CASE REPORT

Pancreatic Metastasis from Papillary Thyroid Carcinoma: A Case Report

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ABSTRACT

Introduction differentiated thyroid carcinoma presents with distant metastasis in 4% of cases, usually occurring in the lungs, bones and thoracic lymph nodes. Pancreatic involvement is extremely rare, with few cases reported in the literature. **Case report** A 47-years-old female patient presented abdominal pain. She had a history of papillary thyroid carcinoma surgically resected in 2009. After 10 years, computed tomography revealed hepatic lesions suggestive of secondary involvement and a solid mass in the pancreatic head. Endoscopic ultrasound fine-needle aspiration was performed in a heterogeneous hypoechoic mass located at pancreatic head. Cell block with immunohistochemistry was positive for thyroglobulin, suggesting papillary thyroid carcinoma metastasis. The patient still survives at present, treating metastasis with Cabozantinib. **Conclusion** endoscopic ultrasound fine-needle aspiration is a minimally invasive and accurate method of sampling lesions of the pancreas. In combination with clinical history and immunohistochemistry, can confirm diagnosis and define management.

INTRODUCTION

Differentiated thyroid carcinoma includes the papillary and follicular subtypes. In general, they are indolent, have a good prognosis, and the follicular variant is more aggressive [1, 2].

The preferred localizations of metastases are regional lymph nodes, bone and lung. Pancreatic metastasis is rare, with few cases reported in the scientific literature [3, 4].

Metastases correspond 1.8% to 7.6% of the pancreatic masses and the diagnosis is important for clinical staging and appropriate management. However, the location of the pancreas makes it challenging to obtain biopsies from these masses [5].

Endoscopic ultrasound (EUS) guided fine needle aspiration (FNA) is a non-invasive and effective method that has 89% accuracy in diagnosing metastasis to pancreas [5].

Thus, the present study aims to report a case of papillary thyroid carcinoma metastatic to pancreas, whose diagnosis was made by EUS-FNA and immunohistochemistry.

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Keywords Pancreatic cancer; Papillary Thyroid Cancer; Endoscopic Ultrasound; Immunohistochemistry
Abbreviations WBS Whole-body scintigraphy; CT computed tomography; PET-CT positron emission tomography - computed tomography; EUS endoscopic ultrasound; EUS-FNA endoscopic ultrasound fine-needle aspiration; TTF-1 thyroid transcription factor 1; CH-EUS contrast-enhanced harmonics EUS; RAI radioiodine therapy; SC Smear cytology; LBC liquid-based cytology; CB and cell block; NETs Neuroendocrine tumors.
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CASE REPORT

This report is about a 47-year-old female patient with an initial diagnosis of papillary thyroid carcinoma (PTC) in January 2009 (BETHESDA IV). On that occasion, total thyroidectomy was performed.

A cervical ultrasound performed in June 2009 identified thyroid tissue and lymph node disease, and adjuvant treatment with radioiodine therapy (RAI) with 100mCi was indicated. After that dose, whole-body scintigraphy (WBS) showed only uptake in the thyroid topography.

In March 2010, she presented elevated levels of thyroglobulin, and a new dose of RAI with 200mCi was indicated. WBS detected uptake in the left hemithorax, confirmed by imaging (presence of bilateral pulmonary nodules).

In September 2012, positron emission tomography - computed tomography (PET-CT) showed an increase in the number of pulmonary nodules. A new dose of RAI with 300mCi was performed.

From July 2015 to June 2017, there was progression of the disease, with development of neoplastic pleural effusion

and bone metastasis. The patient started treatment with tyrosine kinase inhibitor (Vandetanib and Lenvatinib).

In June 2019, a metastatic brain lesion was discovered and treated with radiosurgery. Computed tomography (CT) was performed to investigate abdominal pain. CT revealed hepatic lesions suggestive of secondary involvement and a solid mass in the pancreatic head. EUS showed a heterogeneous hypoechoic nodule with well-defined borders, measuring 19 mm x 17 mm, located at the pancreatic head, promoting dilation of the main pancreatic duct (8.8 mm) **(Figure 1)**.

EUS-FNA was performed with a 22G needle through the duodenal wall. A part of material aspirated was used to prepare slides with panoptic and papanicolau staining. The other part was centrifuged and paraffin embedded. Cytology identified epithelioid cell neoplasia, and cell block material was positive for thyroglobulin, thyroid transcription factor 1 (TTF-1), Ki-67 and cytokeratin AE1/AE3 **(Figure 2)**. The patient started treatment with Cabozantinib and still survives at present moment.

