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COLONIC CARCINOMA METASTASIZING TO INTRATHYROIDAL PRIMARY MALIGNANCY WITH PARATHYROID NEOPLASM

Oncology/Radiotherapy

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ABSTRACT

Background: Carcinoma colon metastasizing to thyroid is very rare and simultaneous coexistence of papillary carcinoma thyroid and metastasis from carcinoma colon to thyroid, tumor to tumor metastasis, is extremely rare. Here we report such a rare case. **Case Report:** 43 year old female with past history of goiter, positive family history; diagnosed as carcinoma colon pT3N2aM0 stage IIIB underwent left hemicolectomy and adjuvant chemotherapy. On routine follow up, after 8 months incidentally detected metabolically active nodule in right lobe of thyroid (SUV 6.7) on PET CT scan. Total thyroidectomy was done and histopathology report showed encapsulated invasive follicular variant of papillary thyroid carcinoma with adenocarcinoma colon deposit with a background of Hashimoto's thyroiditis. Also detected Parathyroid lesion with possibilities of hyperplasia/ adenoma. TTF 1 and CDX2 were positive. All these pointed towards a tumor to tumor metastasis and also a rare possibility of genetic syndrome to be considered due to young age and occurrence of 3 neoplasms. Patient was treated with 30mCi radioactive Iodine 131.After 2 months she developed liver and ovarian metastasis and started on second line chemotherapy. **Conclusion:** Carcinoma colon metastasizing to thyroid gland although very rare, needs to be detected early for a favorable prognosis. The substantial genotype heterogeneity and lack of understanding of its clinical utility, psychosocial impact makes it difficult for clinicians to recommend Hereditary cancer predisposition panel. Hence future research is necessary to guide clinicians to predict cancer risk, counsel patients, estimate frequency and predictive values of panel testing.

KEYWORDS

Carcinoma Colon, Thyroid Metastasis, Papillary Carcinoma Thyroid

INTRODUCTION

Colorectal cancer is the third most common cancer worldwide and approximately 15%-30% of patients present with metastases at presentation and 20%-50% with localized disease later develop metastases.[1]The most common location of metastases being liver, lung, peritoneum and distant lymph nodes.[2] Thyroid metastasis constitute 1.5-7.5% of all thyroid malignancies commonly from carcinoma lung and renal cell carcinoma.[3] In general metastasis to thyroid is rare and metastasis from carcinoma colon to thyroid is very rare. Furthermore, simultaneous coexistence of papillary carcinoma thyroid and metastasis from carcinoma colon to thyroid, tumor to tumor metastasis, is extremely rare. Here we report a very rare case of tumor to tumor metastasis involving metastatic colonic adenocarcinoma and papillary carcinoma thyroid and review of related literature.

Case Report

43 year old female with past history of goiter since 15 years, family history of breast cancer in second degree relative, diagnosed as carcinoma colon pT3N2aM0 stage IIIB post left hemicolectomy reported to us for adjuvant chemotherapy with CAPOX regimen (8 cycles). Histopathology report suggestive of well differentiated adenocarcinoma colon. Tumor deposits (4) in pericolonic tissue. Lymphovascular invasion present. 4/7 lymph nodes involved.

Reassessment CECT scan post chemotherapy showed asymmetric circumferential wall thickening along left side of colon and multiple liver lesions likely metastasis. PET CT showed no metabolic activity in the tumor bed. Fat infiltration in hepatic parenchyma with no abnormal metabolic activity suggestive of post chemotherapy (oxaliplatin) induced hepatic changes. The scan showed metabolically active nodule in right lobe of thyroid (SUV 6.7) which was an incidental finding. USG thyroid suggestive of benign lesion and FNAC was inconclusive. She underwent total thyroidectomy in view of metabolically active thyroid nodule on PET CT. The post op histopathology report showed an encapsulated invasive follicular variant of papillary thyroid carcinoma (2.8 x 2.5cm) reaching up to thyroid capsule with adenocarcinoma colon deposit. No angioinvasion or lymphatic or perineural invasion or extra thyroidal invasion. Background showed Hashimoto's thyroiditis. Parathyroid lesion with possibilities of parathyroid hyperplasia/ adenoma seen. Immuno histochemistry was done. TTF1 positive in papillary carcinoma thyroid cells and CDX2 positive in atypical cells within the tumour.TSH was highly elevated with low T3 and T4. Serum CEA was elevated (14.37ng/ml). Patient was treated with 30mCi radioactive Iodine 131 and put on a suppressive dose of thyroxine and put on follow up. But unfortunately after 2 months she presented with ascites and serum CEA was 46.4ng/ml. On evaluation detected liver and ovarian metastasis and started on second line chemotherapy.

