Diagnostic clue of nodular fasciitis mimicking metastasis in papillary thyroid cancer, mismatching findings on ^{18}F-FDG PET/CT and ^{123}I whole body scan: A case report

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Abstract. This study reports a case of nodular fasciitis incidentally detected in a patient with papillary thyroid cancer. A 47-year-old woman underwent a total thyroidectomy and radioactive iodine therapy for papillary thyroid cancer. On a follow-up fluorodeoxyglucose (^{18}F-FDG) PET/computed tomography (CT) scan after 12 months, a focal ^{18}F-FDG-avid lesion was incidentally detected in the paraspinal muscle. It was well-enhanced on CT and magnetic resonance imaging, indicating metastasis. However, the lesion was not iodine avid on the ^{123}I whole body scan, which favored benign etiology over metastasis from thyroid cancer. For pathological confirmation, surgical excision was performed and the paraspinal lesion was finally confirmed as nodular fasciitis. Therefore, it was suggested that nodular fasciitis may be included in the differential diagnosis of a ^{18}F-FDG avid/iodine non-avid soft tissue lesion in patients with thyroid cancer. In such circumstances, ^{123}I whole body scans may serve a role in non-invasive work-up, and prevent unnecessary surgical procedures.

Introduction

Nodular fasciitis is a benign soft tissue tumor that is characterized by the proliferation of fibroblasts and myofibroblasts in the deep subcutaneous layer, as well as the muscular fascia (1). Its occurrence is common in the upper extremities of young to middle aged adults and is equal in distribution among men and women. Its risk factors remain unknown and it is often mistaken for soft tissue malignancy or metastasis (2,3). Complete excision is currently the gold standard for diagnosis and treatment. Nodular fasciitis exhibits good prognosis with a low recurrence rate and thus, is considered benign (3). There are few case reports on the clinical implications of nodular fasciitis using ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT), in which ^{18}F-FDG uptake was distributed to areas of rich cellularity and high mitotic activity (4,5). The present study exhibits a case of nodular fasciitis incidentally detected on ^{18}F-FDG PET/CT in a patient followed up for papillary thyroid cancer (PTC).

Case report

A 47-year-old woman was diagnosed with PTC and was admitted to Ulsan University Hospital (Ulsan, Republic of Korea) in March 2013 for a total thyroidectomy. The final pathological stage was T3N1b in accordance with the American Joint Committee on Cancer staging system (6), with a size of 0.9x0.9x0.8 cm extending to the perithyroidal soft tissue with a clear resection margin and no lymphovascular invasion, and 9 lymph node metastases in the left cervical levels II-IV. Radioactive iodine therapy of 150 mCi was performed.

A 12-month follow-up using ^{18}F-FDG PET/CT revealed an unexpected focal ^{18}F-FDG-avid lesion (SUV_{max}, 9.8) in the left paraspinal muscle at the T3 level (Fig. 1A and B). Enhanced chest CT and magnetic resonance imaging (MRI) were performed to evaluate the possibility of metastasis. The two modalities showed a well-enhanced nodule of 9 mm, indicative of metastasis (Fig. 1C and D). No abnormalities were observed in the laboratory findings at that time. The levels of thyroid stimulating hormone, thyroglobulin (Tg), thyroxine (T4) and anti-Tg antibodies measured using chemiluminescence immunoassays were 0.017 μIU/ml, <0.1 ng/ml, 1.85 ng/dl and <20 IU/ml, respectively. An ^{123}I diagnostic whole body scan, which was performed to exclude metastasis from thyroid cancer, showed no abnormal iodine uptake in the left upper back (Fig. 2). These findings favored a benign condition over metastasis. The level of stimulated Tg at this time was 0.89 ng/ml.

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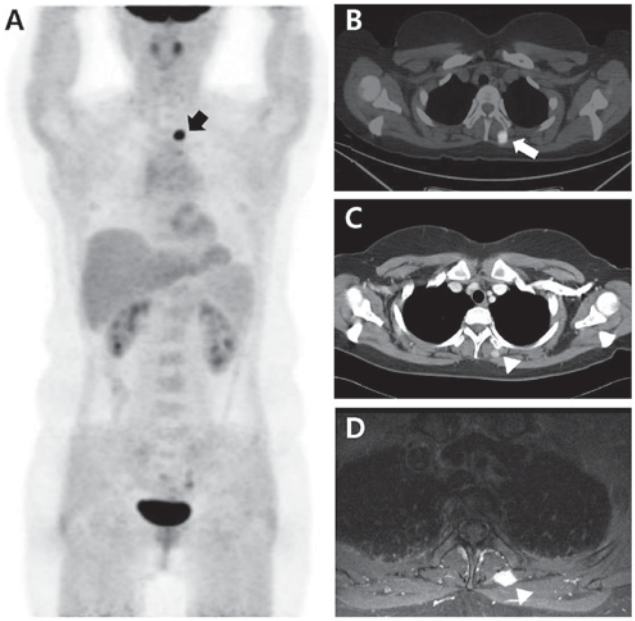

