14] Muller R, Liu YY, Brent GA. Thyroid hormone regulation of metabolism. Physiol Rev 2014;94:353–82.
[15] Sethra RA, Singh BK, Yen PM. Thyroid hormone regulation of hepatic lipid and carbohydrate metabolism. Trends Endocrinol Metab 2014;25:538–45.
[16] Barrio M, Czernin J, Yeh MW, et al. The incidence of thyroid cancer in 15,000 patients. Nucl Med Commun 2016;37:1290–6.
[17] Garberoglio S, Testori O. Role of nuclear medicine in the diagnosis of benign thyroid diseases. Front Horm Res 2016;45:24–36.
[18] Busing KA, Schonberg SO, Brade J, et al. Impact of blood glucose, diabetes, insulin, and obesity on standardized uptake values in tumors and healthy organs on 18F-FDG PET/CT. Nucl Med Biol 2013;40:206–13.