

CASE REPORT

Thyroid metastasis of bladder transitional cell carcinoma

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Abstract

The thyroid gland is a rare site for cancer metastasis. We report a 75-year-old man who was referred with a history of hematuria and generalized bone pain for the past few months. He had a past history of partial left lobe thyroidectomy for follicular adenoma. Subsequently he was referred for a thyroid mass and a subtotal thyroidectomy showed a poorly-differentiated carcinoma. On the latest admission, the patient underwent resection of a bladder tumour with malignant histology and an immunohistochemical profile of CK7+/CK20+/34 Beta E12+/CEA-/PSA-. Re-examination of thyroid sections with immunohistochemical stains revealed the malignant cells to be CK7+/CK20+/34 Beta E12+/CEA-/TTF1-. The findings were compatible with metastasis of the bladder transitional cell carcinoma to the thyroid gland. Scans revealed multiple liver and bone metastases. The patient died 2 months after the diagnosis.

Keywords: transitional cell carcinoma of bladder; thyroid metastasis

INTRODUCTION

The thyroid gland is a rare site for cancers metastasis,¹ but the number of case reports of such occurrences have increased in recent years.² The incidence of metastasis to the thyroid gland in autopsy series varies from 1.25% to 24%.³ While up to 24% of metastatic cancers have been reported to spread to the thyroid gland, it is not detected in clinical practice in most cases.¹ The mean age of patients with secondary thyroid cancer has been reported to be 55.3±6.7 years.¹ Metastasis to the thyroid gland is usually considered a terminal event and the effectiveness of its conventional treatment has been questioned.³ Most of the reported patients had widespread metastasis to many other organs as well and have died within 9 months of the diagnosis.¹ The patients have very short survival times mainly attributed to delayed diagnosis.¹ The cancers that usually metastasize to the thyroid include those of the breast, lung, colon, and kidney.² The kidney was the most common primary tumour site (33%), followed by the lung (16%), breast (16%), esophagus (9%) and uterus (7%).³ Among kidney cancers, renal cell carcinoma was the most common type that metastasized to the thyroid gland.⁴

Transitional cell carcinoma is the most

common cancer of the bladder, ureter, urethra, and urachus.⁵ The common sites for metastasis of bladder cancer are liver, lung, and bone.¹ There are only few reports of thyroid metastasis from renal transitional cell carcinoma.⁶ In this report, we describe a rare metastasis of bladder transitional cell carcinoma to the thyroid gland. It has not been reported in the literature till now. This case was diagnosed by histology and confirmed with immunohistochemistry.

CASE REPORT

A 75-year-old man presented with a history of mild haematuria, dysuria, frequency and generalized bone pain for the previous recent months. He had a past history of partial left lobe thyroidectomy for follicular adenoma some years prior. He was referred to a surgeon for a large left hemi-lateral immobile, firm thyroid mass 1 month previously. Subtotal thyroidectomy was performed. Histopathology of the excised thyroid mass revealed a poorly-differentiated carcinoma. Immunohistochemical study was recommended but was not performed at that point.

Radiological investigations included a computed tomography scan of the abdomen and chest. Abdominal sonography showed a large



FIG. 1: Whole body scans showed multiple bone metastases

hypochoic mass in the bladder. No pathological changes were found in the lungs, but multiple metastatic lesions were seen in the liver. Whole body scan showed abnormal lesions in the skull, ribs, humeri, vertebrae and pelvic bones, compatible with generalized bone metastasis (Fig.1).

The patient was scheduled for transurethral resection of a solid bladder tumour in our center.

Histopathology

Histology of the bladder tumour showed multiple fused and delicate papillary architectures composed of epithelial cells with severe pleomorphism, prominent nucleoli, and

many atypical mitoses. There were multiple foci of vascular and muscular bladder wall invasions(Fig. 2).

Re-examination of sections of the previous thyroid tumour revealed sheets of malignant epithelial cells admixed with scattered thyroid follicles that were embedded in malignant cells (Fig.3).

