



## **Fracture of the Humeral Bone as the First Clinical Presentation of Metastatic Papillary Thyroid Carcinoma in Ibadan**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Author MAA conceived and designed the study. Author BLA wrote the first draft of the manuscript. Authors EOF, OOA and AAS managed the literature searches. Authors MAA and BLA managed the photomicrographs and the literature review. All authors read and approved the final manuscript.*

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**Case Study**

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### **ABSTRACT**

Papillary thyroid carcinoma is the commonest type of thyroid cancer representing 75 to 85 per cent of all thyroid cancer cases. It is often well-differentiated, slow-growing, and localized, although it can metastasize. This is a case of a 49-year-old male who presented with a pathological fracture of the left humerus. A bone biopsy was done at the surgery which had a histological diagnosis of metastatic thyroid carcinoma. A total thyroidectomy was subsequently done and was histologically reported as a follicular variant of papillary thyroid carcinoma. The patient was clinically stable post-thyroidectomy and was discharged home on the 10<sup>th</sup> postoperative day and he is currently being followed-up in the surgical outpatient clinic. Pathological fracture as the initial clinical presentation is an unusual manifestation of metastatic thyroid carcinoma; therefore a high index of suspicion is needed to make this diagnosis. In any patient presenting with a pathologic fracture, the possibility of metastatic carcinoma from the thyroid gland should always be considered.

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## 1. INTRODUCTION

Thyroid cancers account for only 1.5% of all cancers in adults and 3% of all cancers in children [1]. Of all thyroid cancers, 75-85% of cases are papillary thyroid carcinomas [1,2,3,4]. Papillary thyroid carcinoma [PTC] is the most common form of well-differentiated thyroid cancer, and the most common form of thyroid cancer to result from exposure to radiation. Follicular carcinoma incidences are higher in regions where goitre is common [5]. Thyroid carcinoma occurs in all age groups, with a mean age of 49 years and an age range of 15-84 years. In the younger population, papillary thyroid carcinoma tends to occur more frequently than follicular carcinoma, with a peak in patients aged 30-50 years [3]. PTC appears as an irregular solid or cystic mass or nodule in normal thyroid parenchyma [3]. Despite its well-differentiated characteristics, papillary carcinoma may be overtly or minimally invasive [3]. These tumours may spread easily to other organs. Papillary tumours have a propensity to invade lymphatics but are less likely to invade blood vessels. PTC has several histologic variants, which show different patterns of behaviour. For example, tall cell PTC [TPPTC] is an uncommon but relatively aggressive variant that is more likely to demonstrate invasion, metastasis, and recurrence [6]. The life expectancy of patients with PTC is also related to their age. The prognosis is better for younger patients than for patients who are older than 45 years. Of all patients with papillary thyroid cancers, about 11% present with metastases outside the neck and mediastinum [7]. Papillary carcinoma shows a propensity to invade locally (the thyroid parenchyma, peri-thyroid soft tissues, and rarely the trachea) and to metastasize to regional lymph nodes (the sites of predilection being cervical-central and ipsilateral cervical-lateral nodes) [3]. Local recurrence in the residual thyroid, soft tissues of the neck, or cervical lymph nodes can occur after treatment. Distant metastasis is uncommon (9%-14%) and generally occurs late in the course of the disease, mostly to the lungs and bone [1,2,3,8].

Pathologic fracture of bone as the initial manifestation of metastatic thyroid carcinoma is an uncommon event. Here we present the case of a 49-year-old male who presented with a pathologic fracture of the right humerus as the

initial manifestation of metastatic papillary thyroid carcinoma.

## 2. CASE REPORT

The case is that of a 49-year-old male driver who presented with a pathologic fracture of the right humerus. He had an open reduction and internal fixation (ORIF) done during which a bone biopsy was taken and submitted for histology. The biopsy showed features suggestive of metastatic thyroid carcinoma [Figs. 1 and 2]. He subsequently had a total thyroidectomy done. Macroscopic findings of thyroidectomy specimen showed enlarged right lobe which measured 5x3x2 cm. The isthmus and the left lobe measured 2x1.5x1 cm and 3x2x1 cm respectively. The weight of the specimen was 10 g. The capsule was moderately congested and cut sections through the specimen showed a central yellowish-white nodule in the right lobe that measured 1.5x1 cm.

