


Papillary Thyroid Cancer Metastases to the Parathyroid Gland

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ABSTRACT

INTRODUCTION: Papillary Thyroid cancer (PTC) is the most common malignancy encountered by endocrine surgeons accounting for up to 85% to 90% of all thyroid malignancies. Parathyroid metastases appear to be an uncommon phenomenon however are likely to be underdiagnosed due to routine parathyroid gland preservation during thyroidectomy.

CASE: We present the case of 63-year-old lady with PTC metastases to the parathyroid gland. She underwent total thyroidectomy, central compartment lymph node dissection and selective left neck (levels IIA-IV) lymph node dissection. Final pathology confirmed a 45mm low grade conventional type papillary carcinoma with microscopic extension into perithyroidal soft tissue focally and into the adjacent left parathyroid gland.

CONCLUSION: Parathyroid gland thyroid cancer infiltration/metastasis is rarely reported and likely underdiagnosed. This is the first case of parathyroid gland metastasis reported from New Zealand or Australia to our knowledge. There is currently limited research available to guide whether parathyroid gland infiltration or metastasis is of clinical or prognostic significance and whether a more aggressive treatment strategy is warranted when present.

KEYWORDS: Pathology, surgical, case reports, clinical, surgery

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Introduction

Papillary Thyroid cancer (PTC) is the most common malignancy encountered by endocrine surgeons accounting for up to 85% to 90% of all thyroid malignancies.¹ Nodal micrometastases are commonly seen in over 90% of PTC cases, with approximately 20% to 30% of patients having pathological lymph nodes on preoperative ultrasound imaging.² Parathyroid metastases appear to be an uncommon phenomenon however are likely to be underdiagnosed due to routine parathyroid gland preservation during thyroidectomy to prevent post-operative hypocalcaemia.³ In this case report we present a patient who had PTC metastasis to a parathyroid gland.

Case

A 63-year-old euthyroid woman was referred by her GP with a 3-month history of a left sided neck swelling. Ultrasound of the neck revealed a large solid hypoechoic lesion in the left hemithyroid with a broad-pushing front expanding the thyroid capsule, measuring 3.2 cm × 3.6 cm × 3.8 cm. Suspicious lymph nodes were also identified in level II as well as the central compartment of the neck. Fine needle aspiration (FNA) biopsy confirmed metastatic papillary thyroid carcinoma with involvement of cervical lymph nodes (Figure 1).

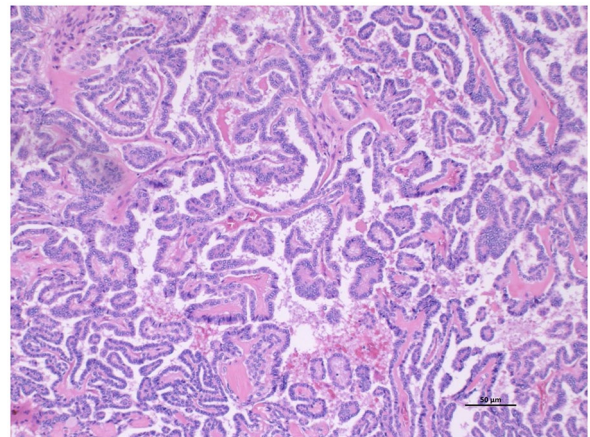


Figure 1. HE stained sample of the papillary thyroid carcinoma.

She had no prior history of surgery or neck radiation and no family history of thyroid or other endocrine disease. Her medical history included hypertension and impaired glucose tolerance testing (IGT). She is a current smoker. There was no history of immunocompromised medical conditions or immunosuppressive drugs.

She underwent total thyroidectomy, central compartment lymph node dissection and selective left neck (levels IIA-IV)



