

## Case Report

# Concurrent Hip Pain and Skull Lump as the First Manifestations of a Silent Follicular Thyroid Carcinoma

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Received: 9 September 2020; Accepted: 18 September 2020; Published: 23 September 2020



**Abstract:** Follicular thyroid carcinoma is a slowly growing cancer with a generally good long-term prognosis. Distant metastasis from follicular thyroid cancer usually occurs in the lung and bones following a long period after diagnosis and treatment for primary cancer. Occult skull metastasis as the first presentation at diagnosis from follicular thyroid cancer is relatively rare. A 51-year-old woman presented with intermittent pain in her right hip that was treated due to the intensely progressed pain, motor weakness, and difficulty walking. The patient was then referred due to swelling in the forehead. Further evaluation revealed that the frontal swelling and the pathological femoral fractures were manifestations of distant metastases from follicular thyroid cancer. In the presence of swelling in the skull, the metastatic lesion should be considered as a differential diagnosis from a silent primary cancer. This report will be beneficial for general practitioners, surgeons, and internists to recognize unusual distant metastatic manifestations from silent differentiated thyroid cancer.

**Keywords:** follicular carcinoma; thyroid; silent cancer; diagnosis; metastasis

## 1. Introduction

Follicular thyroid carcinoma is considered an indolent tumor with a favorable clinical outcome unless it presents as a metastatic disease [1]. The 10-year survival rate of differentiated thyroid carcinoma is 90% and the rate decreases to 40% in patients with distant metastasis [1,2]. In follicular thyroid cancer, distant metastasis at diagnosis is detected in 3–10% of cases but usually will develop later as a disease progression in 6–20% of patients [2]. The lung and bones are the most common sites of distant metastasis from thyroid cancer [1,3]. Skull metastasis at diagnosis is relatively rare and occurs in 2.5% of patients with thyroid cancer usually after a long period of follow-up [1,3,4].

The presentation of metastatic disease in the first point of care is considered a delayed cancer diagnosis and has recently emerged as a significant challenge in low- and middle-income countries [1,5]. Several factors, including sociodemographic and cultural barriers, in addition to a retarded referral system are associated with a delayed cancer diagnosis. In thyroid cancer, however, early detection and active surveillance are not recommended because they can cause over-diagnosis and over-treatment [6]. Although the incidence of thyroid cancer has tripled during the past 40 years, the mortality rates remain relatively low, suggesting the excess detection of subclinical diseases [6]. Although delayed diagnosis in differentiated thyroid cancer might not affect long term survival, it can affect a patient's

quality of life if the disease presents with distant organ metastasis. We reported manifestations of distant metastases in the skull and proximal femur in a patient with silent follicular thyroid cancer.

## 2. Case Presentation Section

### 2.1. Patient

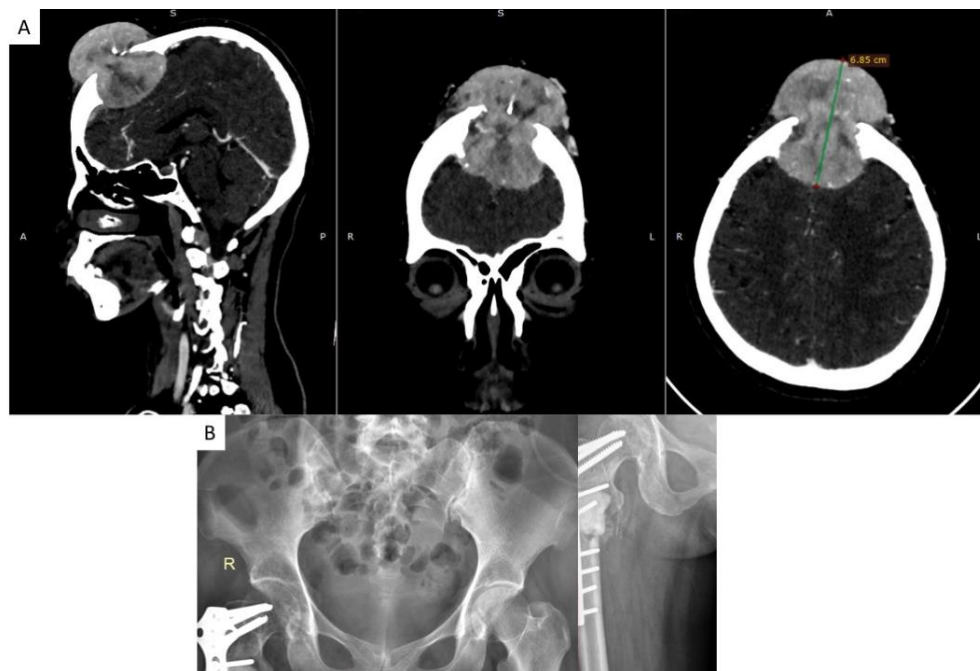
A 51-year-old woman presented with intermittent pain in her right hip and swelling in the forehead for 6 months. She was then brought to an orthopedic hospital because of the intensely progressed pain, motor weakness, and difficulty walking. Written informed consent was obtained from the patient for the presentation in this case report.