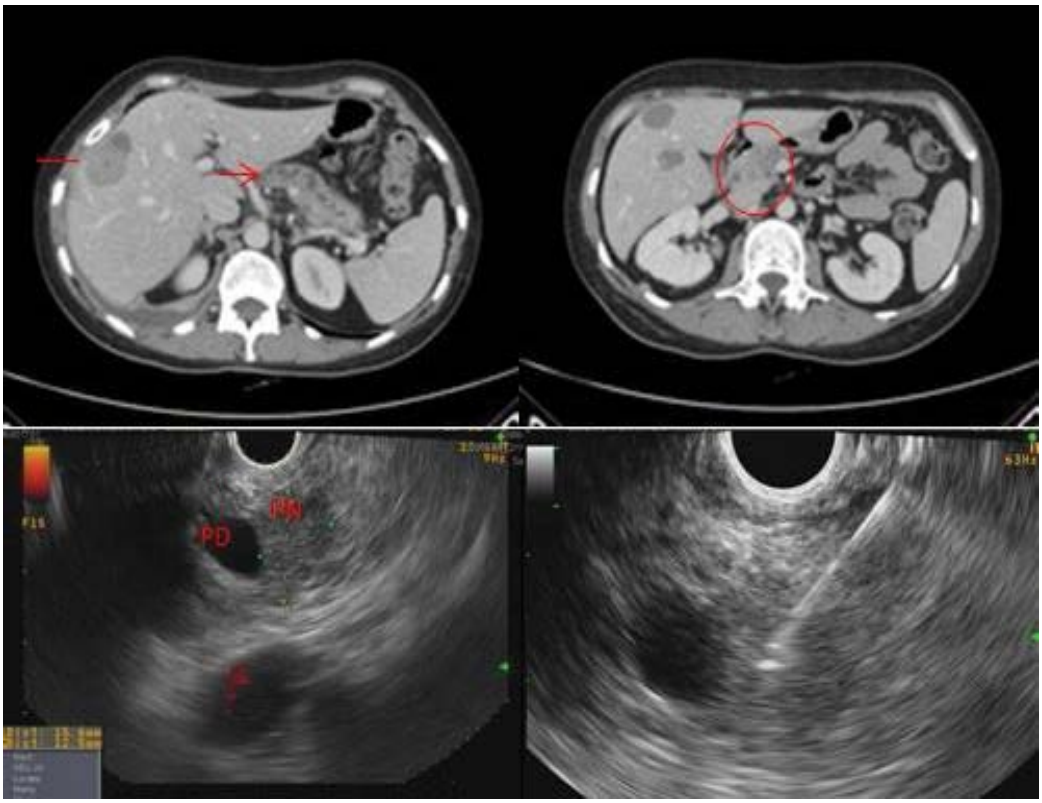

Figure 1. CT and EUS images of the pancreatic lesion. Arrow - hepatic metastases, arrowhead - Wirsung duct dilatation, circle-pancreatic nodule, PD Pancreatic Duct; PN Pancreatic Nodule.

