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CASE REPORT

Pancreatic Metastasis of Tall Cell Variant of Papillary Thyroid Carcinoma: Diagnosis by Endoscopic Ultrasound-Guided Fine Needle Aspiration

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ABSTRACT

Context The incidence of tall cell variant of papillary thyroid carcinoma that has metastasized to the pancreas is extremely rare. There has been only one previously reported case of pancreatic metastasis of the tall cell variant of papillary thyroid carcinoma.

Case report We present the case of a patient who presented with tall cell variant of papillary thyroid carcinoma with metastasis to the pancreas detected and confirmed cytologically by EUS-FNA after finding of the CT scan were equivocal.

Discussion EUS-FNA is a powerful new tool that can be used for the detection and diagnosis of primary and metastatic lesions of the pancreas.

INTRODUCTION

Endoscopic ultrasound (EUS) is emerging as a powerful tool in the clinical evaluation of pancreatic lesions. This procedure is capable of both detecting and facilitating the biopsy of small (less than 2 cm) lesions within the pancreas that may not be visualized by helical computed tomography (HCT). Indeed, recent studies have found EUS to have a higher detection rate for small pancreatic tumors than HCT [1, 2].

Clinically evident metastasis of thyroid cancer to the pancreas is rare and, in fact, there has been only one previously reported case of pancreatic metastasis of the tall cell variant of papillary thyroid carcinoma (TCV-PTC) [3]. We present the case of a patient who presented with TCV-PTC with metastasis to the pancreas detected and confirmed cytologically by EUS- guided fine needle aspiration (FNA) after finding of the CT scan were equivocal. We also give a brief overview of TCV-PTC, and discuss the role of EUS in the evaluation of metastatic pancreatic lesions.

CASE REPORT

In May 1997, a 62-year-old man with no significant past medical history was referred to another institution for investigation of dysphagia. On physical examination, he was noted to have nodular enlargement of the right lobe of the thyroid gland with displacement of the trachea to the left. A CT scan of the neck confirmed the presence of a 4 cm mass in the right thyroid lobe, and a diagnosis of “large cell carcinoma” was made by ultrasound-guided fine-needle aspiration biopsy.

The patient next underwent total thyroid

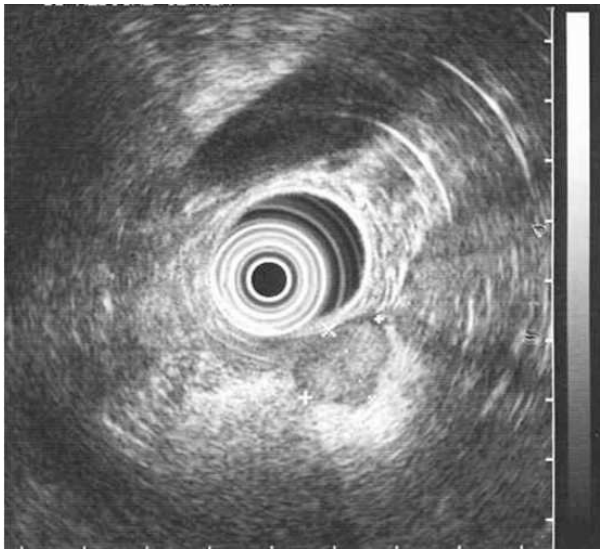

Figure 1. EUS showing a well-defined, 15x11 mm hypoechoic, homogeneous mass in the pancreatic head.

ectomy with bilateral paratracheal lymph node, and left modified radical neck dissections. A histopathologic diagnosis of TCV-PTC, with extensive involvement of the right thyroid lobe and isthmus, invasion of the tracheal perichondrium, and metastases to multiple cervical, paratracheal, and superior mediastinal lymph nodes, was made. With the definitive diagnosis of TCV-PTC stage T4 N1b M0, adjuvant radiotherapy was given. The patient received 5,000 rads (radiation absorbed dose) of external beam radiation to the neck, and was maintained on levothyroxine sodium (175 μg daily). A post-treatment iodine scan showed residual uptake