### 2.2. Diagnosis

She was diagnosed with a pathological femoral neck fracture and treated with internal fixation. A pathology examination of the bone lesion indicated a metastatic lesion, and she was then referred to our oncology clinic. The painless lump of the frontal skull region was rapidly expansive (Figure 1) in the past 2 months. Inspection of the neck did not show a significant abnormality, while palpation revealed a firm nodule with a clear border in the left thyroid lobe around 3 cm in diameter with positive central neck lymphadenopathy. No sign of thyroid hyperfunctioning was found. A head CT-scan showed a lobulated, heterogeneously contrast-enhancing lesion with a diameter of 7 cm in the frontal region of the cranium (Figure 2). Lytic bone destruction was observed in the overlying frontal lesion. The extra-axial metastatic lesion did not cause midline shift nor ventricular system obstruction. Pelvic X-rays showed lytic lesions in the proximal femur (Figure 2). Needle aspiration biopsy guided with sonography in the thyroid revealed follicular neoplasm and needle biopsy from the skull lump indicated metastatic lesions from well-differentiated thyroid carcinoma. Sonography of the neck showed hypoechoic lesions in the right thyroid lobe with enlargement of the cervical lymph nodes.



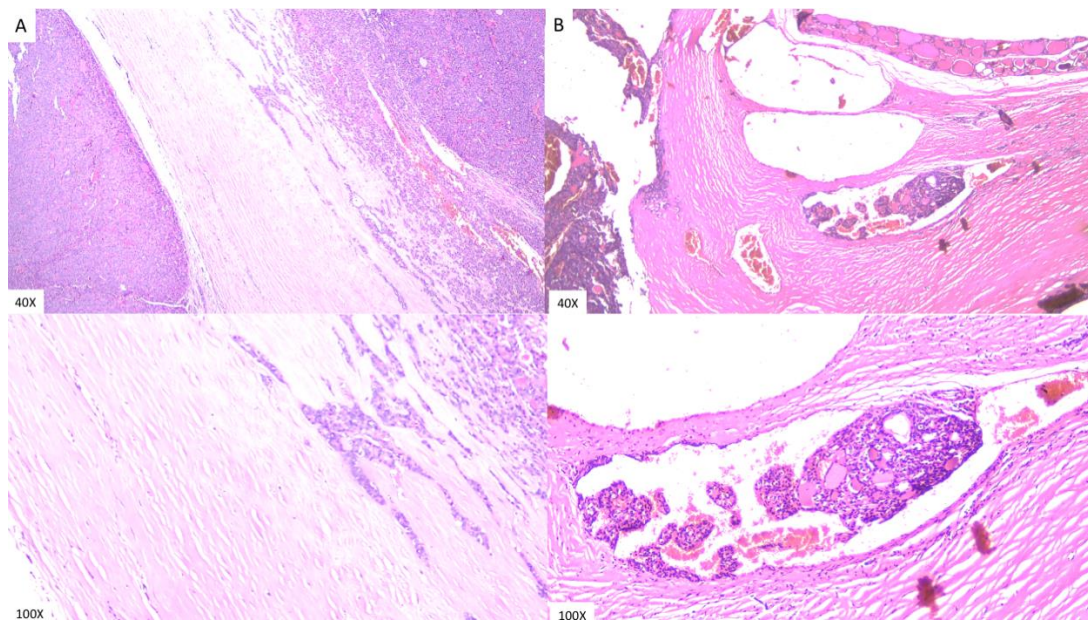
**Figure 1.** Clinical presentation of the skeletal lump in the frontal region.