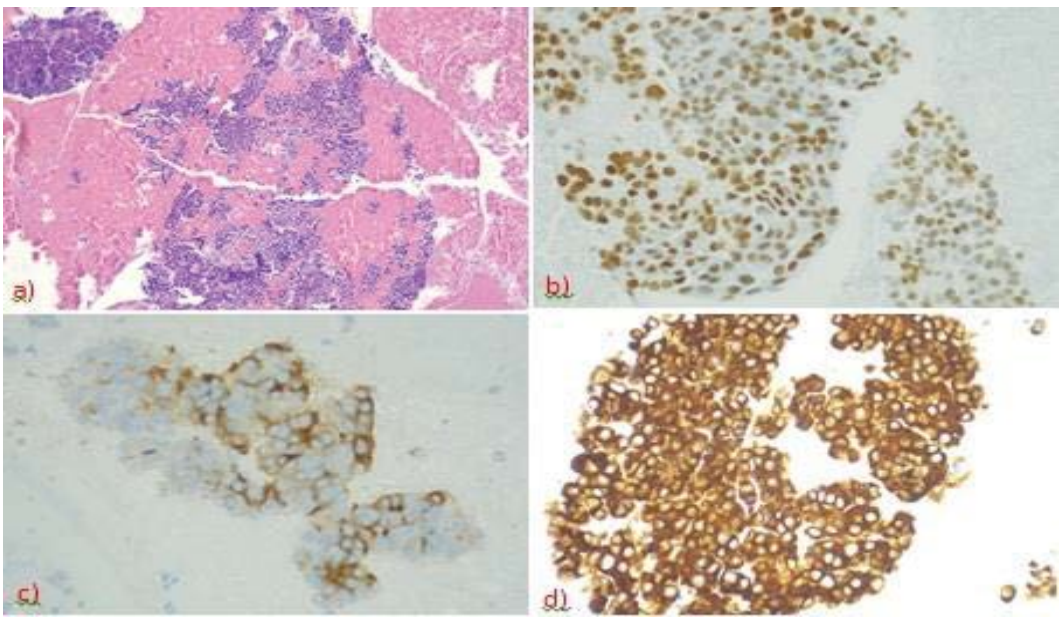

Figure 2. (2a) Hematoxylin-eosin–stained section, (2b) immunohistochemistry positive for TTF-1, (2c) immunohistochemistry positive for thyroglobulin, (2d) immunohistochemistry positive for AE1/AE3.

Table 1. Cases of pancreatic metastases from PTC.

Demographic			Primary lesion				Metastatic lesion				
Author	**Age at PTC diagnosis**	**Gender**	**Size**	**Location**	**Histology**	**TNM classification**	**Time after diagnosis of primary lesion**	**Location in pancreas**	**Other distant metastasis**	**Stain**	**Treatment**
Sugimura et al	32	F	N/A	N/A	PTC	N/A	7 years	Head	None	Tg	Surgery
Jobran et al	53	M	5.5 cm	Left	PTC (TCV)	T4N1M0	1 month	Head	Lung, bone	Tg	Surgery+Carboplatin/ Adriamycin
Meyer et al	62	M	N/A	N/A	PTC	T4N0M0	4 years	Head	Adrenal, lung, liver, kidney	Tg	Surgery
Siddiqui et al	62	M	4 cm	Right	PTC (TCV)	T4N1bM0	7years	Head	Lung	Tg, TTF-1, CD15	Surgery
Angeles at al	72	M	N/A	Intrathoracic	PTC (classic)	TxNxM1	N/A	Body and tail	Brain	Tg, TTF-1, cytokeratin 7, cytokeratin 19, HMBE-1	Surgery
Borschitz et al	34	F	6 cm	Right	PTC (FV)	T3N1aM0	9 years	Head	None	Tg	Surgery
Borschitz et al	46	M	N/A	Right, multifocal	PTC	T3N1cM0	13 years	Body	Lung, bone	Tg	Surgery
Chen et al	82	M	N/A	N/A	PTC (classic)	TxN1M0	5 years	Neck	None	Tg	Unknown
Alzahrani et al	55	M	2 cm	Right	PTC (classic)	T4aN1bM0	7 years	Uncinate process	Lung, liver, bone, omentum	Tg, TTF-1	Sorafenib
Tunio et al	56	F	4 cm	Right	PTC (FV)	T2N1cM0	7 years	Neck	Lung	N/A	Surgery+Sorafenib
Li et al	55	M	N/A	N/A	PTC	N/A	11 years	Body and tail	None	Tg, TTF-1, Ki67, CK19, CgA, Syn, CEA, CD56	Surgery
Davidson et al	82	F	3.3 cm	Left and isthmus	PTC (TCV)	T3N1bM0	2 years	Body	None	Tg,TTF-1, CD57, CEA	Monitoring
Ren et al	47	M	10 cm	Left and isthmus	PTC	N/A	Diagnosis of primary and metastasis at the same time	Body and tail	Liver, diaphragm	Tg, TTF-1, PAX-8, CK19, HBME-1, Galectin-3, P53, WT, DPC4, CA19-9, MUC1	Surgery
Cho et al	71	Male	N/A	N/A	PTC (classic)	N/A	10 years	Head and body	Lung	TTF-1, PAX-8	Unknown
Present case	38	Female	2.5 cm	Right	PTC (classic and FV)	T1NxMx	10 years	Head	Lung, liver, bone, brain	Tg, TTF-1, PAX-8, Ki-67, AE1/AE3, Beta-catenin, Vimentin, alpha 1-anti-chymotrypsin	Cabozantinib

PTC papillary thyroid carcinoma; TCV tall cell variant; FV follicular variant; N/A not available; Tg thyroglobulin; TTF-1 thyroid transcription factor 1; CEA carcinoembryonic antigen; CgA chromogranin A; HMBE-1 Hector Battifora mesothelial-1; F Female; M Male.