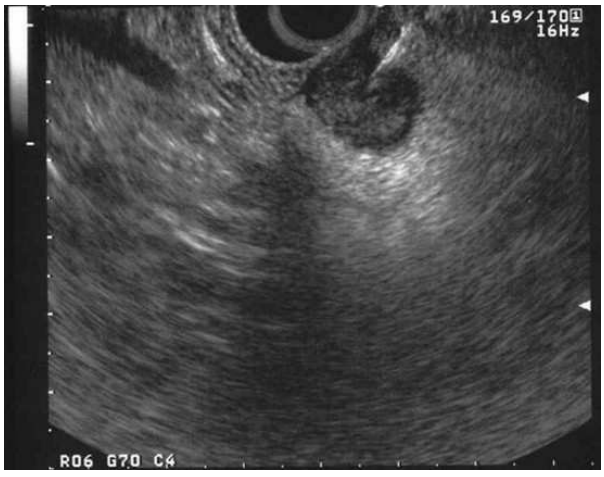

Figure 2. EUS-guided FNA of pancreatic head mass. Cytology confirmed tall cell variant of papillary thyroid carcinoma (TCV-PTC).

only in the thyroid bed, and serum thyroglobulin levels were undetectable. In January of 1998, a follow-up scan again demonstrated iodine uptake in the neck and the thyroglobulin level was now 50 ng/mL (reference range: 3-40 ng/mL). Radioactive ^{131}I (158 mCi) was given to treat residual disease. The patient received a second treatment of radioactive ^{131}I in 2001 due to a rising thyroglobulin, and follow-up imaging showed only a small area of uptake in the thyroid bed. Due to a rising thyroglobulin (90 ng/mL) over the next year, a repeat chest CT scan was performed and this showed multiple pulmonary nodules with no evidence of residual thyroid disease. In light of the clinical stability of his disease, the patient was treated conservatively and no tests or treatment was offered.

In February 2004, the patient presented to his physician with complaints of abdominal pain and fullness. The serum thyroglobulin level was now 167 ng/mL, having increased from 96 ng/mL some four months previously. An iodine scan showed no residual uptake. A positron emission tomography (PET) scan revealed a hypermetabolic lesion in the abdomen, and a follow up HCT scan suggested the presence of a low-density lesion in the head of the pancreas. However, the HCT findings were equivocal with the radiologic differential diagnosis including focal tumor, metastatic disease, and chronic pancreatitis. The patient subsequently underwent EUS and this showed a well-defined, 15x11 mm hypoechoic, homogeneous mass in the head of the pancreas (Figure 1). EUS-FNA of the mass was performed (Figure 2) and cytologic examination of the direct smears showed papillary groups of tumor cells with nuclear features typical of PTC, including frequent grooves and intranuclear cytoplasmic inclusions (Figure 3a). In addition, rare soap bubble-type intranuclear inclusions were identified (Figure 3b). Tissue sections of a cell block prepared from the specimen showed papillary groups of eosinophilic tumor cells that were more than twice as tall as they were wide (Figure 4). Immuno-

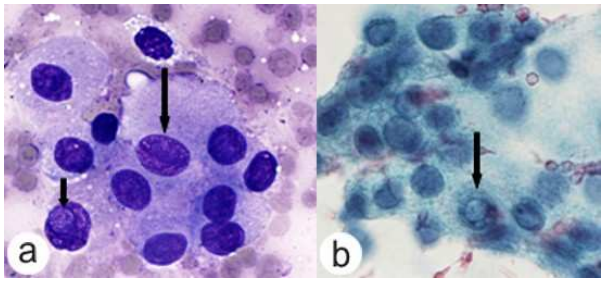

Figure 3. Fine needle aspiration biopsy findings. **a.** Tumor cells with longitudinal nuclear groove (long arrow) and intranuclear cytoplasmic inclusion (short arrow) (Diff-Quik™ stain x1,000). **b.** Tumor cell with "soap-bubble"-type intranuclear inclusion (arrow) (Papanicolaou stain x1000)

histochemical stains revealed that the tumor cells were positive for both thyroglobulin and thyroid transcription factor-1, confirmatory of thyroidal origin. The tumor cells were also immunoreactive for CD15 which, in concert with the morphologic findings, supported a diagnosis of metastatic TCV-PTC. Slides from the patient's thyroidectomy specimen were requested from the outside hospital and, upon review, his original tumor was found to show morphologic features consistent with TCV-PTC.

