

Ectopic thyroid of the pancreas

A case report and literature review

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Abstract

Rationale: Ectopic thyroid is commonly found in the neck region. Intra-abdominal ectopic thyroid is extremely rare, with only 2 cases reported in the pancreatic region. Very few reports have described detailed imaging findings of intra-abdominal ectopic thyroid.

Patient concerns: A 73-year-old woman with aggravated recurrent right upper quadrant pain was found to have a retroperitoneal mass at the head of pancreas. Abdominal computed tomography (CT) showed a well-defined, high attenuated (56HU) mass measured of 60 × 50 mm in diameter, that exhibited heterogeneous contrast enhancement throughout the 3 phases.

Diagnosis: Neuroendocrine neoplasm was suspected.

Interventions: Following discussions with the patient, she refused fine needle aspiration cytology; however, she underwent total resection of the mass and had an uneventful clinical course. Histopathological examination showed thyroid tissue with TTF-1 and TGB positivity, and BRAF negativity, indicating a benign variant.

Outcomes: The patient had no signs of relapse with normal thyroid hormone levels after 2 years of follow up.

Lessons: Ectopic thyroid tissue should be considered when patients present with similar imaging findings in abdomen. We review all reported cases of abdominal ectopic thyroid tissue to provide specific evidence for the diagnosis and treatment of this rare entity.

Abbreviations: CT = computed tomography, FNAC = fine needle aspiration cytology, IHC = immunohistochemistry, TGB = thyroglobulin, TTF-1 = thyroid transcription factor-1, USG = ultrasonography.

Keywords: ectopic thyroid, pancreas, thyroid gland

1. Introduction

Ectopic thyroid is a rare developmental abnormality that occurs during the migration of the thyroid anlage. It can be found anywhere along the path of the thyroid descent, from the floor of the primitive foregut to the final position of the thyroid in the neck. The estimated frequency of ectopic thyroid is 0.17 per 1000 patients,^[1] with lingual thyroid accounting for 90% of cases.^[2] Sublingual types are less frequently encountered, and ectopic thyroid below the diaphragm is an even more rare condition.

Experience with intraabdominal ectopic thyroid in the clinical literature is limited, and doctors could mistake ectopic thyroid tissue for neoplasms of adjacent tissues. The most appropriate management of this entity has not been established; however, surgical removal is common to exclude malignancy. We herein report a case of intraabdominal thyroid tissue located in the

pancreas and review of all the reported cases of ectopic thyroid in the abdomen to provide evidence for diagnosis and treatment.

2. Case presentation

A 73-year-old woman was admitted to Peking Union Medical College Hospital in Beijing, China, with a 6-year history of recurrent mild right upper quadrant pain, which was aggravated during the past month and could no longer be relieved by painkillers (not known). She had not previously been diagnosed with any other diseases.

A retroperitoneal hyperechoic mass was detected using abdominal ultrasonography (USG). A further abdominal computed tomography (CT) scan was performed, which indicated an inhomogeneous, ovoid mass measured 60 × 50 mm; the mass was hypodense (56 HU) in comparison with the normal liver parenchyma (Fig. 1A). It had a well-defined margin with small sheet-like calcifications and cystic degeneration. The mass was surrounded by the duodenum, was in front of the inferior vena cava, and compressed the head of the pancreas. After contrast medium administration, there was obvious enhancement in the arterial phase, which was hyperdense to the liver and lasted throughout the portal and delay phases (Fig. 1B–D). The coronal axes showed the accurate location of the mass, and 3D reconstruction suggested a rich blood supply from the celiac trunk (Fig. 1E, F).