The specimen was fixed in 10% neutral buffered formalin before surgical grossing. It was afterwards put in tissue cassettes and sent to the lab for processing. It was dehydrated by passing it through a series of increasing concentrations of alcohol, then the dehydrator was cleared with xylene. The tissue was subsequently embedded with paraffin wax and cut into 4 micrometre thick sections using a rotary microtome machine and floated in a water bath, a microscopic glass slide was then used to pick up the cut sections. The glass slides were then placed in a warm oven for about 15 minutes to help the section adhere to the slides. Slide and was subsequently deparaffinized with xylene and stained with haematoxylin and eosin stains. The stained slides were taken through a series of alcohol solutions to remove the water, then through clearing agents to a point at which a glass coverslip was placed on the stained sections. The stained slides were then examined by two Pathologists and a consensus diagnosis of follicular variant of papillary thyroid carcinoma was made.

Histological sections of the thyroid gland showed a malignant epithelial neoplasm [Figs. 3 and 4]. This malignant neoplasm was composed of mildly pleomorphic follicular epithelial cells that were disposed of predominantly in follicles, trabeculae and focal papillary patterns. The component cells had optically clear nuclei,

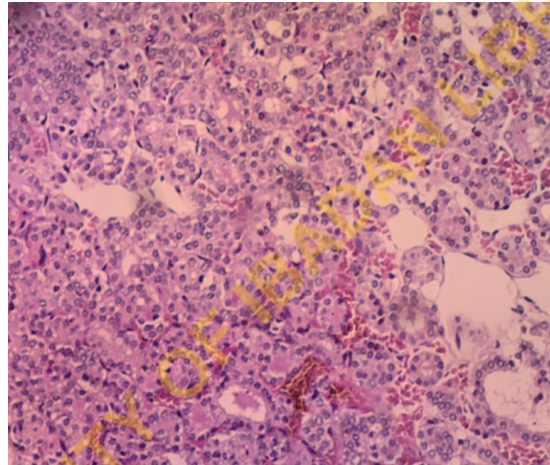
nuclear grooves and nuclear pseudo-inclusions. Some areas also showed prominent oncocytic changes. There was marked stromal fibrosis with some areas containing dystrophic calcifications and psammoma bodies. There were also areas of stromal inflammation and hyalinization. Tumour was also seen invading into the thyroid capsule and beyond it. The overall features are seen were those of a follicular variant of papillary thyroid carcinoma.

The patient was clinically stable post-thyroidectomy. He was discharged home on the 10<sup>th</sup> postoperative day to be followed up at the surgical outpatient clinic. He is also being planned for radioiodine therapy.

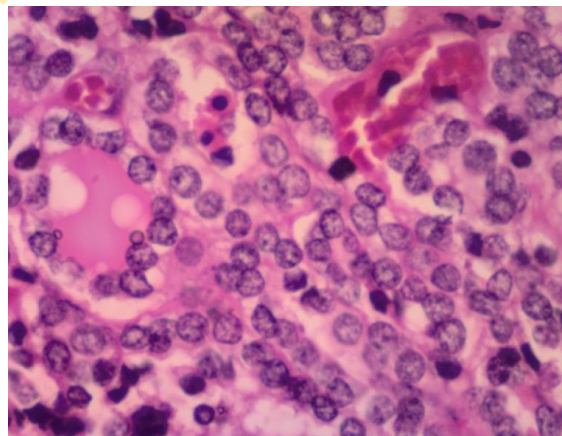
### 3. DISCUSSION

Thyroid cancer is the most common malignancy of the endocrine system, with increasing incidence in the past three decades [9]. Well-differentiated thyroid cancers, including papillary and follicular carcinomas, comprise approximately 85% to 90% of all thyroid cancers and usually have an excellent prognosis following appropriate treatment [10].

