Papillary thyroid carcinoma presenting as metastases at unexpected sites: Report of two cases

Renu Thomas,* Elezabeth Manuel

Department of Histopathology, VPS Lakeshore Hospital and Research Centre, Kochi, India

ABSTRACT

Papillary thyroid carcinoma (PTC) is the most common form of differentiated thyroid carcinoma (DTC). It is generally confined to the neck with or without spread to regional lymph nodes. Distant metastases is rare, if occurs, it usually involves lung and bone. Additional locations have only been sporadically reported and were identified during the course of follow-up, subsequently to a thyroid surgery. Distant metastases as the initial presentation of PTC is a rare event. We, herein, report two cases of PTC presenting initially as metastases at unusual sites and discuss the importance of meticulous histopathological and immunohistochemical examination in such situations. Our aim is to increase awareness of the unique possibility of PTC presenting as metastatic deposits at unexpected sites.

Key Words: Thyroid carcinoma, Papillary, Metastases

1. INTRODUCTION

Papillary and follicular carcinomas of thyroid are the differentiated thyroid carcinoma (DTC), characterized by a slowly progressive course with 10 year survival rates as high as 80%-95%.[1] Papillary thyroid carcinoma (PTC) which is the most common thyroid tumour represent 79% of thyroid malignancies, is generally confined to the neck with or without spread to regional lymph nodes, with 10 year mortality rate less than 7%.[2] However, 4%-8% of patients develop distant metastasis, most common sites being bone and lung.[3] Presence of distant metastasis is the most significant poor prognostic factor with 10 year survival rate falling to less than 50%.[4] Herein, we report two rare presentations of PTC as metastases at unusual sites.

2. CASE REPORT

2.1 Case 1

A 47-year-old male patient presented with one month history of fever to an outside hospital. Ultrasonogram of abdomen done at that centre along with routine laboratory investigations, revealed a large mass lesion over left kidney. Therefore an MRI scan of abdomen was taken, which confirmed a large, 10 cm–12 cm mass lesion arising from left adrenal gland and adhering to left kidney. He was thereafter, referred to our hospital and underwent left adrenalectomy and radical nephrectomy.

Resected specimen was composed of kidney measuring 17 cm × 13 cm × 9 cm with an adhering encapsulated tumour measuring 12 cm × 8 cm × 7 cm in the suprarenal region. Cut section of the growth was whitish solid and vaguely...
lobulated. Central necrosis and cystic changes were present. Microscopic examination showed an encapsulated malignant epithelial neoplasm composed of rather regular cells forming follicles (see Figure 1A). Individual cells showed vesicular round to oval nuclei with clearing, inconspicuous nucleoli and eosinophilic granular cytoplasm. Several cells showed nuclear grooving. Large areas of necrosis, lymphovascular emboli and frequent mitosis > 10/10 HPF were observed.

The possibilities considered, based on this morphology were a neuroendocrine neoplasm, thyroid like follicular renal cell carcinoma arising from the kidney and metastatic follicular patterned carcinoma of thyroid origin. Immunohistochemical studies (Bond Polymer refine detection method using Leica BOND MAX fully automated IHC machine) were performed which showed tumour cells staining positive for Cytokeratin 7 (Dako), thyroid transcription factor1 (TTF1-Dako) (see Figure 1B), thyroglobulin (PathNsitu) (see Figure 1C) and Pax8 (PathNsitu) (see Figure 1D). Cytokeratin 20 (PathNsitu), neuroendocrine markers - synaptophysin (PathNsitu) and chromogranin (PathNsitu) and inhibin (Biogenex) – a marker for adrenocortical carcinoma were negative. This led to a diagnosis of metastatic thyroid carcinoma with features favouring follicular variant of papillary carcinoma.

Following this, an ultrasound scan of the neck was done which showed multiple nodules in both thyroid lobes with a suspicious nodule in the inferior pole of right lobe, measuring 3 cm × 2 cm in size. Fine needle aspiration cytology from this nodule confirmed PTC. CT thorax and PET scan did not detect any other metastatic deposits.

Patient underwent total thyroidectomy which revealed multifocal PTC - follicular variant (see Figure 2), involving right and left lobes; tumour size ranging from 0.4 cm to 4 cm × 2.5 cm × 2 cm in a background of nodular hyperplasia with lymphocytic thyroiditis. Extrathyroidal extension was not present and regional lymphnodes were free of tumour.

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**Figure 1.** Histopathology of adrenal tumour

A. Tumour showing cells forming follicles, individual cells have clear nuclei with grooving-hematoxylin-eosin, original magnification ×400; B. Immunohistochemical staining with TTF1 showing diffuse nuclear staining-original magnification ×400; C. Immunohistochemical staining with thyroglobulin showing diffuse cytoplasmic staining- original magnification ×200; D. Immunohistochemical staining with Pax8 showing diffuse nuclear staining- original magnification ×200.
Figure 2. Histopathology of tumour in the thyroid

Left: Low power view showing tumour nodules surrounded by normal thyroid tissue, hematoxylin-eosin, original magnification ×100;
Right: High power view showing features of papillary carcinoma-follicular variant, similar to the adrenal tumour, hematoxylin-eosin, original magnification ×400.