Immunohistochemistry

Immunohistochemistry of the bladder tumour showed positivity for CK7, CK20, and 34 Beta E12 (Fig. 4) while negative staining for CEA and PSA(Fig. 5). The thyroid tumour showed positivity for CK7, CK20 and 34 Beta E12

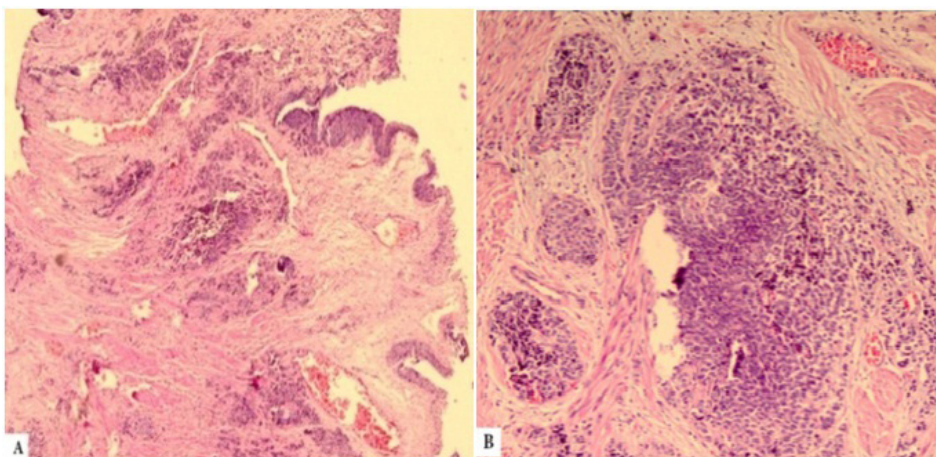


FIG. 2: (A) Transitional cell carcinoma, H&E ×4. (B) Tumour cell nest infiltration in bladder wall, H&E ×10.

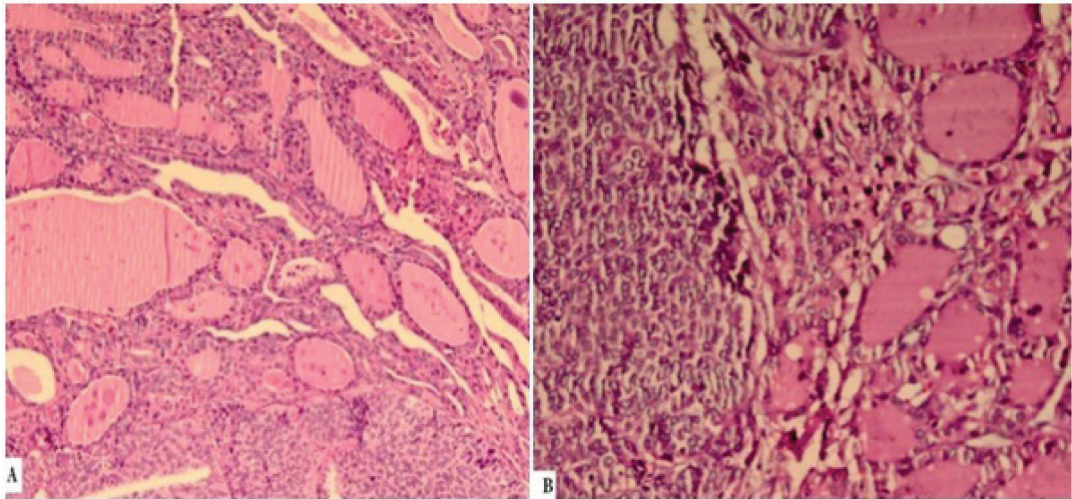


FIG. 3: Metastatic transitional cell carcinoma in thyroid, (A) H&E x4 (B) H&E x10.

(Fig. 6) and negative reaction to CEA and TTF1 (Fig. 7).