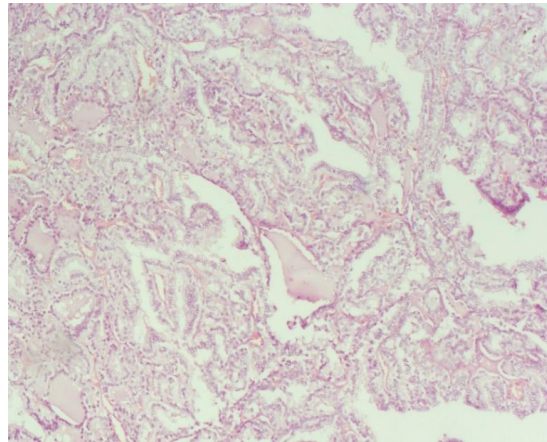
Metastases to the skeletal system from thyroid carcinoma is a well-known event, constituting the second most common systemic site of involvement after the lungs [7]. Depending on the study design, such as duration of follow-up, the



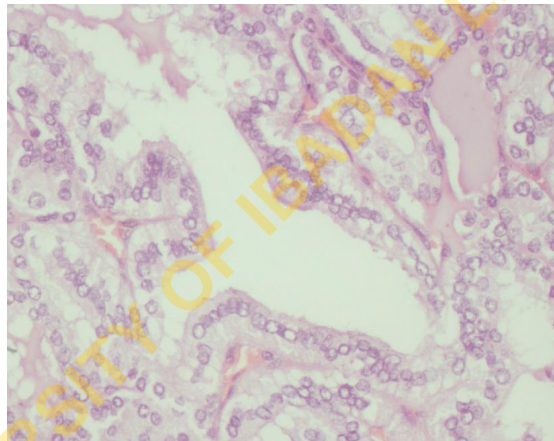
**Fig. 1. Section of the right humeral bone biopsy showing sheets and follicles of malignant follicular epithelial cells having optically clear nuclei, nuclear grooves and nuclear pseudo-inclusion. (Haematoxylin and eosin stains, X40)**



**Fig. 2. Section of the right humeral bone biopsy at high magnification showing sheets and follicles of malignant follicular epithelial cells having optically clear nuclei, nuclear grooves and nuclear pseudo-inclusion. (Haematoxylin and eosin stains, X400)**



**Fig. 3. Section of the thyroid tissue showing malignant follicular epithelial cells disposed in follicles and papillary patterns consistent with papillary thyroid carcinoma. (Haematoxylin and eosin stains, X40)**



**Fig. 4. Sections of the thyroid tissue at high magnification showing malignant follicular epithelial cells disposed in follicles and papillary patterns. The cells have optically clear nuclei, nuclear grooves and nuclear pseudo-inclusion consistent with papillary thyroid carcinoma. (Haematoxylin and eosin stains, X400)**

type of pathology practice (community practice versus large centers with a significant number of referred cases), or the diagnostic parameters used (RAI uptake, histologic evaluation of the resection or biopsy material, or postmortem examination), the overall reported incidence of bone metastasis from thyroid carcinoma has ranged from less than 1% to more than 40% [11]. Distant metastases of papillary carcinoma to lungs and bones occur in 5–7% of cases [12].

Among the different histologic subtypes, follicular carcinoma is most likely to show bone metastases, with reported incidences ranging from 7% to approximately 28% [11]. This contrasts with the index case which had the

histological diagnosis of papillary thyroid carcinoma. Some studies report Hürthle cell carcinoma to be the most common subtype with bone metastases [13,14]. In most studies, papillary carcinoma has been found the least likely subtype to show bone metastases (1.4%–7%) [11]. Among tumours that metastasize to the bone, thyroid cancers are the third most common. Bone metastasis rate in differentiated thyroid carcinomas has been reported to be between 2% and 13%. Bone metastasis is especially common in advanced stages of follicular carcinoma. Bone metastasis in follicular cancer is between 7% and 28%, whereas in papillary thyroid cancer this rate is 1.4–7%. Approximately 12% of Hürthle cell carcinomas

show vertebral metastases [15,16,17]. In medullary thyroid carcinomas; at the time of diagnosis, distant metastases are present in up to 13% of cases and are usually accompanied by elevated calcitonin levels above 150 pg/mL. Metastatic medullary thyroid carcinoma frequently involves multiple sites and often produces multiple metastases at each site [18].