**Figure 2.** (A) Head CT-scan demonstrated a skull lesion in the frontal region with the overlying lytic bone lesion. (B) Pelvic X-ray showed multiple lytic lesions at the proximal right femur and internally fixated pathological femoral neck fracture from the previous hospital treatment.

### 2.3. Treatment

She was treated with total thyroidectomy and level VI node dissection. A histopathological examination revealed follicular thyroid carcinoma with capsular and vascular invasion (Figure 3). Resected lymph nodes were negative for tumor infiltration. Surgery of the skull lesion was considered as a high-risk procedure because of the proximity to the dural sinuses. Since the metastatic lesion was radioactive iodine-avid, Radioisotope I-131 ablation (RAI) was then delivered after levothyroxine withdrawal at 2 months and 8 months post-surgery. She also received external radiotherapy in the pelvic bone and frontal regions with a cumulative dose of 20 Gy in five fractions. Monthly zoledronic acid and daily levothyroxine suppression in between radioisotope ablation were also routinely administered. After a period of follow-up for 9 months, she expressed that her health was improved. Pelvic pain was significantly reduced although she still independently walked with a crutch.



**Figure 3.** Histology examination revealed that the tumor was arranged in variably-sized follicles containing colloid with capsular invasion (A) and vascular infiltration (B). The cancer cells consisted of polymorphic cells with nuclear enlargement and hyperchromasia.

### 3. Discussion

Thyroid cancer has emerged as the most common endocrine malignancy with significantly increasing incidence over the past few decades [1,5]. Thyroid cancers consist of four subtypes according to the histological differentiation, including papillary, follicular, medullary, and anaplastic thyroid cancer [1]. Papillary and follicular thyroid cancers are considered differentiated thyroid cancer and account for almost 90% of all thyroid cancer [1]. Although differentiated thyroid cancers generally have an excellent prognosis and overall survival, 5–20% of patients develop distant metastasis during the follow-up which has a worse prognosis despite receiving sufficient treatment [3,7].

Pelvic bones and skull account for 20% of all metastatic sites from breast, lung, and prostate cancers. Bone metastases from follicular thyroid cancer are usually multiple, involving long and flat bones such as ribs, sternum, and spine [3]. Metastasis of thyroid cancer to the pelvic bones is rare and accounts for only around 1–4% of all metastasis [3,5]. In addition, skull metastasis at the initial diagnosis is very rare in thyroid cancer ranging from 1.0–2.2% and is usually manifested as a painless soft lump in the occipital region [5]. Predilection sites of skull metastases are at the midline of the frontal and parietooccipital regions as well as in the cranial base at sella turcica, petrous ridge, sphenoid sinus, cavernous sinus, and infratemporal sinus [8]. The most common symptoms of skull metastasis from differentiated thyroid cancer are cranial nerve dysfunction and increased intracranial pressure including hemiparesis, consciousness deficit, and headaches [4]. Most of the reported skull metastases from follicular thyroid cancer were diagnosed following a long period of follow-up after more than 2 years [4,9]. In imaging, metastatic lesions usually appear as local bone destruction and invasion to the adjacent soft tissues that are often misinterpreted as chordoma, melanoma, and chondrosarcoma [4]. At primary diagnosis, our case revealed an unusual case of an osteolytic skull and femoral metastases from silent follicular thyroid cancer. The primary thyroid cancer was not clinically prominent and asymptomatic. In our patient, the main complaint was the pathological fracture in the proximal femur that initiated her to seek medical help. Only two previous reports have shown that large cranial metastases with confined lesions within the dura were presented without any neurological deficit [4,10].

