Differentiated thyroid cancer: Case report of false positive ^{131}I uptake on whole body scintigraphy in a patient with bilateral femur osteonecrosis

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Abstract

Objective: Differentiated thyroid cancer (DTC) is one of the fastest growing cancers worldwide. Despite the generally good prognosis of thyroid carcinoma, about 5% of patients will develop metastatic disease, exhibiting a more aggressive behavior. Radioiodine whole-body scintigraphy (WBS) has been used in the detection of DTC. Radioiodine is a sensitive marker for detection of thyroid cancer; however, radioiodine uptake is not specific for thyroid tissue. It can also be seen in healthy tissue as well as in inflammation, or in a variety of benign and malignant non-thyroidal entities. **Subject and Methods:** The subject of the present case report is a 52 years old man with brain metastatic DTC who received radioiodine therapy and corticosteroids as palliative therapy. Whole-body scintigraphy revealed bilateral iodine uptake of the femur. Corticosteroid therapy is among the most widely recognized risk factor for osteonecrosis, which at the present case had to be recognized as a false positive (iodine-131) ^{131}I uptake in order to avoid diagnostic error. **Results:** Post therapeutic whole body scintigraphy revealed no uptake in the thyroid bed as well as pathologic uptake of radioiodine in both femurs. The magnetic resonance imaging (MRI) of the femurs combined with the history of long term exposition on high doses of corticosteroids evidenced diagnosis of steroid-induced osteonecrosis of the femurs. **Conclusion:** Radioiodine WBS plays an important role in clinical decision making for the evaluation and the management of patients with DTC. Despite its high range of sensitivity and specificity, a variety of reports of false positive whole body scans has demonstrated a diversity of causes. Comprehension of the physiology of iodine uptake and of the pathophysiology of clinical entities which end up giving false positives scans, provides clinicians a useful tool in order to avoid diagnostic and therapeutic errors as far as DTC is concerned.

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Introduction

Differentiated thyroid cancer (DTC) which is a favorable malignant tumor, includes papillary and follicular cancer and constitutes approximately 90% of all thyroid cancers [1]. This type of thyroid cancer is accossiated with a lower risk of death compared with other malignancies [2]. The 10-year overall cause-specific survival for patients with DTC is estimated at 85%, as the 10-year survival rate in cases of distant metastasis does not exceed 25%-40% [3-5]. Female sex, race, age especially between 20 and 50 years old, genetic background, family history and exposure to moderate levels of radiation to the head and neck, particularly in childhood age are risk factors known to increase the chance of developing thyroid cancer [6]. According to current medical studies, ionizing radiation is the best documented risk factor for thyroid cancer based on the anatomical position and radiosensitivity of thyroid tissue [7, 8]. Relative risk is linearly related to exposure dose, starting as low as 0.1Gy, and at least up to 30Gy. The latency period after exposure is at least 3 to 5 years and according to studies, the relative risk is increased even after 40 years in comparison to non-irradiated population [9, 10]. The therapy of DTC includes total thyroidectomy, selective neck dissection, radioiodine therapy (RAIT) and thyroid stimulating hormone (TSH) suppressive thyroid hormone treatment [11, 12]. Radioiodine therapy is defined as the systemic administration of 131-sodium or potassium iodide for selective irradiation of thyroid remnants, microscopic DTC or other non-resectable or incompletely resectable DTC as well as metastatic disease, either as a component of primary treatment of DTC or to address persistent or recurrent disease [13]. This method of treatment is generally well-tolerated which targets thyroid cells so there is little exposure to

the rest of body's cells. As for the follow-up of differentiated thyroid cancer after total thyroidectomy and thyroid ablation, serum Tg determination and iodine-131 (^{131}I) diagnostic whole-body scan (WBS) performed in the hypothyroid state 6-12 months after thyroid ablation are mainly used.

The present case report describes a 52 years old male patient who appeared with brain metastatic DTC and received RAIT under the administration of corticosteroids. The following post-therapy whole body scan revealed no iodine uptake in thyroid bed, physiologic uptake in the liver as well as pathologic uptake in both femurs. Post therapeutic whole body scintigraphy is acquired to localize ^{131}I uptake with a specificity which ranges between 96%-100%. False positive results of ^{131}I are described in malignant and non-malignant diseases other than thyroid cancer, including pathologies such as a vascular necrosis which was observed in our patient [14-16].