The patient died 2 months after the diagnosis.

DISCUSSION

Metastases to the thyroid are not as rare as previously believed. It has been shown in autopsy series that it is more prevalent.^{7,8} Primary malignant tumours occur mostly in the elderly population.⁹ The same is true for metastatic malignancies to the gland, where most patients are in their sixth or seventh decades of life.^{1,10} The age of our patient was also approximately 75 years.

A search of the literature did not yielded case reports of thyroid metastasis from primary bladder transitional cell carcinoma. However, there is a report of thyroid metastasis from renal transitional cell carcinoma. The evidence shows that this situation is rare, compared to thyroid

metastasis from other common sites and carries a poor prognosis. The primary sites for metastatic bladder cancer are the liver, lung, and bone.¹ Most of the metastatic lesions occur in advanced stages of primary cancer with multiple organ involvement.¹ In our patient, the lung showed no pathologic change, but the liver had multiple metastatic lesions. Moreover, whole body scan showed generalized bone metastasis.

Metastatic lesions often preserve histological similarity to the primary lesion, but they can be poorly-differentiated and anaplastic, making their comparison difficult.¹¹ Furthermore, some degree of morphological overlap is seen in carcinomas that arise from different organs.¹² This poses challenges in determining the origin of a neoplasm with conventional histology. The site of origin of the cancer has prognostic and therapeutic significance.¹³ Immunohistochemistry (IHC) can help the pathologist to determine the site of origin of the metastatic tumours.

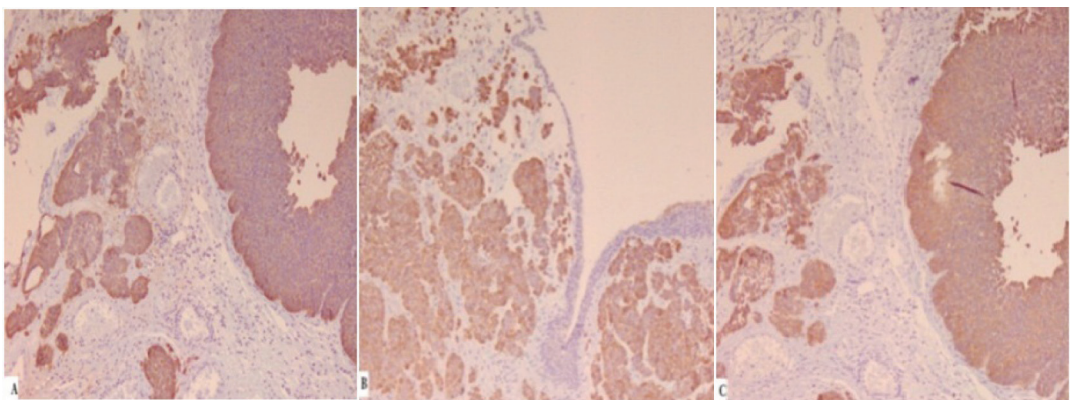


FIG. 4: Bladder tumour showing immunopositivity for (A) CK7, (B) CK20 and (C) 34BE12. Magnifications x4.

