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Metachronous Collision Tumors of the Thyroid Gland Unveiled in Real Time by a Change in the Thyroid Nodule Phenotype

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Abstract

Introduction: The term collision tumor refers to the coexistence of two histologically distinct neoplastic tumors within the same mass. Collision tumor of the thyroid (also referred to as tumor-to-tumor metastasis) with metastatic colorectal carcinoma to a preexisting thyroid adenomatoid nodule is rare. Preoperative diagnosis of this disorder is exceedingly difficult. This report highlights the rare occurrence of a tumor-to-tumor metastasis of colorectal cancer to a preexisting thyroid adenomatoid nodule unveiled in real time by serial positron emission tomography CT scans (PET/CT). Since cytological diagnosis of these lesions is often insufficient, we present a stepwise diagnostic approach with a combination of investigations in the preoperative setting. The patient management is reviewed together with a rationalized use of targeted therapy based on the genetic status of the tumor.

Methods: Ultrasound (US)-guided fine needle aspiration (FNA) biopsies of the collision tumor of thyroid were performed and analyzed for cytologic, immunologic, and molecular tumor phenotyping. KRAS gene analysis of the metastatic lesion was also performed.

Results: The samples revealed adenocarcinoma of the colon (Tg-negative, TTF-1-negative, HBME-1-negative, galectin-3 negative, CEA-positive, CK-20 positive) intense glucose transporter-1(GLUT-1) expression and KRAS positivity. The patient was then brought to surgery for a left hemithyroidectomy and ipsilateral central compartment node dissection. Final histology revealed metastatic colonic carcinoma, invading the benign adenomatoid nodule. His recovery was uneventful and the post-op chemotherapeutic regimen was guided by the KRAS analysis of the tumor.

Conclusion: Once a collision tumor of the thyroid gland is suspected on PET/CT, the lesion should be corroborated by sonography of the thyroid gland. FNA with combined cytological, immunocytochemical and when necessary KRAS gene analysis can lead to a timely diagnosis and a treatment plan. In the context of limited systemic malignant disease and good performance status, palliative thyroidectomy with or without combined chemotherapy may control local disease and prevent tracheal invasion.

Keywords: Collision tumor; Tumor-to-tumor metastatsis; Thyroid metastatsis; FDG-avid thyroid metastatsis; Tumor GLUT-4 expression

Introduction

Clinically significant metastases from nonthyroidal malignancies (NTM) to the thyroid gland have been reported in 1.4% to 3% patients who have undergone surgery for thyroid malignancies [1]. The term collision tumor refers to the coexistence of two histologically distinct neoplastic tumors within the same mass. Collision tumor of the thyroid (also referred to as tumor-to-tumor metastasis) of a colorectal carcinoma to a preexisting thyroid tumor is exceedingly rare. Preoperative diagnosis of this disorder is difficult but aided by a composite of investigations including: structural/functional imaging and fine needle aspiration (FNA)-based cytologic, immunologic, and molecular tumor phenotyping [1-4].

This report demonstrates the very rare tumor-to-tumor metastasis of a colorectal carcinoma to a pre-existing thyroid adenomatoid nodule unveiled in real time. A contemporary approach, using a combination of diagnostic tools, allowed for timely preoperative confirmation and management of the colorectal metastasis. Indeed, palliative hemithyroidectomy allowed for prevention of possible tracheal invasion and rationalized use of targeted therapy based on the KRAS status of the colorectal lesion.

Case Presentation

A 67-year-old man underwent a right hemicolectomy December 2009 for an adenocarcinoma (T2N0M0, Dukes B). Ultrasonography (US) of the neck confirmed a left thyroid nodule felt on palpation, which appeared as an encapsulated, solid, isoechoic lesion, without calcifications, and measured 2.80×3.07×4.01 cm (height to width ratio

<1). Doppler flow interrogation revealed scant peripheral blood flow. The serum thyrotropin was 1.23 (normal 0.5-4.5 mU/L), and an US-guided FNA of the lesion revealed follicular cells with mild cytological atypia in a microfollicular architecture: Bethesda category III, follicular lesion of undetermined significance (FLUS).

