

## Medullary Thyroid Carcinoma Metastatic to the Pancreas: An Unusual Site of Metastasis

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### ABSTRACT

Metastasis to the pancreas, are uncommon and usually sign of extensive disease ; they remain asymptomatic or are associated with nonspecific complaints . it may be difficult to differentiate a pancreatic metastasis from a primary pancreatic tumor, being the clinical presentation and the radiological characteristics similar for both primary and secondary neoplasms. The cytomorphology in combination with the clinical history and immune his to chemical findings can indicate a definitive diagnosis and avoid additional time-consuming diagnostic procedures for appropriate clinical management ; We aim to expose an exceptional case of a patient with a medullary thyroid carcinoma metastatic to the pancreas.

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### Introduction

Medullary thyroid carcinoma (MTC) accounts for 4% of thyroid carcinoma and originates from parafollicular cells, secreting calcitonin and carcinoembryonic antigen (CEA) [1]. Most of them are sporadic (80%), although a minority may occur in a hereditary form [2].

Calcitonin is the most sensitive and specific tumor marker at the preoperative diagnosis [3] and the post surgery follow up [4]. More than 50% of patients have lymph node involvement at the time of surgery. Despite the fact that thyroidectomy and neck dissection is rarely curative, the 5-year survival rate is approximately from 78% to 91% with continued mortality at 10 and 15 years [5].

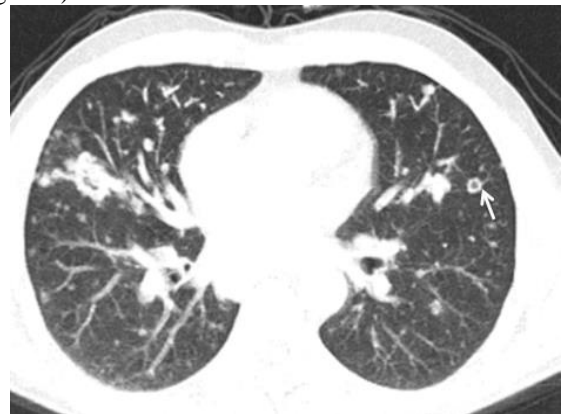
Pancreatic metastasis are extremely rare, accounting for 3–16% of pancreatic tumors [6]. The most common tumors to secondarily involve the pancreas include melanoma, lymphoma and carcinomas of the lung, kidney and breast. To our knowledge, this is the first report of MTC metastatic to the pancreas.

### Case report

A 38-year-old male north African patient, with no family history of thyroid cancer or multiple endocrine neoplasia 2 (MEN 2)-associated malignancies, who was originally diagnosed with medullary thyroid carcinoma in 2014. At that time, he presented with a voluminous left cervical lymphadenopathy. Cervical ultrasound revealed left thyroid nodule classified as TI-RADS 5 with multiple suspicious left jugular adenopathy. After witch a fine needle aspiration was performed under US. Histological finding were consistent with a diagnosis of medullary thyroid carcinoma confirmed through the use of immunohistochemistry.

The patient was referred to a thyroid surgeon and total thyroidectomy with left cervical dissection was carried out. According to pathology lab report, the tumor was in dimension of 6 cm with focal capsular invasion and with lymph node metastasis 41N+/50 including 7 with capsular effraction.

The patient did not carry any mutations of exons 10 and 11 of the RET gene found in MEN2b and familial medullary cancers. Thus allowing to exclude a family nature to the carcinoma. On thyroid hormone replacement, he had a TSH of 0.199 mIU/L and free T4 0.54ng/dL. FT3 < 1 pg/l ,thyrostimuline 70,9 uUI/ml ,calcemie 103mg/l, and calcitonin 458 ng/L .Whole body iodine scintigraphy was noniodine avid and a total body CT was run for the evaluation of the extension, and revealed multiple lung metastasis (Figure 1).



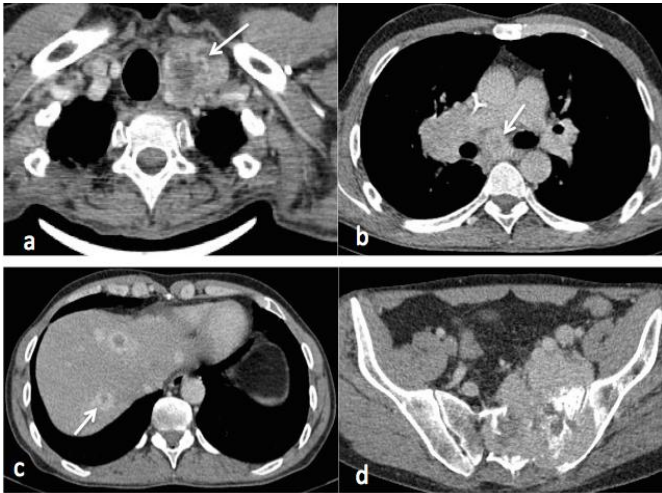
**Figure 1. High-resolution CT scan on lung window showing multiple bilateral pulmonary nodules of variable size with Feeding vessel sign, highly suggestive of metastatic dissemination.**