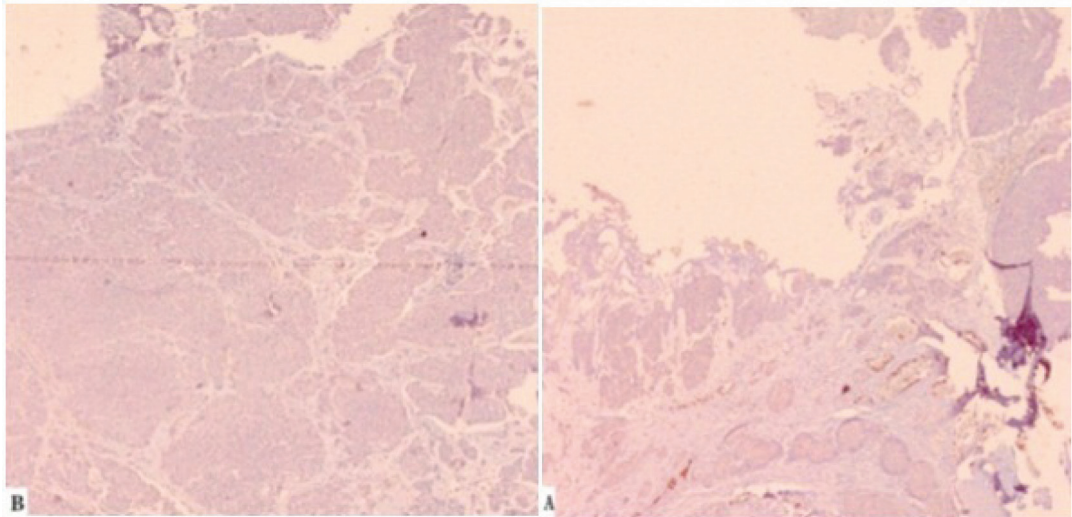


FIG. 5: Bladder tumour showing negative staining for (A) CEA and (B) PSA. Magnifications x4.

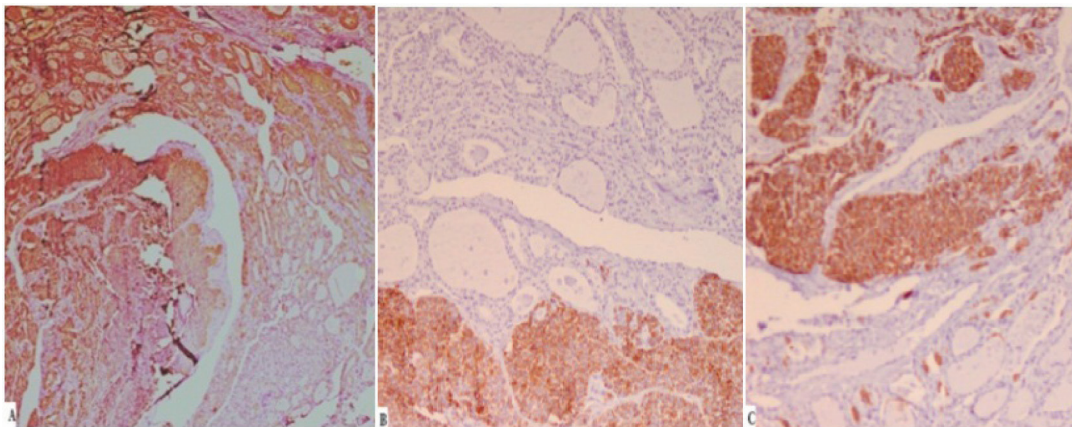


FIG. 6: Metastatic tumour cells in thyroid showing positive immunohistochemistry for (A) CK7, (B) CK20 and (C) 34BE12. Magnifications x4.