There was no evidence of recurrent malignancy on surveillance with conventional imaging studies (CIS) and serial serum carcinoembryonic antigen (CEA) levels. Twenty-two months from primary surgery, a total body 18F fluorodeoxyglucose: positive emission tomography computerized tomography (FDG PET/CT) scan revealed the previously known left thyroid nodule measuring 3.50 cm, with no significant FDG activity. An US –guided FNA of the thyroid nodule was repeated and again showed findings of Bethesda category III, FLUS.

Four years and 6 months after primary therapy, serum CEA slowly rose to 8.5 µg/L. A repeat PET/CT now showed interval growth of the left thyroid lesion to 4.80 cm and increased metabolic activity with SUV 13 (Figure 1); there was no evidence of metastasis elsewhere. Ultrasonography of the neck identified the left thyroid nodule, which now displayed a different echotexture highlighted by focal areas of internal hyperechogenicity, no calcifications and increased blood flow on Doppler interrogation (Figure 2) . With a suspicion of collision tumor, a third FNA was directed at this area of the left thyroid nodule with the goal of preparing cell blocks and performing KRAS genetic analysis.

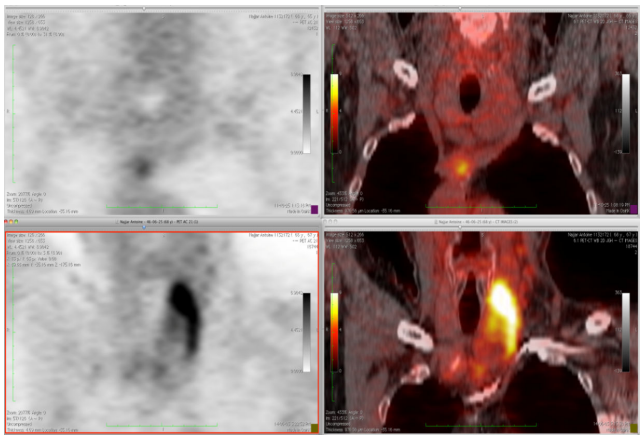

Figure 1: FDG: PET/CT: (Top frames): left thyroid nodule measuring 3.50 cm, with no significant FDG activity (isometabolic left thyroid nodule). (Bottom frames): A repeat PET/CT after 32 months showed interval growth of the left thyroid lesion to 4.80 cm and increased metabolic activity with SUV 13 (the hypermetabolic collision tumor).

Methods

Prior to the PET/CT study the patient fasted overnight. 18F-FDG was injected intravenously (599 megabecquerels, MBq) and scanning began 75 minutes later. The patient had a fasting blood glucose blood of 5.1 mmol/L. Studies were acquired on a hybrid PET/CT scanner (Discovery ST, General Electric Medical Systems, Waukesha, WI, USA). The FNA biopsies were performed under sonographic guidance with 21-gauge needles mounted on 10 cc syringes. Two passes were suspended in 10 mls of formalin and cell blocks were prepared for cytological assessment and immunocytochemical stains using specific monoclonal antibodies directed against TG, thyroid transcription factor-1(TTF-1) HBME-1, galectin-3, CEA, and CK-20. The third pass was collected in 500 µl of nucleic acid preservative (RNAlater, Ambion) for KRAS gene mutation analysis.

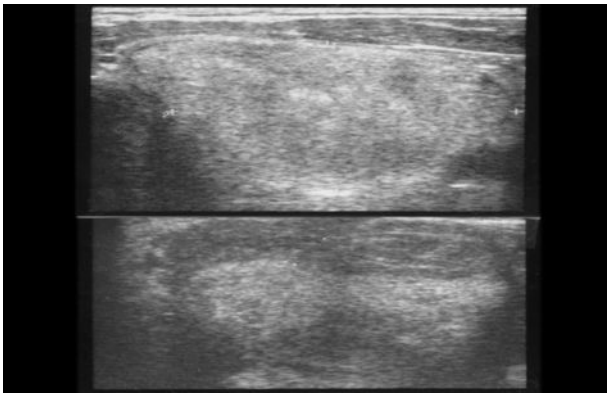

Figure 2: Longitudinal views of sonographic image of left thyroid lobe (A) thyroid adenomatoid nodule, measured 4.01 cm, encapsulated, solid, isoechoic, without calcifications. (B) Collision tumor within a pre-existing thyroid adenomatoid nodule. This is a 54 months follow up ultrasound, which showed interval growth of the left thyroid lesion to 4.80 cmand displayed a different echotexture highlighted by focal areas of internal hyperechogenicity, without calcifications