Osteonecrosis, also known as a vascular necrosis or ischemic necrosis of the femoral head, is a pathologic process that results from interruption of blood supply to the bone. Risk factors are several but in 5%-25% osteonecrosis occurs in patients who take corticosteroids [17]. However, only 8% to 10% of patients exposed to corticosteroid therapy may develop osteonecrosis. More specifically, a dosage >2gr of prednisone or its equivalent is associated with the disease which appears within a 2 to 3 months period. However, the period from the beginning of corticosteroid treatment to the diagnosis of osteonecrosis ranges from 1 to 16 months on average 5.3 months. The majority of patients are diagnosed within 12 months [18].

Case report

A 52 years old man with metastatic thyroid cancer was admitted in our department for further treatment. At the age of 17 there was a history of metastatic squamous cell carcinoma from the nasopharynx with no recurrence found at follow up for 29 years. At the age of 46 he underwent total thyroidectomy and selective node neck dissection and was diagnosed with metastatic (to lymph nodes) differentiated papillary thyroid cancer (DPTC). Till the time he referred to our department he had already received a total amount of 200mCi of ^{131}I in other institutions. Three years after initial diagnosis he presented in our department and received radioiodine therapy of 150mCi. Post therapeutic whole body scintigraphy showed no thyroid remnants or distant metastases. A brain magnetic resonance imaging (MRI) which was performed a year later showed metastases of the frontal and temporal lobe. In order to avoid cerebral oedema radioiodine therapy was excluded at least until the patient had undergone metastasectomy. Following, he underwent external brain radiotherapy of 30Gy utilizing linear accelerator. After neurosurgery our patient was set in corticosteroid treatment. He has been receiving 15mg of dexamethasone per day for three weeks. Under the administration of corticosteroids, our patient received a fourth dose of 200mCi of ^{131}I in our hospital. Post therapeutic whole body scintigraphy showed no thyroid remnants or distant metastases. During surveillance the following year, nodal locoregional recurrence in the neck was detected and treated with modified neck dissection followed by radioiodine therapy of 250 mCi that the 52 years old man received in our department. Post therapeutic whole body scintigraphy revealed no uptake in the thyroid bed as well as pathologic uptake of radioiodine in both femurs. The MRI of the femurs which was performed right after, combined with the history of long term exposition on high doses of corticosteroids evidenced diagnosis of steroid-induced osteonecrosis of the femurs.

Results

Post therapeutic whole body scintigraphy revealed no uptake in the thyroid bed as well as pathologic uptake of radioiodine in both femurs. The MRI of the femurs which was performed right after, combined with the history of long term exposition on high doses of corticosteroids evidenced diagnosis of steroid-induced osteonecrosis of the femurs.

Discussion

Radioiodine whole body scan plays an important role in clinical decision making for the evaluation and the management of patients with DTC. It is a highly accurate and cost-effective post-thyroidectomy imaging procedure combined with serum thyroglobulin (Tg) determinations and ultrasound evaluation of the neck in order to manage DTC. Whole body scan can detect thyroid tissue remnants after total thyroidectomy and local nodes and distant metastaseseither after surgery or during the follow-up of DTC [19]. Despite its high range of sensitivity and specificity, a variety of reports of false positive whole body scans has demonstrated a diversity of causes such as effusions, tumors, delayed excertion, contamination, retention and functional NIS expression [20]. False positive uptakes on radioiodine scintigraphy are not only result of the normal metabolic circuit of iodine but also due to several other machanisms. Among these are described: increased perfusion, vasodilatation, enhanced capillary permeability, accumulation of inflammatory exudates and mucous secreted by the hypertrophied glands and mucinous cells, inflammatory reaction and retention of radioiodine in the leukocytes or in clots, passive diffusion and retention of radioiodine, intravascular blood pooling etc. Comprehension of the physiology of iodine uptake and of the pathophysiology of clinical entities which end up giving false positives scans, provides clinicians a useful tool in order to avoid diagnostic and therapeutic errors as far as DTC is concerned [21]. Iodine uptake is medicated via the sodium/iodine symporter-NIS (iodization), a transmembrane protein expressed by the basolateral membrane of the thyrocytes. The main role of NIS is to transport actively iodide, which is required for thyroid hormone synthesis, against concentration and electrochemical gradients [22, 23]. NIS expression is regulated by TSH. Its expression in other tissues except thyroid gland, reflects iodine accumulation in such regions [19].

