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Fluorine-18-Fluorodeoxyglucose Uptake in Rheumatoid Arthritis-Associated Lung Disease in a Patient with Thyroid Cancer

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An ¹⁸F-fluorodeoxyglucose (FDG) whole-body PET scan was performed on a thyroid cancer patient with long-standing rheumatoid arthritis who presented with pulmonary nodules. A recent diagnostic radioiodine whole-body scan was negative. However, the ¹⁸F-FDG scan demonstrated intense uptake in the chest lesions as well as in several joints affected by rheumatoid arthritis. Fine-needle aspiration of a pulmonary nodule revealed inflammatory reaction and absence of malignant cells, fungus and tuberculous infection. A repeat chest CT scan after 7 mo of steroid therapy showed a marked decrease in the size and number of nodules. In thyroid cancer patients, ¹⁸F-FDG uptake in the lung may not necessarily represent pulmonary metastases. This case illustrates a benign, unrelated pathology namely, rheumatoid arthritis-associated lung disease.

Key Words: fluorine-18-fluorodeoxyglucose; PET; rheumatoid arthritis; thyroid cancer; false-positive results

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Fluorine-18-fluorodeoxyglucose (FDG) PET imaging has a proven role in the assessment of patients with cancer (1). It has been useful in detecting suspected or proven recurrence and/or metastases of differentiated thyroid cancer (2). Since differentiated thyroid cancer is not uncommon, coexistent unrelated pathology in thyroid cancer patients may represent a diagnostic problem. We report on a thyroid cancer patient who presented with chest lesions with ¹⁸F-FDG uptake due to rheumatoid arthritis-associated lung disease.

CASE REPORT

A 57-yr-old woman with long-standing rheumatoid arthritis and a history of papillary thyroid cancer presented with pulmonary nodules on a chest radiograph. The patient had a 12-yr history of rheumatoid arthritis with secondary Sjogren's syndrome. Two years earlier, she had a right, followed by complete, thyroidectomy

for a large cold nodule in the right lower lobe. The histology showed a follicular variant of papillary thyroid cancer confined to the thyroid gland. A laboratory workup showed an erythrocyte sedimentation rate of 69 mm/hr, a rheumatoid factor of 43 IU/ml (normal range 0-19) and positive for antinuclear antibodies (speckled) 1:640 with a diagnostic 555 MBq (15 mCi).

A ¹²³I whole-body scan showed 18% neck uptake, for which the patient received 4440 MBq (120 mCi) ¹³¹I treatment. An initial chest radiograph revealed several pulmonary nodules that were subsequently shown on a chest CT scan (Fig. 1A). One year later, a follow-up chest CT scan showed an increase in the size and number of pulmonary nodules as well as some cavitation (Fig. 1B and 1C). A concurrent radioiodine diagnostic scan was negative (thyroid-stimulating hormone 170 mU/liter; thyroglobulin 2.6 μ/liter). Sputum samples were consistently negative for tuberculosis and malignancy. Several months later, a whole-body ¹⁸F-FDG PET scan 1 hr postinjection of 370 MBq (10 mCi) showed corresponding uptake in all lung nodules as well as in several joints (Fig. 2). A CT scan-guided fine-needle aspiration of the lesion in the basal part of the right lung revealed giant inflammatory cells and the absence of malignant cells, fungus and tuberculous infection.

The patient was given 40 mg prednisone orally daily for 5 wk, with a gradual tapering of the dose to 10 mg daily over a period of 8 wk. A chest CT scan 7 mo later showed considerable resolution of the chest lesions (Fig. 1D). The patient had no clinical, biochemical or scintigraphic evidence of persistent or recurrent thyroid cancer up to 2.5 yr after radioiodine treatment and was maintained on thyroxine 150 μg and prednisone 10 mg daily.

DISCUSSION

We present rheumatoid arthritis-associated lung disease causing FDG uptake in a patient with papillary thyroid cancer. The presence of pulmonary nodules on a routine chest radiograph suggested pulmonary metastases. The absence of radioiodine uptake in the chest lesions together with the undetectable thyroglobulin levels argued against it.