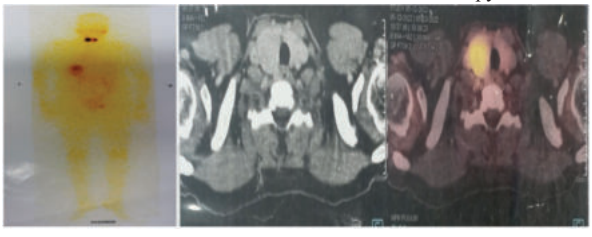

Fig 1 **Fig 2**
Radioactive Iodine scan(Figure 1) and PET CT (Figure 2) showing metabolically active nodule in right lobe of thyroid

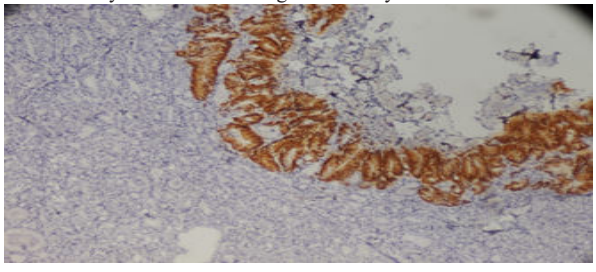

Figure 3 CDX2 positive in metastatic adenocarcinoma

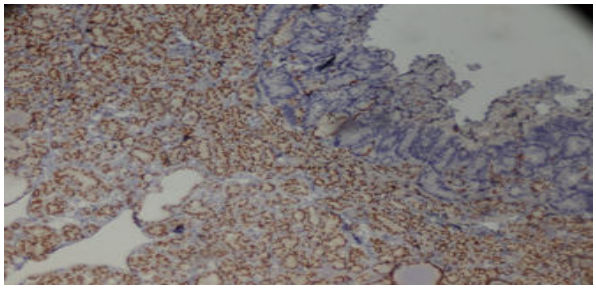

Figure 4 TTF1 positivity in papillary carcinoma, negative in metastatic carcinoma

DISCUSSION

A systematic review published in 2013 found only 34 cases of colorectal metastasis in thyroid since 1931. Since the review in 2013 there have been at least 14 cases of thyroid metastasis with colorectal origin.[4] Given the extensive blood supply to the gland, the low incidence of metastases to the thyroid is surprising .Willis suggested that this is influenced by the glandular microenvironment; the fast arterial blood flow, high concentration of oxygen and iodine could thus prevent the anchorage and secondary growth of circulating tumor cells.[5]

While, metastasis of colorectal cancer to thyroid gland is uncommon, which only accounts for about 0.1% , metastasis to an intrathyroidal primary neoplasm that is tumor to tumor metastasis is exceptionally uncommon. Tumor to tumor metastasis is defined as metastases of one tumor to another including both malignant to benign tumor and malignant to malignant tumor. The first case of tumor to tumor metastasis was reported by Berent in 1902. Criterias for its diagnosis are

(1) More than one primary tumor must exist. (2)The recipient tumor should be a true benign or malignant tumor. (3)The donor malignancy must be true metastasis and (4) The exception of contiguous growth of one tumor into another adjacent tumor i.e. Colonization tumor, embolisation of tumor cells and metastasis to the lymphatic system.[6] Our patient has met all the above mentioned criterias.

Less than 50 case reports of tumor to tumor metastasis, in which the recipient tumor was a primary thyroid neoplasm were reported in the literature. Also only 8 cases of primary colorectal carcinoma metastasizing to primary thyroid carcinoma were identified in the scientific literature.[6] (Table 1).Here we describe a case of adenocarcinoma colon metastasizing to the primary follicular variant of papillary thyroid carcinoma.