Thereafter the patient received 3 cures of chemotherapy (5FU-CDDP). Over the next year a post therapeutic ct-scann was performed and showed new lesions in the hila, mediastinum, liver and bones (Figure 2). For witch he received a second line chemotherapy and a palliative RTH for spine and sacrum metastasis.

After 6 cures of dacarbazine- cyclotide-vincristine the patient remained well and stable on the surveillance CT, until 4years after, he presented to the emergency department with a 4-week history of vomiting and epigastric pain. On physical examination, he was in good general condition and his vitals

were stable. Per abdomen examination revealed deep tenderness in epigastrium; however, there was no palpable mass.

His calcitonin at this time was 2500 pg/ml. Given the clinical symptoms and the increase of calcitonin levels a CT scan of the neck, chest, abdomen, and pelvis was performed and demonstrated the appearance of a pancreatic hypodense node with peripheral enhancement giving a target appearance to the n (figure 3), this radiological aspect was similar to the hepatic and lymphnodes metastasis of the patient (Figure 3).



**Figure 2.** CT of neck, chest, abdomen and pelvis showing lymphnodes (a), mediastinum(b), liver(c) and bones (d) metastasis.



**Figure 3.** CT imaging demonstrating a pancreatic metastasis from medullary thyroid cancer appearing as an hypodense lesion with peripheral enhancement within the pancreatic body.

MTC metastatic to the pancreas has not been previously described; therefore a US-guided FNA of the pancreatic mass was performed and showed pancreatic metastasis of carcinomatous process primarily suggestive of an MTC. A third line chemo was started (5FU-Dacarbazine), and a restaging CT imaging revealed progressive disease in multiple sites, including the pancreas with an increase in size of the pancreatic node and the appearance of a new lesion with the same radiological appearance (Figure 4).

Ultimately, he continued to deteriorate and passed away 6 months after.



**Figure 4.** Ct imaging on axial (a) and coronal (b) planes showing a new node in the pancreatic body resembling the prior pancreatic lesion.

### Discussion

Pancreatic metastases are extremely rare and are only found in a minority (3-12%) of patients with widespread metastatic disease. They account for only 2-16% of all pancreatic tumors [6]. The demographic features match those of the primary tumor. They can occur over a wide age range, but are most common to the elderly patient.

Most pancreatic metastases are asymptomatic and are found incidentally on imaging or at autopsy [7].

Clinically they behave as benign tumors or low-grade malignancies. Symptoms can be seen in large lesion located at the head of the pancreas, such as: Icterus, malabsorption due to pancreatic insufficiency or epigastric pain.

Imaging findings are nonspecific, the pancreatic metastasis can have a variety of appearances. In general, and they tend to appear in ultrasound; as solid hypoechogenic masses located within the pancreatic parenchyma. On CT there appearance has also varied widely with typically a well circumscribed mass which is iso or hypodense to normal pancreas on non-contrast scans [8]. In general, the enhancement pattern resembles that of the primary tumor, but tends to be homogeneous in smaller lesions, and peripheral in larger lesions [7-9], as in our case (Fig.3).

The optimal approach to treatment of pancreatic metastases has not been fully established; surgical treatment is usually not an option but can be proposed for solitary RCC metastasis [9]. In general, patients are treated with palliative intent, due to widespread metastatic disease. However, biliary stents or gastroenteric bypass are also proposed for obstruction as it improves the local control rate. Prognosis is poor, matching that of the primary tumor.

Although any primary tumor may eventually deposit in the pancreas, the most common primaries encountered include renal cell carcinoma, melanoma and breast cancer [7-8]. To our knowledge, this is the first report of medullary thyroid cancer metastatic to the pancreas.

MTC is an aggressive form of thyroid cancer, and an uncommon malignancy. The disease progresses from C cell hyperplasia (CCH), often with elevated calcitonin levels, to microscopically invasive carcinoma, then grossly evident carcinoma[10]. Medullary thyroid cancer occurs in both heritable and sporadic forms. The majority of medullary thyroid cancers is sporadic, but 20% of cases are a result of a germline mutation in the ret proto-oncogene as is seen in multiple endocrine neoplasia types 2A and 2B (MEN2), and familial MTC syndrome [10].