In light of the long-term stability of the patient's lung nodules by CT, and their low standardized uptake value by PET, it was felt that his pancreatic tumor deposit was the most likely source of his increasing serum thyroglobulin level. Therefore, a pylorus-sparing pancreaticoduodenectomy was performed as a means of metastectomy. At the time of surgery, the serum thyroglobulin had increased to 362 ng/mL. Examination of the surgical resection specimen revealed a 1.4x1.4x1.2 cm nodule in the head of the pancreas that was histologically confirmed to be metastatic TCV-PTC. Post-operatively, the patient's levothyroxine was resumed and serial thyroglobulin levels showed a decrease to 107 ng/mL. The patient has done well 24 months post-operatively but, at the time of submission of this report, his thyroglobulin level had risen to 224 ng/mL, presumably due to progression of his pulmonary disease as evidenced by increasing size of his lung nodules on chest CT.

DISCUSSION

We report an unusual case of TCV-PTC metastatic to the pancreas in which the diagnosis was accomplished by EUS-FNA. This is only the second such case reported in literature [3]. TCV-PTC is a clinically aggressive morphologic variant of PTC that, by definition, differs from conventional PTC in being composed of eosinophilic tumor cells (more than 30%) that are twice as tall as they are wide [4, 5]. Immunohistochemically, the tumor cells differ from those of conventional PTC by expressing the human myelo-monocytic antigen, CD15 [6]. The cytologic features of TCV-PTC as observed by FNA have been recently reviewed and, in contrast to conventional cases of PTC, the intranuclear cytoplasmic inclusions characteristic of PTC cells were reported to be frequently multiple, imparting a soap bubble appearance to the involved nuclei [7]. In our case, in addition to many typically single intranuclear inclusions (Figure 3a), rare soap bubble-type inclusions were also identified (Figure 3b). Compared to conventional PTC, TCV-PTC occurs in a slightly older population, and has a greater incidence of both regional and distant metastases with the most common sites of metastases being the regional lymph nodes and the lungs. Transformation to anaplastic carcinoma is rare [8]. While conventional CT scans have been traditionally used to diagnose thyroid cancers, new studies have suggested

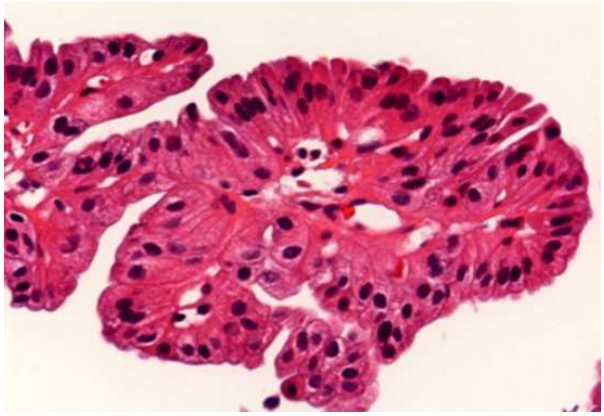

Figure 4. Cell block tissue section showing papillary cluster of columnar tumor cells with abundant oncocytic cytoplasm (H&E x200).

that the new integrated PET/CT modality may have a higher accuracy to diagnose and stage differentiated thyroid malignancies [9]. The 10-year mortality for TCV-PTC has been quoted as 25%, with death due to disease usually resulting from either local tissue destruction or distant metastases [10, 11, 12].