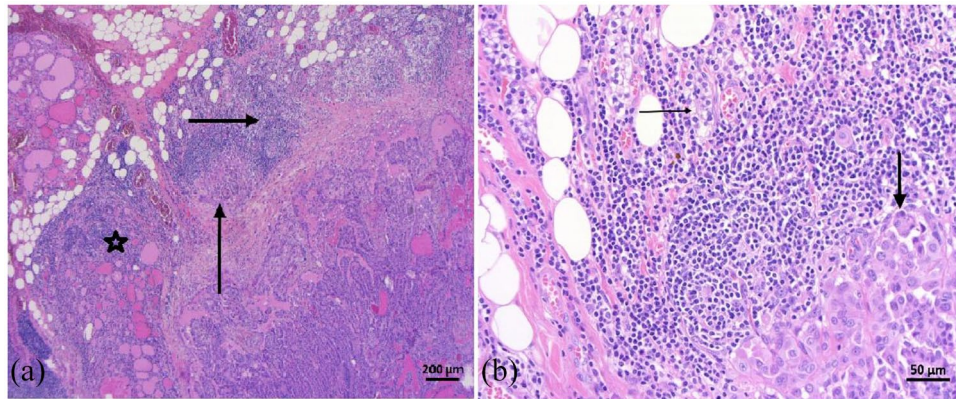


Figure 2. HE stained sample at low (a) and high (b) power magnification showing direct invasion of PTC (vertical arrow) into perithyroidal soft tissue and parathyroid tissue (horizontal arrow), with no demonstrable capsule and background thyroid tissue with Hashimoto's thyroiditis (a, star).

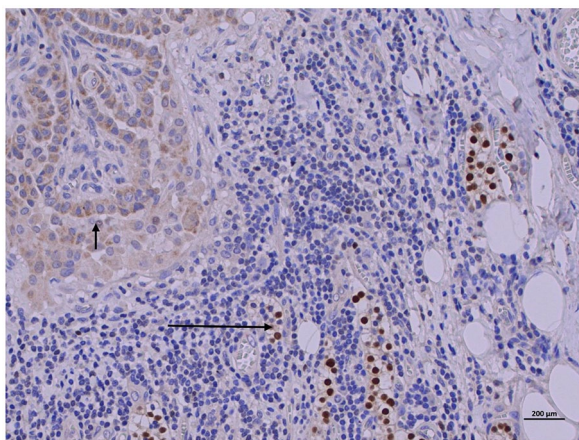


Figure 3. GATA-3 positive stained parathyroid tissue (long arrow) demonstrating direct invasion of PTC (short arrow) into parathyroid tissue that has no evidence of a capsule.

lymph node dissection. Neither of the left superior or left inferior parathyroid glands were definitively identified. Both right parathyroid glands were clearly identified, well vascularised and preserved.

Final pathology confirmed a 45 mm low grade conventional type papillary carcinoma in the left thyroid lobe with microscopic extension into perithyroidal soft tissue focally and into the adjacent left parathyroid gland (Figures 2 and 3). Thyroid capsular and vascular invasion were also present. The background thyroid parenchyma showed features suggestive of Hashimoto's thyroiditis (Figure 2(a)). Immunohistochemistry was positive for BRAFv600E (Figure 4). A 10mm focus of conventional type papillary thyroid cancer was seen in the right thyroid lobe. Six of the nineteen left sided lymph nodes excised were positive for metastatic disease. Final pathological staging was pT3a, N1b, Mx

Discussion

Metastasis to the parathyroid gland from primary thyroid cancer is poorly understood and likely an underdiagnosed phenomenon due to the routine practice of preserving parathyroid

glands during thyroidectomy to prevent post-operative hypocalcaemia.³ To our knowledge we report the first published case of PTC metastasis to the parathyroid gland in New Zealand or Australia.

Six different series describing this phenomenon have been published; 1 from Greece,³ 1 from Saudi Arabia,⁴ 1 from Italy⁶ and 3 from Japan.^{5,7} These studies suggest a predominance in women; however, it must be noted that the sample size is very small. A 2012 retrospective review in the World Journal of Surgical Oncology by Chrisoulidou et al³ described a 0.5% incidence of parathyroid gland involvement in thyroidectomy patients (10 of 1770) This increased to 3.94% when looking at cases where the parathyroid gland was excised (10 of 254 cases).³ Similarly, Al Qahtani et al, reported a prevalence of 1.94% of cases with parathyroid metastasis over all but 8.38% in those who had a parathyroid gland excised.⁴ Kakudo et al⁵ found the prevalence to be 3.9% increasing to 7.9% when only parathyroidectomy samples were included. These studies suggest the prevalence is likely to be higher than recognised and that in many cases parathyroid gland thyroid metastasis may be left in situ with parathyroid gland preservation.

Parathyroid gland metastasis from thyroid cancer is thought to occur via 2 main potential pathways.³ Infiltration of tumour through the thyroid capsule with direct invasion to the adjacent parathyroid gland tissue is the most common. Histological features of haematogenous spread with foci of metastatic spread are also described although less common.⁷

Papi et al⁶ found the most predominant form of spread was through direct invasion (6 of 10 cases). This is in keeping with our patient, seen in the pathological specimen (Figures 2 and 3). Extension of the primary tumour through an intervening pseudocapsule was also described but found to be less common. One patient in the study exhibited both types of metastatic spread.