Table 1The duration of diagnosis of primary colorectal cancer and its metastasis to a thyroid malignancy was in the range of 18 months to 9 years. Hematogenous dissemination can be reason for colon to thyroid metastasis. Paget's seed and soil theory suggest that metastasis develops when viable tumor cells(seed) can proliferate at the favorable growth environment of the recipient tumor (soil) via hematogenous dissemination.

The literature review also found 2 cases had colorectal cancer with isolated thyroid metastasis with a history of long standing thyroid goiter.Based on the Batsons new theory of vertebral venous metastasis Luo et al hypothesized that tumor cells migrate through the vertebral veins and directly enter the thyroid without entering the thoracic and abdominal cavity, or without involving the caval, pulmonary and portal vein. In fact the thyroid diseases are vulnerable to primary or secondary thyroid cancer growth due to alteration of the thyroid environment so that it becomes a favourable site for tumour cell to grow and settle.[6]

Our patient developed isolated thyroid metastasis in a long standing Hashimoto's thyroiditis within 8 months of diagnosis of primary colorectal cancer (explained by Batson's theory) but later after a period of 1 year she developed liver and ovarian metastasis probably via hematogenous route.

Thyroid metastasis may be symptomatic but data suggest that 28% presents as an incidental diagnosis.[4]Our patient was asymptomatic and it was purely an incidental finding on PET CT scan. The NCCN guidelines recommend use of PET/CT scan for detection of recurrence. A recent systematic review and meta-analysis of 11 studies found that PET/CT scan can detect tumor recurrence with a sensitivity of 94.1% and a specificity of 77.2%.[6] In thyroid metastasis, PET CT showed focal nodular or multiple discrete nodular or diffuse uptake with standardized uptake value (SUV) ranging between 3.9 and 4.2. In our case PETCT scan showed metabolically active nodule in right lobe of thyroid (SUV 6.7) which raised suspicion of a second thyroid primary or metastasis and had raised CEA value of 14.37ng/ml. FNAC was inconclusive.In view of high suspicion of malignancy our patient underwent thyroidectomy.

The current study demonstrates the importance of IHC in confirming tumor to tumor metastasis. Immunostaining with thyroid specific markers TTF1 and Thyroglobulin will be positive in PTC, while CDX2 is a marker for gastrointestinal malignancies. In our case TTF1 was positive in follicular variant of papillary carcinoma thyroid cells and CDX2 positive in atypical cells within the tumor.[6]

Through the literature review we found that the majority of the secondary lesions were diagnosed above the age of 52yrs, except for Luo et al and the current case. Our patient is unique in that she had a parathyroid neoplasm as well. She being young with 3 neoplasms , raises the suspicion of a genetic syndrome.

Genetic evaluation is highly recommended in case of strong family history of colorectal cancer, diagnosed at early age and multiple primary cancers in CRC cases. The two well known genetic syndromes associated with colorectal cancers are the Familial Adenomatous Polyposis(FAP) and Lynch syndrome (Hereditary Non Polyposis colon cancer).FAP can be associated with thyroid tumors up to 12%. MEN syndrome can present with parathyroid and thyroid neoplasms, colorectal and gastrointestinal polyps.Cowden syndrome is associated with thyroid cancer up to 10% and CRC 9%.The ongoing efforts towards massive genomic sequencing may lead to the discovery of new, previously unknown rare syndromes in the coming years. This would help in identification of high risk young population and assigning polygenic risk scores will allow for personalized risk assessments, which are beneficial for prevention, early diagnosis and disease management.[14]

CONCLUSION

Carcinoma colon metastasizing to thyroid gland although very rare, needs to be detected early for a favorable prognosis. The substantial genotype heterogeneity and lack of understanding of its clinical utility, psychosocial impact makes it difficult for clinicians to recommend Hereditary cancer predisposition panels. Future research is necessary to guide clinicians to predict cancer risk, counsel patients, estimate frequency and predictive values of panel testing.

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