Fluorine-18-FDG uptake was noted in all nodules seen on the CT scan as well as in the inflamed joints. The scan appearance

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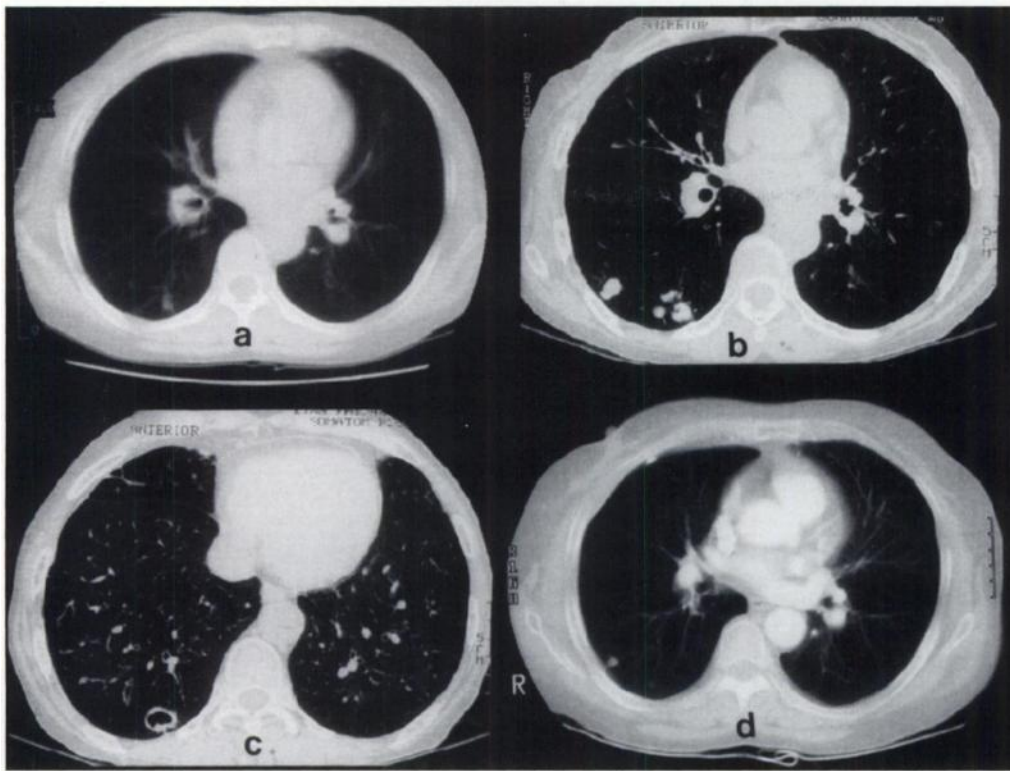


FIGURE 1. (A) Initial chest CT scan showing a small nodule in the lower lobe of the right lung. (B) A follow-up CT scan of the chest, 1 yr later, showing an increase in the number and size of the pulmonary nodules as well as cavitation (C). (D) Scan of chest 7 mo after steroid treatment showing considerable resolution of pulmonary nodules.

was nonspecific and could represent multifocal pulmonary metastases as well as rheumatoid nodules. However, the rapid progression and cavitation of the pulmonary nodules along with the long-standing history of rheumatoid arthritis and Sjogren's syndrome favored diagnosis of rheumatoid nodules. This was confirmed pathologically, and the patient was treated with high-dose steroids. A follow-up chest CT scan at 7 mo showed a marked decrease in size and number of rheumatoid nodules. Pulmonary involvement in rheumatoid arthritis could be in the form of diffuse interstitial fibrosis, single or multiple nodules in the lung parenchyma or a pleural effusion, and it may lead to cavitation (3).

The lung uptake in this patient is not unexpected since ^{18}F -FDG is not a cancer-specific agent (1) and has been reported in association with sarcoidosis (4), tuberculosis (5), fungal infections (1) and other inflammatory conditions such as pancreatitis (6) and abdominal (7) and brain abscesses (8). Moreover, ^{18}F -FDG uptake has been noted in active synovitis in rheumatoid arthritis patients. The quantification of synovial deoxyglucose metabolism correlates well with standard outcome measures and has been suggested to assess disease activity and effectiveness of antirheumatoid medications (9).

Despite these reported cases of ^{18}F -FDG uptake in associa-

tion with benign inflammatory diseases, whole-body ^{18}F -FDG PET scanning has a proven role in evaluating single pulmonary nodules (10) and in assessing patients with different neoplasms (1). The value of ^{18}F -FDG whole-body imaging has been documented in the follow-up of thyroid cancer patients (2,11,12). Previous studies documented intense ^{18}F -FDG uptake in pulmonary metastases that concentrated relatively little ^{131}I (11). Thyroid cancer metastases that have ceased to accumulate ^{131}I after treatment with radioiodine may still be demonstrated with ^{18}F -FDG (12). Whole-body ^{18}F -FDG scintigraphy may be useful in cases of suspected recurrence and/or metastases of differentiated thyroid cancer, but it is particularly useful in cases with negative radioiodine whole-body scans and elevated thyroglobulin levels (2).