Figure 3. Histopathology of scalp swelling showing papillary thyroid carcinoma

A. Nests of cells showing nuclear clearing, grooving and pseudoinclusions(arrow)-hematoxylin-eosin, original magnification ×400;
B. Tumour eroding through skull bone-hematoxylin-eosin, original magnification ×100; C. Immunohistochemical staining with thyroglobulin showing diffuse cytoplasmic staining-original magnification ×200; D. Immunohistochemical staining with TTF1 showing diffuse nuclear staining- original magnification ×200.
2.2 Case 2

A 54-year-old male patient presented with one month history of scalp swelling, which was not associated with pain. CT and MRI scan showed enhancing dural based mass eroding through the bone and elevating overlying skin, suggestive of meningioma. He underwent excision of the same. Intra-operatively, firm vascular mass, densely adherent to dura, eroding the bone but sparing arachnoid mater was found. Excised specimen consisted of a nodular, fairly circumscribed mass, measuring 3.5 cm × 3.5 cm × 1.5 cm, attached to dura and eroding through attached bone. Cut section had tan, focally haemorrhagic appearance. Microscopic examination showed a cellular neoplasm composed of closely packed cells with round to ovoid vesicular nuclei with clearing and grooving and eosinophilic granular cytoplasm, arranged in nests and trabeculae with intervening thin walled vascular channels (see Figure 3A, B). Frequent mitoses, 8-10/10HPF were observed. These morphological features were suggestive of a malignant neoplasm, differential diagnoses were anaplastic meningioma and metastatic carcinoma.

On immunohistochemical studies (Bond Polymer refine detection method using Leica BOND MAX fully automated IHC machine), tumour cells stained diffusely for pancytokeratin (Zytomed), cytokeratin 7 (Dako), Vimentin (Dako), thyroglobulin (PathNsitu) (see Figure 3C), TTF1 (Dako) (see Figure 3D) and Pax8 (PathNsitu), confirming metastatic carcinoma of thyroid origin. Cytokeratin 20 (PathNsitu), epithelial membrane antigen (Dako), neuroendocrine markers synaptophysin (PathNsitu), markers for lung carcinoma-Napsin (PathNsitu) and P63 (PathNsitu) and marker for GI tumours CDX2 (PathNsitu) were negative. The patient then underwent ultrasound scan of the neck which showed a 1.6 cm hypoechoic nodule in the right thyroid lobe. The patient was not willing for further investigations due to financial constraints and was lost to follow up.

3. Discussion

Distant metastases prior to a primary thyroid cancer diagnosis are extremely infrequent but when occurs, pose diagnostic challenges, especially when presenting at unusual sites. Rare distant metastatic locations of PTC that have been sporadically reported include the following: liver, pancreas, spleen, kidney, adrenal gland, brain, cerebellum, skeletal muscle, parotid gland, skin, and so on.\(^5\)\(^{-14}\) Less than 1/2,000 thyroid tumours initially manifest as adrenal metastasis\(^15\) and they are usually multiple, bilateral and often associated with lung or bone metastases.\(^16\),\(^17\)

In our case, metastasis was solitary and unilateral in the left adrenal gland without evidence of involvement of other common locations like lung or bone.
roidectomies over long periods found doubling of both while DTC specific mortality rate remains unchanged; therefore suggesting watchful waiting as a safe route for management of these cases, especially the early stage and papillary subtype, to reduce the economic burden of potentially avoidable thyroidectomies.\textsuperscript{[28,29]} The two cases illustrated here raise concerns to such an approach. Distant metastases in DTC represents advanced disease stage and are often associated with poor prognosis. Therefore, earlier detection of clinically silent primary tumours has a significant impact on prognosis of these patients and clinical decision-making. Incorporation of molecular diagnostics may evolve as a promising tool in risk stratification in these cases.

To date, the best therapeutic option for PTC with distant metastases is resection of metastatic tumour along with total thyroidectomy, followed by radioactive iodine ablation therapy.\textsuperscript{[30]}

4. Conclusion

Our cases are rare presentations of PTC as a solitary metastatic lesion at unusual sites without involvement of commonly affected organs like lung or bone. These cases highlight the importance of early detection of thyroid carcinoma before the development of metastases. Meticulous histopathological and immunohistochemical examination are crucial to arrive at the correct diagnosis while encountering rare tumours.

CONFLICTS OF INTEREST DISCLOSURE

The authors declare they have no conflicts of interest.

REFERENCES