Figure 1. Fluorodeoxyglucose PET/CT shows a focal hypermetabolic lesion in the left paraspinal muscle at the level of T3 on (A) maximum intensity (black arrow) and (B) axial fused PET/CT images (white arrow). (C) Enhanced CT and (D) magnetic resonance imaging show a well-demarcated nodule with enhancement (white arrowhead). PET, positron emission tomography; CT, computed tomography.

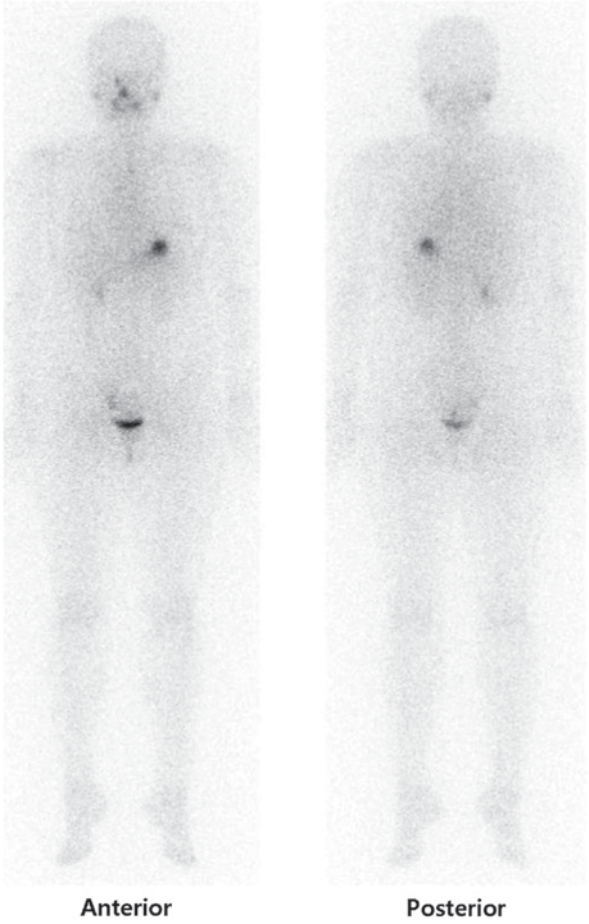

Figure 2. ^{123}I diagnostic whole body scan shows no abnormal iodine uptake associating with the hypermetabolic lesion in the left paraspinal muscle. Focal iodine uptakes in the major salivary gland areas, nasal cavity, upper abdomen and pelvic cavity are presumed to result from physiological activities.

Surgical excision was performed and the pathological diagnosis was nodular fasciitis. The gross pathological specimen was a 1.7x1.1 cm well demarcated firm mass (Fig. 3). Following hematoxylin and eosin staining, the specimen was observed under a light microscope (Olympus BX51; Olympus Corporation, Tokyo, Japan). Spindle cells were identified to be arranged in storiform fascicles and normal mitotic figures were present (Fig. 3). Immunohistochemical analysis for CD68 (cat. no. M0876; dilution, 1:200; Dako; Agilent Technologies, Inc., Santa Clara, CA, USA), smooth muscle actin (cat. no. 18-0106; dilution, 1:250; Invitrogen; Thermo Fisher Scientific, Inc., Waltham, MA, USA), CD34 (cat. no. MS-363-P; dilution, 1:1,000; Thermo Fisher Scientific, Inc.) and S-100 protein (cat. no. LCL-L-S100P; dilution, 1:1,000; Novocastra; Leica Biosystems GmbH, Wetzlar, Germany) were performed on formalin-fixed paraffin-embedded 4 μm-thick tissue sections using Bond-Max with a Bond Polymer Refine Detection kit (Leica Biosystems GmbH) according to the manufacturer's protocol. All antigen vs. antibody reactions were performed with a Bond Polymer Refine Detection kit (Leica Biosystems GmbH), and non-specific binding was blocked by the hydrogen peroxide in the kit according to the protocol of the manufacturer. The specimen exhibited positive expression levels of CD68 (Fig. 4A) and smooth muscle actin (Fig. 4B), while CD34 (Fig. 4C) and S-100 (Fig. 4D) proteins were not expressed (Fig. 4).