One of the most important points of discussion around this case is the impact, if any, parathyroid gland metastasis has on disease severity and outcomes for the patient. PTC usually follows an indolent course with an excellent 5-year survival rate.¹

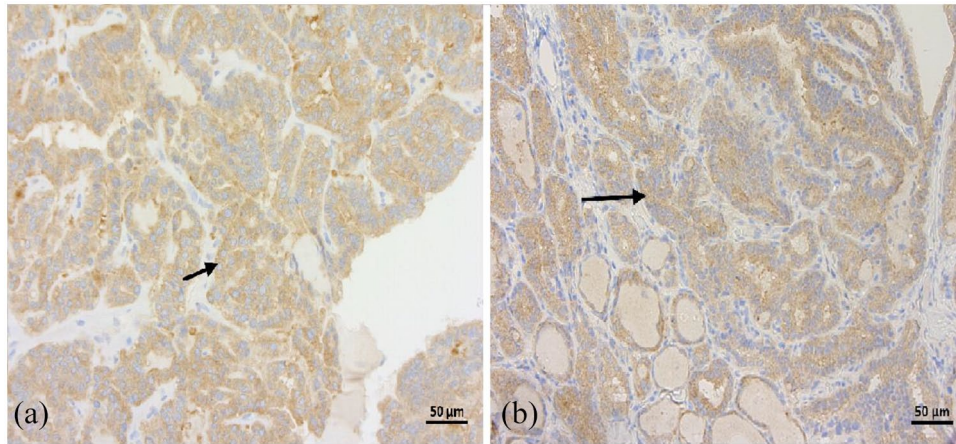


Figure 4. PTC cells showing cytoplasmic positivity for BRAFV600E mutation on both the right (a) and left (b) side.

TNM staging currently does not account for parathyroid gland involvement. This is likely due to it being an uncommon diagnosis and any impact on thyroid cancer outcomes either negligible or not yet defined. However, the presence of parathyroid gland metastasis would upstage a thyroid cancer if applied when a parathyroid gland metastasis is present to, that is, T3a/T4a if direct invasion is present or M1 if hematogenous spread to the parathyroid gland is recognised.⁴

Several studies have tried to define whether the presence of parathyroid gland metastasis has an impact on outcomes in thyroid cancer. In Papi et al's review, all cases with parathyroid gland metastasis fell within the intermediate risk category for disease recurrence.⁶ However, none of the patients in this study (n=10) had a detectable thyroglobulin level after a mean of 5.6 years. Ito et al⁷ suggested invasion of the parathyroid gland had minimal clinical significance or prognostic impact and should be classified as T3a disease. However, in this study, those with pT4 disease had significantly worse disease-free survival (DFS) rates compared to those with pT3 disease with or without parathyroid involvement. Kakudo et al⁵ also found parathyroid gland involvement corresponded with worse DFS rates and correlated with a more aggressive thyroid cancer. Al-Qahtani et al⁴ found DFS in patients with parathyroid gland metastasis to be similar to T4a stage differentiated thyroid cancers, with a higher risk of recurrence and therefore likely to benefit from post-operative RAI.⁴ All these studies have low numbers of patients and will have diagnostic bias. This limited data necessitates further study into this area to ascertain if parathyroid involvement is, in fact, a significant prognostic indicator.

Of interest in our case is the presence of a BRAFV600E mutation. The left sided PTC showed direct invasion into the parathyroid as well as lymph node metastases. The small right sided lesion had not metastasised. Both lesions were BRAFV600E positive on molecular testing (Figure 4). This mutation is associated with more aggressive biological behaviour and increased risk of thyroid cancer related mortality amongst patients with PTC¹ and therefore likely higher incidence of parathyroid gland metastasis. A positive BRAFV600E

mutation could be associated with a with a higher likelihood of parathyroid gland invasion/metastasis Current literature does not clarify the status of this mutation in those reported to have parathyroid gland thyroid cancer metastasis and is an area where further research could be initiated.

In conclusion, parathyroid gland thyroid cancer infiltration/metastasis is rarely reported and likely underdiagnosed. This is the first case of parathyroid gland metastasis reported from New Zealand or Australia to our knowledge. There is currently limited research available to guide whether parathyroid gland infiltration or metastasis is of clinical or prognostic significance and whether a more aggressive treatment strategy is warranted when present.

Author Contributions

Brian O'Sullivan: Literature review, writing and revising manuscript. Tom Burton: Writing and revision of manuscript. Fouzia Ziad: Writing and revision of manuscript. Oversight around histopathology. Goswin Meyer Rochow: Chief investigator, conceptualization, writing and revision of manuscript.

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