CONCLUSION

We report on a patient with a history of thyroid cancer who demonstrated ^{18}F -FDG uptake in rheumatoid arthritis-associated lung disease as well as in arthritic joints. Inflammatory rheumatoid nodules should be added to the causes of ^{18}F -FDG uptake in the lung and should be considered in thyroid cancer patients with long-standing rheumatoid arthritis, especially when



FIGURE 2. (A,B) Fluorine-18-fluorodeoxyglucose PET whole-body scan acquired without attenuation correction showing intense uptake in pulmonary nodules as well as in elbow joints.

the radioiodine scan is negative and the thyroglobulin level is undetectable.

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Thallium-201 Uptake with Negative Iodine-131 Scintigraphy and Serum Thyroglobulin in Metastatic Oxyphilic Papillary Thyroid Carcinoma

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We report a case of a 48-yr-old woman who underwent surgery because of papillary oxyphilic thyroid carcinoma pT3. After total thyroidectomy, we administered 2960 MBq ^{131}I for ablation of the residual tissue. Initial follow-up visits showed no clinical, radiological or scintigraphic evidence of residual or metastatic thyroid tissue. Serum thyroglobulin levels (Tg) and ^{131}I whole-body scintigraphy were negative. Three years after thyroidectomy, the patient experienced seizures, and as a consequence a brain tumor was removed. It was an undetected metastasis of the primary thyroid carcinoma. Histological examinations showed that neither the primary tumor nor the metastasis produced any Tg. With this fact in mind and the knowledge of negative ^{131}I whole-body scans we had to concentrate on radiological (CT and MRI scans) and nonspecific scintigraphic methods such as ^{201}Tl whole-body scintigraphy in our management of the patient. Further follow-up demonstrated multiple metastasis by ^{201}Tl whole-body scan (mediastinum, bones and soft tissue), and most of them have been removed by surgery. This case report demonstrates that, in addition to ^{131}I whole-body scans and measurement of serum Tg, the use of nonspecific tracers like ^{201}Tl is important to detect ^{131}I and/or Tg negative metastases.

Key Words: thallium-201; iodine-131; serum thyroglobulin; thyroid carcinoma; negative Tg expression

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In the follow-up of differentiated thyroid carcinoma, ^{131}I whole-body scan, ultrasonography of the neck, measurement of serum Tg levels and nonspecific radionuclides and tracers such as ^{201}Tl , $^{99\text{m}}\text{Tc}$ -sestamibi or $^{99\text{m}}\text{Tc}$ -tetrofosmin are in use. The combination of these methods is considered to give the best diagnostic results and the biggest benefit for the patient (1-7). Some studies emphasize the diagnostic capabilities of ^{201}Tl scans in the management of patients with differentiated thyroid

carcinoma (8-12). It has been well known for years that there are some patients with elevated serum Tg, but negative, even post-therapeutic, ^{131}I whole-body scans representing metastatic disease. Our case report refers to a patient in whom neither ^{131}I whole-body scan nor increase in serum Tg gave evidence of developing metastases. Thallium-201 scans were the only nuclear medicine imaging techniques that showed pathologic uptake.

CASE REPORT

A 48-yr-old woman was referred to our department after thyroidectomy because of a papillary oxyphilic carcinoma pT3. We administered an ablative ^{131}I therapy with 2960 MBq. Iodine-131 whole-body scan showed uptake in the remnants but no pathological extrathyroidal uptake; the Tg serum measurement was also negative (<0,5 ng/ml, recovery 114% (Tg-Selco Medipan, Germany); functional assay sensitivity 0,5 ng Tg/ml). Clinical and radiological findings confirmed the absence of metastatic activity. During further follow-up 4 mo after radioiodine ablation of the remnant, no pathological ^{131}I uptake was seen and the Tg level after withdrawing L-thyroxine treatment (bTSH >30 mU/l) was <0.5 ng/ml, indicating complete remission. Three years after thyroidectomy, the patient underwent brain surgery because of seizures, and a tumor was removed. Histological examination showed a metastasis of the primary thyroid carcinoma. Because of the absence of any signs of metastatic activity before brain surgery (negative ^{131}I whole-body scan, negative Tg with a recovery between 70%-130% and negative Tg antibodies during the follow-up), we investigated the Tg expression on both the primary and the metastatic tumor (Fig. 1). Neither the primary carcinoma nor the brain metastasis produced any Tg.

For further follow-up, in addition to ^{131}I whole-body scan and serum Tg measurement, we performed a ^{201}Tl whole-body scan (20 min after intravenous injection of 74 MBq ^{201}Tl) using a dual-head, high-resolution camera. Only the ^{201}Tl scan showed a pathological activity in the mediastinal region (Fig. 2). Findings were confirmed

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