Results

Cytology and immunocytochemistry performed on the third FNA specimen obtained from left thyroid nodule now revealed metastatic colonic carcinoma (Tg-negative, TTF-1-negative, HBME-1-negative, galectin-3 negative, CEA-positive, and CK-20 positive). In addition, a KRAS gene mutation, Gly13Asp (which suggests response to a epidermal growth factor receptor (EGFR) antagonist) was identified. Considering the significant risk for mass effect on surrounding vital structures in the lower neck, the absence of concomitant distant metastases, and his good performance status, the patient was brought to surgery for a left hemithyroidectomy and ipsilateral central compartment node dissection. Histology revealed metastatic colonic carcinoma, invading the benign adenomatoid nodule and infiltrating the normal thyroid parenchyma and perithyroidal soft tissue and nodal metastases. The pathology specimen confirmed the suspected preoperative tumor-to-tumor metastasis and in addition an immunohistochemical stain for the glucose transporter 1(GLUT-1) correlated well with the intense FDG-avidity of the CRC but not the thyroid adenoma (Figure 3). He was then treated with targeted chemotherapy and as of the writing of this manuscript, four years and 11 months after primary surgery; the patient continues to do well.

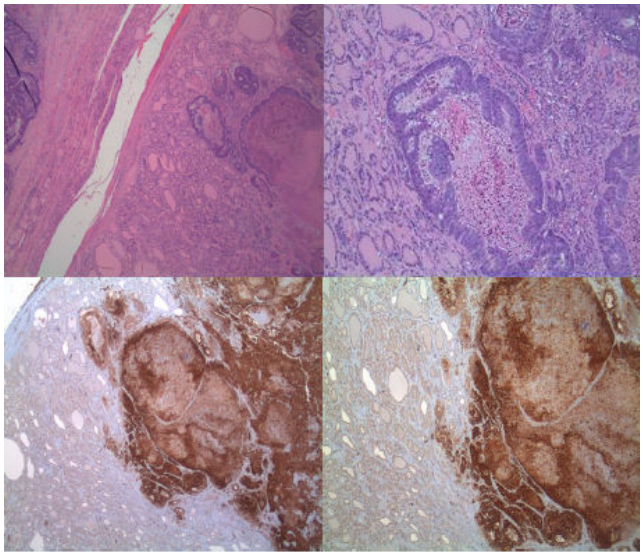

Figure 3: The top two images of the final histology of the left hemithyroidectomy specimen viewed under A) low power magnification. B) high power magnification (600X). The metastatic CRC is pictured invading the pre-existing thyroid adenomatoid nodule. The bottom two images of the immunohistochemical stain for GLUT-1 expression of the collision tumor seen under C) low magnification and D) high magnification (600X).

Conclusion

We described the case of metastatic colonic carcinoma, that collided with a pre-existing benign thyroid nodule, and which was unveiled by an interval change in the morphology and metabolic activity of the thyroidal lesion. The collision tumor appeared approximately four years and 6 months following the adenocarcinoma of the colon. We deployed a composite of investigations to diagnosis this rare tumor-to-tumor metastasis that developed metachronously prior to the hemithyroidectomy [4]. A timely diagnosis allowed for palliative surgery in an effort to reduce the risk of tracheal invasion by the metastatic lesion. The excised collision tumor revealed intense GLUT-1 staining of the colorectal cancer compared with the adenomatoid nodule and correlated with the FDG-avidity. The identified KRAS gene mutation of the colorectal tumor supported a role of EGFR antagonist therapy.

Chung et al. in their seminal review of 374 reported cases of nonthyroidal metastases to the thyroid gland in the past decade, reported that colorectal carcinoma (CRC) represented 10.4% of this cohort [1]. The metastasis to the thyroid could present itself either at the same time as the primary lesion (synchronous) or, as in our case after a time interval, (metachronous), as reported in 261/374(69.7%) in that cohort. For colorectal carcinoma the mean interval between the diagnosis of the CRC and known metastasis to the thyroid gland was 41.5 months, which approximates 53 months in our case. The authors underlined that 69/156 (44.2%) cases of the NTM occurred in pre-existing, abnormal thyroid glands; the most common being goiters and follicular thyroid adenoma, as was revealed by the first FNA in our case prior to the collision phenomenon. An altered microenvironment characterized by decreased local blood flow, oxygen content and iodine concentration (Willis hypothesis) may be pathogenetic. Interestingly, the blood flow by Doppler interrogation of the thyroid nodule was scanty.