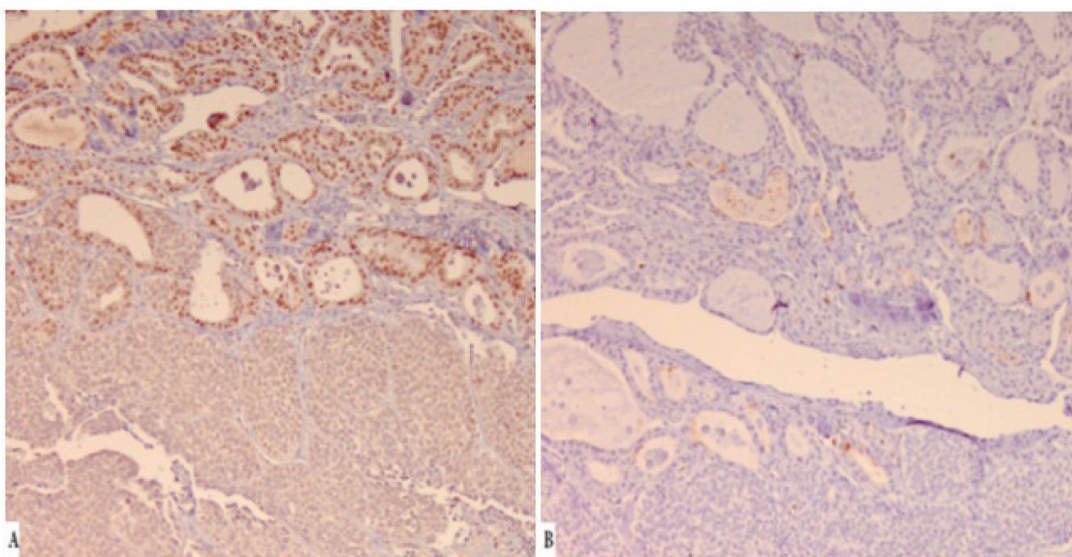


FIG. 7: Metastatic tumour cells in thyroid with negative immunohistochemical staining for (A) TTF1 and (B) CEA. Magnifications x10.

The pathology report of the thyroid mass in our cases was a poorly-differentiated carcinoma. The CK7+ /CK20+ and 34BE12+ immunophenotype is highly characteristic for transitional cell carcinoma of urinary bladder,^{5,14} while primary thyroid tumours are usually CK7+ /CK20 - and TTF 1 +.¹⁵

Cytokeratin 20 (CK20), a low-molecular-weight cytokeratin is specifically expressed in the superficial and some intermediate cells of normalurothelium. Aberrant cytokeratin 20 expression is detected in some urothelial carcinomas.^{16,17} Cytokeratin 7 (CK7) is another intermediate filament that is found in urothelial neoplasia of the urinary bladder.^{9,18}

It is anticipated that the pattern of CK7 and CK20 expression in metastatic urothelial carcinoma is similar to its primary counterpart.¹⁹ CK7 and CK20 are helpful when both are positive, supporting the diagnosis of urothelial carcinoma.²⁰ However, if only one marker is positive or both are negative, these markers have limited usefulness for distinguishing these carcinomas.²¹ Our case shows positive CK7, CK20, and 34BE12 in the primary bladder neoplasm. This pattern is in favour of bladder transitional carcinoma. The thyroid tumour shows also positive CK7, CK20, and 34BE 12 with negative TTF1. This is compatible with metastatic transitional cell carcinoma.

High-grade urothelial and prostate carcinomas have overlapping morphological characteristics and clinical manifestations. The majority of poorly-differentiated prostate adenocarcinomas stain positive for prostate specific antigen (PSA),¹⁸ but CK7 usually is negative in prostate adenocarcinoma.²² Prostate adenocarcinoma usually does not exhibit CK20 staining, but when positive, it often is focal.^{9,18,23} In this patient, IHC showed negative PSA in both primary and secondary tumours which is not compatible with prostatic cancer.

Negativity for TTF-1 and thyroglobulin level of tumour cells might be helpful in differentiating metastatic carcinoma from primary malignancy of the thyroid. In our case, CK7+ /CK20+/34BE12+ were confirmed, while markers like thyroglobulin, TTF-1, CEA and calcitonin were negative.

Metastasis into a thyroid neoplastic tumour or tumour to tumour metastasis is exceedingly rare. Metastasis into a primary thyroid neoplasm is synchronous in 33% of cases and metachronous in 67%.²⁴ Metachronous tumour to tumour metastasis may be considered in our case in view of previous thyroid adenoma.

Conclusion

Most patients with thyroid metastases had widespread metastases to many other organs, in addition to the thyroid gland.¹ These patients have short survival.¹ It mainly occurs in patients with high-grade and high-stage tumours. Immunohistochemical staining can be used to confirm the source of the primary tumour, because the metastatic lesion may be poorly differentiated and render the comparison difficult.

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