No additional treatment was performed. At a 9-month follow-up post-excision, the patient was disease-free, with an unstimulated Tg level of <0.01 ng/ml.

Discussion

This is a case of nodular fasciitis, which was mistaken for muscle metastasis, in a patient being followed up for PTC.

The majority of thyroid cancers are localized at the time of diagnosis with only a small proportion (10-35%), depending on the histology, presenting with distant metastasis (7,8). This proportion is only 4-15% in the case of differentiated thyroid cancers (7,8). Common sites of metastasis include the lungs and bones (8-11), while soft tissue metastasis is reportedly extremely rare (12-14). Although distant metastasis in patients with thyroid cancer is not as grave as that in other cancers, it significantly affects survival; therefore, a thorough work-up including ^{18}F-FDG PET/CT is required (9,15,16).

^{18}F-FDG PET/CT visualizes glucose metabolism and is widely used to differentiate between benign and malignant lesions, as well as to stage/restage various malignances (17-22). In a number of cases, the intensity of FDG accumulation is used to differentiate between malignant and benign lesions (23-26). However, numerous other benign conditions, including abscess, pulmonary granuloma, tuberculosis and sarcoidosis, may also present with increased ^{18}F-FDG uptake (23,27-32). Thus, there is a high chance of encountering false-positive conditions in a clinical setting.

The patient in the present case showed a focal ^{18}F-FDG avid lesion that did not show abnormal iodine uptake, and the patient exhibited a low stimulated Tg level. The differential diagnosis in this case includes primary (such as schwannoma, dermatofibroma and sarcoma) and metastatic (from

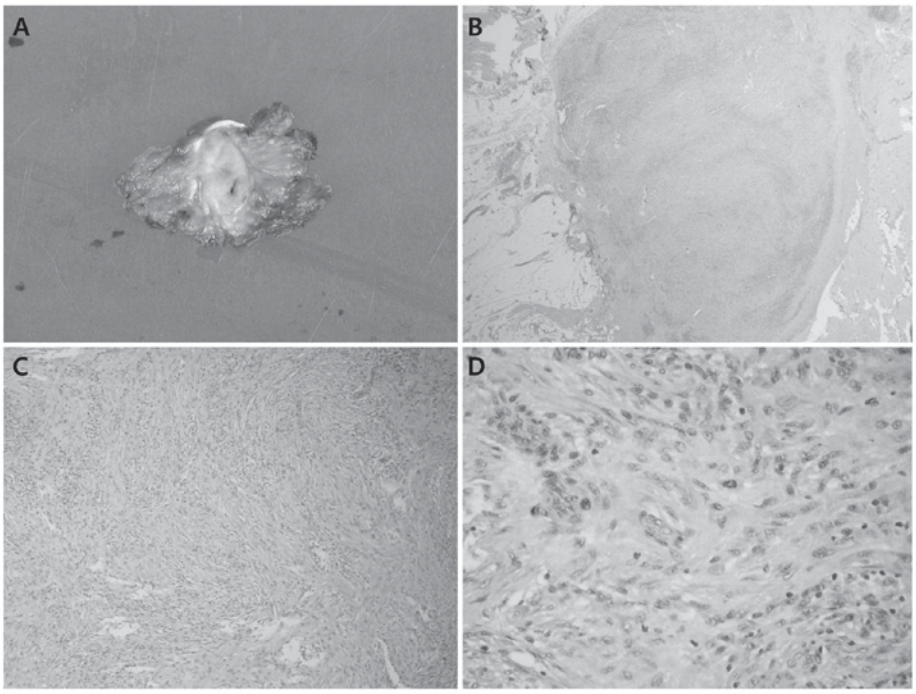

Figure 3. (A) Gross inspection of the pathological specimen shows a well-demarcated, firm soft tissue mass of 1.7x1.1 cm, with a tan white, solid and smooth cut surface. Tissue sections were stained with hematoxylin and eosin and magnified by (B) x20, (C) x100 and (D) x400. The specimen is partially encapsulated with focal capsular infiltration and is composed of spindle cells. The tumor cells are arranged in storiform fascicles. The uniform plump tumor cells with pale nuclei show normal mitotic figures in the image magnified by x400.