EUS is now recognized to be one of the most sensitive tests for the detection of both primary and metastatic lesions of the pancreas. Studies indicate that the sensitivity of EUS for detecting localized pancreatic lesions may be as high as 94-100 % [13, 14, 15]. Additionally, EUS may be helpful in distinguishing between primary pancreatic tumors and metastatic lesions. Primary adenocarcinoma of the pancreas typically appears as an echo-poor mass with irregular borders, whereas metastatic lesions are often rounded and well-delineated with a homogeneous echotexture that is either isoechoic or slightly hypoechoic in comparison with the adjacent pancreas. There may be either intensification or no peripheral attenuation of the ultrasound beam [16].

Newer imaging techniques have become available in recent years for the diagnosis of pancreatic lesions. HCT is an advance in CT technology in which higher resolution images of the pancreas can be obtained through rapid acquisition of images during arterial and venous phases of contrast enhancement. Initial studies in radiological publications reported HCT to have an extremely high detection rate for pancreatic tumors (97%) [17]. However, more recent studies in the gastroenterology literature have dampened enthusiasm for HCT. In a prospective study of 35 patients with presumed respectable pancreatic adenocarcinoma evaluated by EUS, HCT, and positron emission tomography (PET), the sensitivity of HCT for detecting the primary tumor was only 53%, far inferior to the sensitivities of 93% and 87% quoted for EUS and PET, respectively [2, 18]. In this study, EUS was also reported as being more sensitive than HCT for the identification of vascular invasion by tumor. However, another study assessing the HCT has demonstrated an important role in assessing respectability and locoregional extension [19]. EUS has been shown to be especially sensitive in detecting small (less than 3 cm) pancreatic lesions [20, 21, 22]. However, with the advent of newer generation CT technology such as multidetector scanners, it is possible that HCT could soon approach the accuracy of EUS in the evaluation of pancreatic malignancy [23]. A reasonable conclusion that can be drawn from these studies is that EUS and HCT should be viewed as complementary tests in the investigation of pancreatic lesions. New prospective well-designed studies are needed to further define the role of each test [24]. EUS is more sensitive in detecting small pancreatic masses and more accurate in predicting vascular invasion, whereas HCT may be better for the evaluation of larger tumors. In our patient, a PET scan performed due to a rising serum thyroglobulin revealed a hypermetabolic lesion in the abdomen. However, the HCT findings were equivocal, and it was only after the patient underwent EUS that a definite pancreatic lesion was detected. In this case, EUS has been superior to HCT in the detection of a small pancreatic tumor.

EUS-FNA can be used to establish a pathologic diagnosis as was done in our case. The sensitivity of EUS-FNA for detecting malignancy ranges from 75% to 90% and is superior to that of CT-guided FNA [25, 26, 27, 28, 29]. Additionally, EUS-FNA has demonstrated significant improvements in terms of safety, sensitivity, and accuracy to diagnose malignancies compared with endoscopic retrograde pancreatography (ERP) [30]. As previously described, EUS may detect smaller malignancies not seen by CT and, consequently, EUS-FNA may be the only feasible option in some patients. EUS-FNA is generally a safe procedure with an overall complication rate of 1% to 2%. The major complications reported are infection, bleeding, and pancreatitis. To date, there has been not reported case of a pancreatic fistula caused by EUS-FNA. The main drawback of EUS-FNA, or any other form of pancreatic biopsy in which minimal tissue is procured, is

that the negative predictive value is less than 100% [31]. Therefore, negative findings on EUS-FNA of a pancreatic mass do not rule out the presence of malignancy. To ensure that diagnostic material is obtained, many large centers are now performing EUS-FNA in the presence of a cytopathologist who can immediately review the specimen for adequacy. We recommend EUS-FNA in all patients in whom a metastatic pancreatic lesion is suspected in order to establish a tissue-based diagnosis and guide therapy.

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Keywords Biopsy, Fine-Needle; Endosonography; Pancreatic Neoplasms; Thyroid Neoplasms

Abbreviations ERP: endoscopic retrograde pancreatography; HCT: helical computed tomography; rads: radiation absorbed dose; TCV-PTC: tall cell variant of papillary thyroid carcinoma

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