DISCUSSION

Differentiated thyroid carcinoma presents with distant metastasis in 4% of cases, usually occurring in the lungs, bone and thoracic lymph nodes. 6 Pancreatic involvements are extremely rare [3].

In a literature review published by Davidson et al cases of pancreatic metastasis from PTC have been found since 1991 to 2017 [6]. The mean age at diagnosis was 55.3 years, with predominance in males. Metastasis was detected 1 month to 13 years after diagnosis of the primary tumor and 7 patients had other sites of metastases beyond the pancreas [6]. We identified 3 more cases in the scientific literature by 2020 **(Table 1)**.

Pancreatic metastasis may remain asymptomatic for a long period or manifest with non-specific symptoms, usually occurring in the context of an extensive disease [5, 7]. It can be detected incidentally or during follow-up investigations, even several years after the removal of the primary tumor [7].

Despite advances in diagnostic imaging techniques, the differentiation of primary pancreatic cancer from pancreatic metastases remains challenging because there is no pathognomonic feature [8]. The finding of a heterogeneous pancreatic mass with well-defined borders in a patient with a previous history of malignancy should be suspected for metastasis, a clear indication for EUS-FNA [9].

It is also not possible to identify a typical image of metastatic tumor in EUS; however, suggestive findings include multiple lesions, dilatation of the main pancreatic duct, atrophy, and well-defined margins [5].

EUS-FNA is a noninvasive and effective method for definite diagnosis of solid pancreatic masses, with a sensitivity of 75% to 93.8% and specificity of 60% to 100% [5].

Smear cytology (SC), liquid-based cytology (LBC), and cell block (CB) preparation are common techniques used for the analysis of specimens collected from EUS-FNA. CB provides more pathological information, when combined with histological examination such as hematoxylin and eosin (H&E) staining and immunostaining of serial sections compared with each method alone [10].

Immunohistochemistry has become a useful ancillary study in the identification and classification of pancreatic neoplasms. The diagnostic accuracy has been significantly improved because of the development of tumor-associated biomarkers and effective immunohistochemistry panels [8, 11, 12, 13].

New technologies have been developed because of the need to improve the EUS-FNA diagnostic rate. Contrast-enhanced harmonics EUS (CH-EUS) enables the dynamic observation of microvessels with slow flows that are not revealed by Doppler color, which differentiates perfused and nonperfused tissue. The hypoenhanced aspect has been reported as predictive for adenocarcinoma. Neuroendocrine tumors (NETs), chronic pancreatitis, autoimmune pancreatitis, serous cystadenoma, and metastasis are iso/hyperenhanced, with a sensitivity of 39%-86% and a specificity of 98% [14, 15].

According to the cases reported in the scientific literature, surgical treatment should be proposed to selected patients, due to the high incidence of adverse events and mortality after pancreatic resection. The selection criteria for surgery may be that the primary tumor has good prognosis and can be resected, the metastasis is isolated to the pancreas and the patient can tolerate pancreatectomy [16]. Patients may need palliative resection in cases of compression of the nearby structures causing obstructive jaundice or gastric outlet obstruction [17, 18, 19, 20, 21].

BRAF V600E mutation is known to be associated with more aggressive forms of thyroid cancer and was detected in select cases of metastatic PTC to the pancreas [1]. Interestingly, sorafenib, a small kinase inhibitor of the BRAF gene product has been reported to show some degree of stabilization of disease in patients with metastatic PTC [17, 22, 23, 24, 25, 26].

CONCLUSION

Pancreatic metastasis from papillary thyroid carcinoma is extremely rare, causing nonspecific clinical symptoms. EUS-FNA with immunohistochemistry is the best method to confirm diagnosis and define management. Metastasis should be considered as the main diagnostic possibility in patients with pancreatic mass and history of extra-pancreatic malignancy.

Conflicts of Interest

The authors declare that there is no conflict of interests in this study.

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