Prognosis of bone metastases from differentiated thyroid cancer is relatively poor with a 10-year survival rate of around 27% [11]. A case series of 12 patients by Nagamine et al. had a mean survival of 4.5 years suggesting that the prognosis might be even worse for patients with bone metastases [9].



Total thyroidectomy and removal of all metastatic lesions remain the first options for the treatment of metastatic differentiated thyroid cancer [2,4]. However, the resection of skull metastases is often not possible because of the potential risk of excessive bleeding and the possible involvement of any vital structure [2,11,12]. In our case, surgical resection was not performed because of the proximity of the metastatic lesion to the cavernous sinus conferring a high risk of profuse bleeding during surgery. In unresectable primary tumors with distant metastatic lesions, external whole-brain radiotherapy should be considered [2,3,12]. Radioactive iodine ablation (RAI) is an essential adjuvant treatment for metastatic differentiated thyroid cancer [2]. Lung metastasis generally responds better to the RAI. However, bone metastases usually do not respond to RAI, causing low remission rates and poor prognosis even after RAI [3]. If possible, surgical removal is the preferred choice of treatment in bone metastases from differentiated thyroid cancer and is associated with better survival particularly in younger patients with a solitary lesion [3,7,13]. In cases with large lesions adjacent to vital brain structures, stereotactic radiation is recommended [2,3]. Despite receiving comprehensive treatment, patients with skull metastases from differentiated thyroid cancer have relatively poor prognoses. However, untreated patients are reported to have even shorter overall survival [14].

In metastatic differentiated thyroid cancer, factors associated with poor prognosis are male gender, older age, incomplete surgical resection, multiple metastases, and poor response to RAI [2,3,5]. The sole intervention that can improve survival is complete surgical resection to achieve both a free margin and local control [2,12]. In the presence of metastasis, total thyroidectomy and resection of metastatic sites are recommended to decrease the tumor load and optimize RAI [2,12,15]. Uptake rates of brain metastasis to radioactive iodine vary between 17% to 23%. Therefore, adjuvant whole-brain radiation therapy, tyrosine kinase inhibitors, or stereotactic radiosurgery should be considered for patients with non-RAI avid metastatic lesions.

The increasing detection rates of thyroid cancer have been associated with the use of imaging to detect small nodules. However, early detection is currently not recommended due to the indirect evidence of overdiagnosis and overtreatment. Over the past decade, the incidence of thyroid cancer increased by 4.5% yearly without any significant increase in mortality rates [1,5]. The current use of imaging for screening and early detection of thyroid cancer has been associated with overdiagnosis and overtreatment of subclinical and low-risk thyroid cancer [5]. However, a lack of cancer awareness in the majority of low-income countries is often related to a delayed diagnosis which adversely affects overall outcomes. Bone and skull metastases from thyroid cancer are associated with significantly decreased functioning, productivity, and quality of life although the overall survival is still relatively high [3,16,17]. Public education regarding the potential risk of widely invasive follicular thyroid cancer is important to prevent delayed diagnosis and impaired functioning due to the advancement of the disease.

#### 4. Conclusions

Skull and proximal femur metastases can arise from silent differentiated thyroid cancer. Although patients with differentiated thyroid cancer generally have excellent overall survival, metastatic disease progression can affect their well-being and quality of life. Although early detection is not generally recommended, improving public awareness concerning the potentially high risk of invasive thyroid cancer is prudent to prevent late presentation and delayed diagnosis.

**Author Contributions:** K.S., W.S.A., H.T.R., and S.L.A. prepared and collected the relevant anamnesis and laboratory findings. W.S.A. analyzed the imaging results, H.T.R. analyzed the histopathology tests, K.S. and S.L.A. collected the clinical data and follow-up. S.L.A. prepared the first draft and finalized the manuscript. All authors have read and agreed to the published version of the manuscript.

**Funding:** No external funding was used for this case report.

**Conflicts of Interest:** The authors declare no conflict of interest.

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