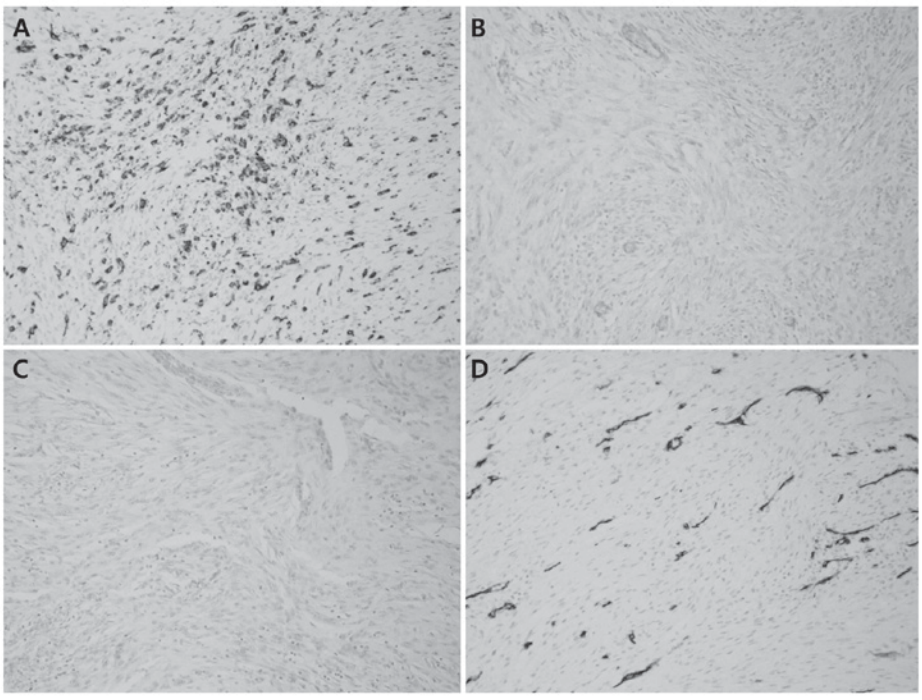

Figure 4. Pathological specimens exhibit positive expression levels of (A) CD68 and (B) smooth muscle actin following immunohistochemical analysis. (C) CD34 and (D) S-100 proteins are not expressed (magnification, x200).

dedifferentiated thyroid cancer or other malignancies) tumors (33,34). The ^{18}F-FDG avid lesion in the current patient turned out to be nodular fasciitis.

Nodular fasciitis is a benign condition, which shows proliferating fibroblasts in the deep subcutaneous layer or the muscular fascia (35). Nodular fasciitis is occasionally clinically mistaken for soft tissue sarcoma. If there is infiltration of mitotically active spindle cell lesions in the connective tissue (35), pathological diagnosis is difficult. The lesion commonly occurs in the first 3 decades of life, with the upper extremities and the trunk being the most commonly affected anatomical sites (36,37). Lesions usually present as

oval nodules with poorly- or well-defined margins, and occasionally microlobulation on CT, MRI and ultrasonography (US) (1,38,39). Lesions show mixed but overall hypoechoic echogenicity on US, as well as variable but typically diffuse contrast enhancement on MRI (1,38,39). Although surgical excision is curative, it usually shows spontaneous involution and is self-limiting (40).

The present case is in agreement with other case reports that describe ^{18}F-FDG-avid nodular fasciitis (4,5,33). The high ^{18}F-FDG uptake in nodular fasciitis may be due to its histological characteristics that are also present in malignancy. These include rapid growth, rich cellularity and high mitotic activity (4,5). Thus, nodular fasciitis is hard to diagnose and the high ^{18}F-FDG uptake may be a limitation of ^{18}F-FDG PET/CT as it mimics malignancy, as in other radiological and pathological modalities as above mentioned (2,3,34-37). To the best of our knowledge, there are no studies on nodular fasciitis mimicking metastasis in PTC. However, since nodular fasciitis exhibited high FDG avidity in the present case, metastasis of PTC could not be excluded and additional diagnostic work-up was necessary. The present histological findings were similar to those aforementioned.

In the present case, the ^{18}F-FDG-avid paraspinal lesion was excised, since the imaging modalities showed findings indicative of soft tissue metastasis. When the lesion was retrospectively reviewed, it had an increased probability of being a primary soft tissue lesion compared with metastasis from thyroid cancer, partly as the patient had a relatively low level of stimulated Tg (0.89 ng/ml) and the ^{123}I whole body scan showed negative iodine uptake. Although these findings may also be shown in the case of a poorly-differentiated metastatic lesion, soft tissue metastasis from thyroid cancer, which is considered a manifestation of a terminal stage, is rare and is usually accompanied by multiple metastases in other sites.

In summary, the present study reported a case of nodular fasciitis with FDG avidity in a patient with thyroid cancer. Nodular fasciitis may be included in the differential diagnosis of an ^{18}F-FDG-avid and iodine non-avid paraspinal soft tissue lesion, when clinical probability of distant metastasis is low. In such circumstances of patients with thyroid cancer, unnecessary surgical procedures may be prevented using a ^{123}I whole body scan as a part of non-invasive work-up.

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