In this particular clinical case a differential diagnosis had to

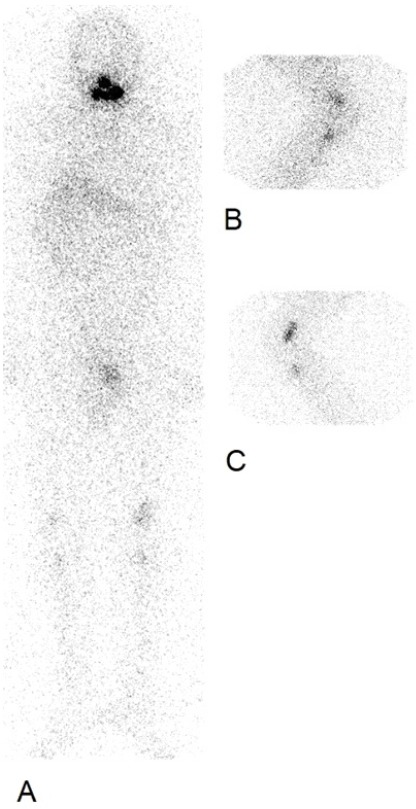

Figure 1. (A) Iodine-131 whole body scintigram and planar images of the right (B) and the left (C) knee show radiopharmaceutical uptake in femoral condyle together with a similar region within the proximal tibial metaphysis of both knees.

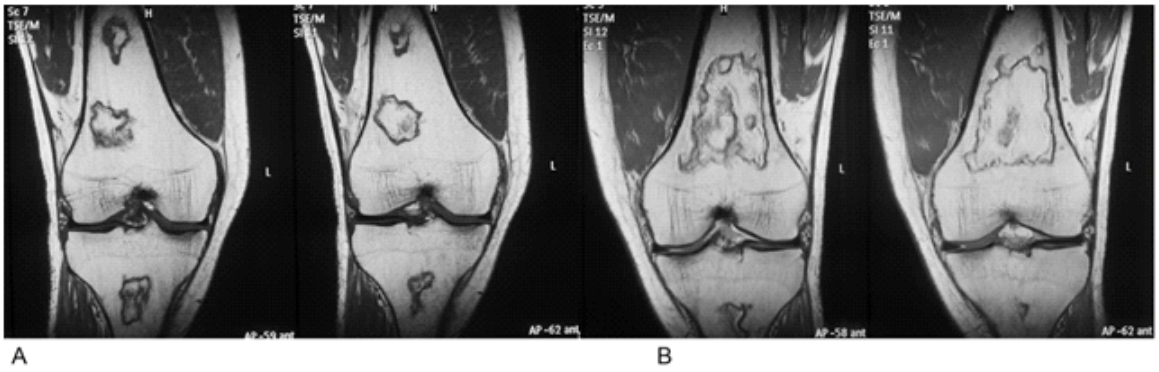

Figure 2. Coronal MRI of right (A) and left (B) knee, show a clearly defined area of bone avascular necrosis and surrounding oedema within femoral condyle together with a similar region within the proximal tibial metaphysic.

be made in order to exclude bone metastases and reveal osteonecrosis. The effects of corticosteroids on bone and bone vasculature are sufficiently complex to affect both phases of osteonecrosis. Corticosteroids can elevate intraosseous pressure by increasing the synthesis of vasoactive peptides and increasing peripheral vascular resistance [24]. They dysregulate the balance of bone formation and resorption by inducing apoptosis of both osteoblasts and osteocytes, increasing the lifespan of osteoclasts, reducing the production of osteoblasts and diminishing bone formation. In addition to this mechanism, adipogenesis may also restrict the number of osteoprogenitor cells by shifting precursors from an osteocytic to an adipocytic lineage [18, 25].

In conclusion, WBS plays an intrinsic role in the management of patients with DTC. A variety of reports of false positive WBS has demonstrated several causes including effusions, tumors, delayed excertion, contamination, retention and functional NIS expression. In order to avoid diagnostic confusion, created by false positive WBS, further investigation should be done by use of complementary imaging techniques such as computed tomography (CT), single photon emission tomography (SPECT)/CT, MRI orpositron emission tomography (PET)/CT. In occasions when uptake occurs in anatomical sites which are common for metastatic disease, such as in our case, careful evaluation should be done so that the therapeutic decision making, is for the best patient's benefit.

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