The most common presentation of thyroid cancer is an asymptomatic thyroid mass or a nodule that can be felt in the neck [3]. Some patients with thyroid cancer have a persistent cough, difficulty in breathing, or difficulty in swallowing. Pain is seldom an early warning sign of thyroid cancer [3]. Other symptoms (e.g., stridor, vocal cord paralysis, hemoptysis, rapid thyroid enlargement) are rare and can be caused by less serious problems [3].

Among the cases of distant metastasis, bone metastasis occurred less frequently than lung metastasis [19]. However, bone metastasis was associated with a poorer prognosis when compared to lung metastasis. The mechanisms underlying the tendency of well-differentiated thyroid carcinoma to lead to bone metastasis is not entirely clear [9]. These bone metastases are usually osteolytic and represent an important source of morbidity and mortality in these patients because they may develop severe complications such as pathological fractures and spinal cord compression [9].

In a study done by Pittas et al using 126 patients with thyroid carcinoma who were referred to Memorial Sloan Kettering Cancer Center (MSKCC) between 1960 and 1998, bone metastases were present at the initial diagnosis in 47% of patients [16]. The vertebrae (29%), pelvis (22%), ribs (17%), and femur (11%) were the most common sites of metastases. Multiple lesions were present in 53% of the cases. The overall 10-year survival rate from the time of diagnosis of thyroid cancer was 35%, and from diagnosis of initial bone, metastasis was 13% [20].

Pathologic fractures occur in about 13% of thyroid carcinoma patients with bone metastasis [20] while bone metastasis is silent in up to 6% of cases. [9] Plain radiographs can show bone destruction and sclerosis in the zone of bone metastases, but lesions may not appear on X-rays for several months before a fracture occurs because the limit of detection of lesions is usually

>1 cm [20]. Computerized tomography scan can evaluate the extent of metastatic lesions even in sites difficult to evaluate such as the spine and pelvis and its diagnostic sensitivity for bone-seeking cancers is 71-100% [16]. The overall survival is best in those whose lesions concentrate radioactive iodine and those who have no non-osseous metastasis [9].

The spread of thyroid carcinoma to the bone is more common in patients over 45 years of age and is usually symptomatic, and often multicentric [21]. This also fits the presentation of this index patient who is a 49-year-old male with pathologic fracture of the humerus although only a single metastatic site was seen at presentation. A similar case was reported at the University Hospital Ramon Cajal, Spain by Gonzalez-García et al. [21]. The case was that of an 83-year-old male patient who presented with a pathologic fracture of the humerus as the initial manifestation of a follicular variant of papillary thyroid carcinoma [21].

The treatments for bone metastasis of well-differentiated thyroid carcinoma include radioactive iodide [11,17], surgical resection, external beam radiation therapy, arterial embolization, systemic bisphosphonates or chemotherapy, and percutaneous image-guided treatments [9]. Despite these therapeutic modalities, the prognosis in patients with bone metastatic disease remains poor, with a 10-year survival rate <50%. However, long-term survival has been demonstrated in a small proportion of patients. The use of prognostic factors in risk stratification and the development of personalized therapy is necessary for this population [9]. The index patient in this case report had an open reduction and internal fixation for the pathologic fracture of the humerus and subsequently had total thyroidectomy and chemotherapy. As at the time of writing this case report, the patient was stable on out-patient follow-up and he is currently being planned for radioiodine therapy.

#### 4. CONCLUSION

Papillary thyroid carcinoma is the most common form of well-differentiated thyroid carcinoma with a wide age range of presentation. The most common presentation is usually neck swelling. They also have the propensity to invade locally and metastasize to regional lymph nodes. Distant metastases commonly occur to the lungs, the central nervous system and the bone. Pathologic

fracture as the initial clinical presentation is an unusual manifestation of metastatic thyroid carcinoma; therefore a high index of suspicion is needed to make this diagnosis. In any patient presenting with a pathologic fracture, the possibility of a metastatic carcinoma should always be considered and a metastatic thyroid carcinoma is included in the differentials.

## CONSENT

As per international standard, patient's written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standard, ethical approval has been collected and preserved by the author.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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