Like other neuroendocrine tumors, MTC can elaborate a variety of products such as calcitonin (CT), carcinoembryonic antigen (CEA), serotonin, and chromograninA [10]. In the context of MTC, the secretion of calcitonin predominates and can be used to confirm the diagnosis, indicate treatment efficacy, and monitor for disease progression or recurrence.

MTC often progresses in an indolent fashion, but has a tendency to spread to locoregional lymph nodes early, making surgical cure difficult [7]. As in the case of our patient, most of the patient present with an advanced MTC with lymph node metastases (80%) and distant metastasis (20%) [11], common sites of distant metastases in MTCs include the lung, liver, and bone [5].

The management of medullary thyroid cancer is predominantly surgical excision, consisting of a total thyroidectomy and lymph node dissection. Total thyroidectomy and lymphadenectomy result in biochemical cure (normalization of calcitonin and CEA) only 40% of the time [10].

Patients with metastatic disease can have significant symptoms from calcitonin excess and may benefit from medical treatment. Unfortunately, the relative rarity of the disease makes clinical trial design and patient accrual difficult. Thus, much of our knowledge about medical treatment of MTC rests upon small prospective series and retrospective reports.

The advent of targeted small-molecule kinase inhibitor drugs has revolutionized medical treatment of medullary thyroid cancer (MTC). Drugs such as vandetanib and cabozantinib produce disease regression in a significant portion of patients, and can extend progression-free survival in advanced; unresectable MTC External beam radiation and radioactive iodine are mostly ineffective [10].

Although it is an aggressive tumor with early metastases, the clinical course is often long, with continued morbidity and mortality extending up to 20 years [11].

### Conclusion

While this case is extremely rare, it serves to highlight a number of useful points. First, it is important to consider the possibility of a metastatic lesion involving the pancreas whenever a neoplasm on pancreatic FNA is not typical of ductal adenocarcinoma. Second, the possibility of more than one primary tumor in a given patient should remain a consideration.

### Competing interests

The authors declare no competing interest.

### References

- [1] Mitra Niafar,\*<sup>a</sup>, Shahram Dabiri,<sup>b</sup> Farshid Bozorgi,<sup>c</sup> Farid Niafar,<sup>d</sup> and Nasrin Gholamie Metastatic medullary thyroid carcinoma: A case report, *J Res Med Sci*. 2011 Apr; 16(4): 568–573
- [2] (Multiple Endocrine Neoplasia type 2 (MEN2) (Saad MF, Ordonez NG, Rashid RK, Guido JJ, Hill Cs, Jr, Hickey RC, et al. Medullary carcinoma of the thyroid. A study of the clinical features and prognostic factors in 191 patients. *Medicine (Baltimore)* 1984;63(6):319–42)
- [3] Ismailov SI, Piulatova NR. Postoperative calcitonin study in medullary thyroid carcinoma. *Endocr Relat Cancer*. 2004;11(2):357–63.
- [4] Moley JF, Debenedetti MK, Dilley WG, Tisell LE, Wells SA. Surgical management of patients with persistent or recurrent medullary thyroid cancer. *J Intern Med*.)
- [5] Michelle D. Williams, MD<sup>a,4</sup>, Sylvia L. Asa, MD, PhD<sup>b</sup>, Gregory N. Fuller, MD, PhD<sup>a</sup> Medullary thyroid carcinoma metastatic to the pituitary gland: an unusual site of metastasis *Annals of Diagnostic Pathology* 12 (2008) 199– 203
- [6] Hamilton SR, Aaltonen LA (editors): *World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of the Digestive System*. Lyon, IARC Press, 2000, pp 250–251 ),
- [7] Scatarige JC, Horton KM, Sheth S et-al. Pancreatic parenchymal metastases: observations on helical CT. *AJR Am J Roentgenol*. 2001;176 (3): 695-9
- [8] Charnsangavej C, Whitley NO. Metastases to the pancreas and peripancreatic lymph nodes from carcinoma of the right side of the colon: CT findings in 12 patients. *AJR Am J Roentgenol*. 1993;160 (1): 49-52.
- [9] Klein KA, Stephens DH, Welch TJ. CT characteristics of metastatic disease of the pancreas. *Radiographics*. 18 (2): 369-78.
- [10] Randolph GW, Maniar D. Medullary carcinoma of the thyroid. *Cancer Control* 2000;7:253 - 61.
- [11] Jessica E. Maxwell, MD MBA, Scott K. Sherman, MD, Thomas M. O’Dorisio, MD, and James R. Howe, MD *Medical Management of Metastatic Medullary Thyroid Cancer* *Cancer*. 2014 November\_1;120(21):3287–3301