One previous study reported metachronous, tumor-to-tumor colorectal carcinoma in preexisting thyroidal lesions, however, ours is the first report highlighting a contemporary diagnostic approach performed in real-time with well documented cytology, immunocytochemistry and KRAS mutational analysis [5]. A collision tumor of the thyroid gland was suspected, even though our patient remained asymptomatic, when rising CEA levels prompted PET/CT scan, which revealed increased metabolic activity of the lesion compared to a baseline study. Choi et al in a retrospective analysis of 245 patients with colorectal carcinoma considered in remission after primary therapy, showed that PET/CT scans detected more recurrences than did conventional imaging studies (CIS) [3]. Indeed one of the four metachronous tumors not detected by CIS was a primary thyroid malignancy. Cheung SY et al in a review of 10 cases of metastatic disease to the thyroid, sonography demonstrated that 8 nodules exhibited an ill-defined hypoechoic character with heterogenous texture and no calcifications; this imaging modality might represent the next diagnostic step in the work up of suspected collision tumors of the thyroid, as was in this case. The preoperative diagnosis of the tumor-to-tumor metastasis can then be established by FNA and cell blocks prepared for a combination of cytological and immunochemical studies and when necessary – additional material collected for molecular studies [4]. Cozzolino et al. reported that reliance on cytology alone to diagnose metastatic colon cancer to the thyroid gland, especially with collision tumor, may be difficult because typical findings are often subtle or absent. Further studies with immunophenotyping of the specimen from cell blocks (TG, TTF-1 and CK20) and if necessary KRAS-gene mutation analysis may corroborate the diagnosis. In our case, cytology and immunocytochemistry sufficed to establish the diagnosis of the colorectal metastasis in the collision tumor, although the KRAS gene analysis provided support for EGFR antagonist therapy.

The management of NTM to the thyroid gland and collision tumors of the thyroid remains to be established. In a retrospective analysis of 36 cases with thyroid metastases, Papi et al reported that there was no survival advantage when comparing those patients who had thyroidectomy versus those who did not (mean survival time 24.3 +/- 4.9 months vs. 39 +/- 9.9 months respectively) [6]. However, partial or total thyroidectomy with or without combination chemotherapy may still represent palliation for prevention of tracheal invasion. Our patient is a testament to a favorable outcome with timely diagnosis of the collision tumor and palliative surgery followed by combination chemotherapy.

Once a collision tumor of the thyroid gland is suspected on PET/CT, the lesion should be corroborated by sonography of the thyroid gland. FNA with combined cytological, immunocytochemical and when necessary KRAS gene analysis can lead to a timely diagnosis. In the context of limited systemic malignant disease and good performance status, palliative thyroidectomy with or without combined chemotherapy may control local disease and prevent tracheal invasion.

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References

1. Chung AY, Tran TB, Brumund KT, Weisman RA, Bouvet M (2012) Metastases to the thyroid: a review of the literature from the last decade. Thyroid 22: 258-268.
2. Cheung WY, Brierley J, Mackay HJ (2008) Treatment of rectal cancer metastases to the thyroid gland: report of two cases. Clin Colorectal Cancer 7: 280-282.
3. Choi, EunKyoung, IeRyungYoo, Hye Lim Park, Hyun Su Choi, et al. (2012) Value of Surveillance 18F-FDG PET/CT in Colorectal Cancer: Comparison with Conventional Imaging Studies. Nuclear medicine and molecular imaging 46: 189-195.
4. Cozzolino, Immacolata, Umberto Malapelle, Chiara Carlomagno, Lucio Palombini, et al. (2012) Metastasis of colon cancer to the thyroid gland: A case diagnosed on fine-needle aspirate by a combined cytological, immunocytochemical, and molecular approach. Diagnostic cytopathology 38: 932-935.
5. Hyun Yoon J, Min Jeon H, Kim EK, Young Kwak J, Jung Moon H, et al. (2010) Metastatic colon carcinoma in a preexisting thyroid nodule. Thyroid 20: 1319.
6. Papi G, Fadda G, Corsello SM, Corrado S, Rossi ED, et al. (2007) Metastases to the thyroid gland: prevalence, clinicopathological aspects and prognosis: a 10-year experience. Clin Endocrinol (Oxf) 66: 565-571.