Fine needle aspiration cytology (FNAC) was suggested to the patient as it is a routine preoperative work-up for pancreatic neoplasms, and may have been especially useful in this difficult case. However, as the mass was deep in the retroperitoneal space and had a rich blood supply, there was a risk of hemorrhage. After a discussion, the patient refused the examination. Surgery was then performed, which revealed a mass of about 8 cm in diameter with a complete capsule. It was found between the liver

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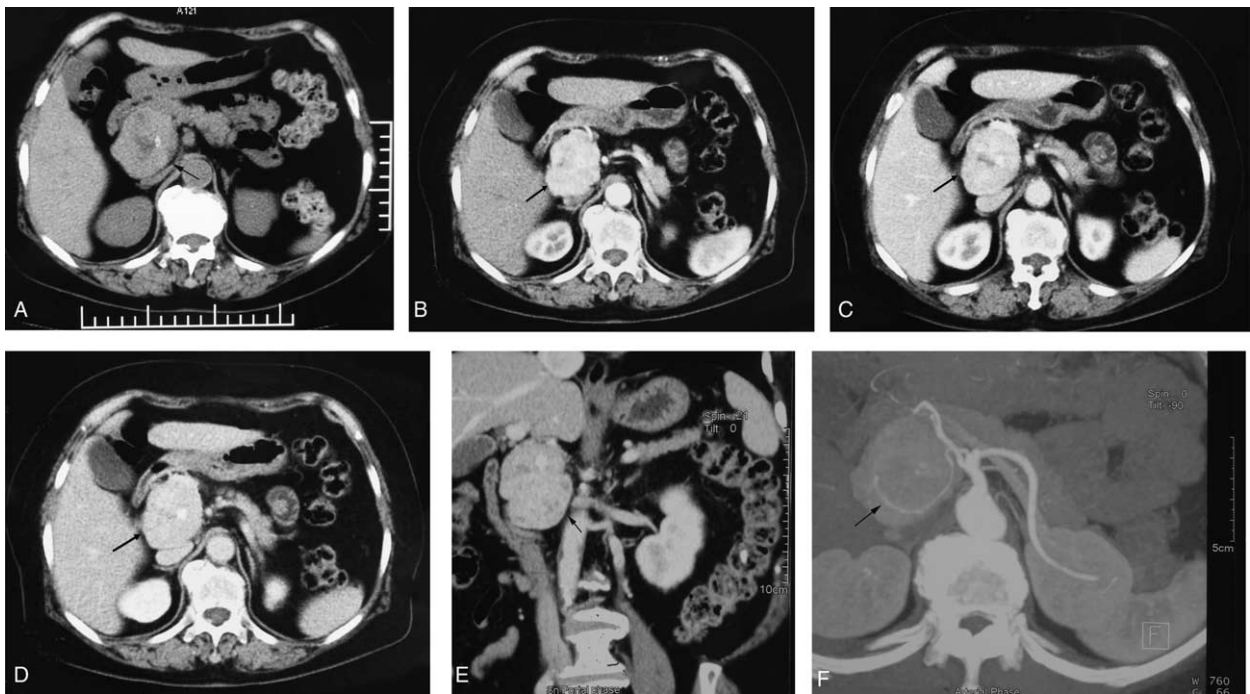


Figure 1. Abdominal computed tomography (CT) scan findings (black arrow). (A) Unenhanced CT showed inhomogeneous, ovoid mass (60 mm × 50 mm), with a well-defined margin and small sheetlike calcification and cystic degeneration. (B–D) The lesion demonstrates heterogeneous contrast enhancement on arterial phase (after 35–40 seconds), portal phase (after 40–60 seconds), and delay phase. (E) Coronal axes showed the location of the mass. (F) 3D reconstruction of vessels showed rich blood supply from the celiac trunk.

and the superior border of the kidney, and had a close interaction with the pancreatic hook. The mass was totally resected with some pancreatic tissue. Postoperatively, the patient had an uneventful course.

Histological examination revealed that the lesion consisted of differentiated thyroid tissue surrounded by some pancreatic tissue, with dilation of pancreatic duct (Fig. 2A). After immunohistochemistry (IHC) staining, strong expression of

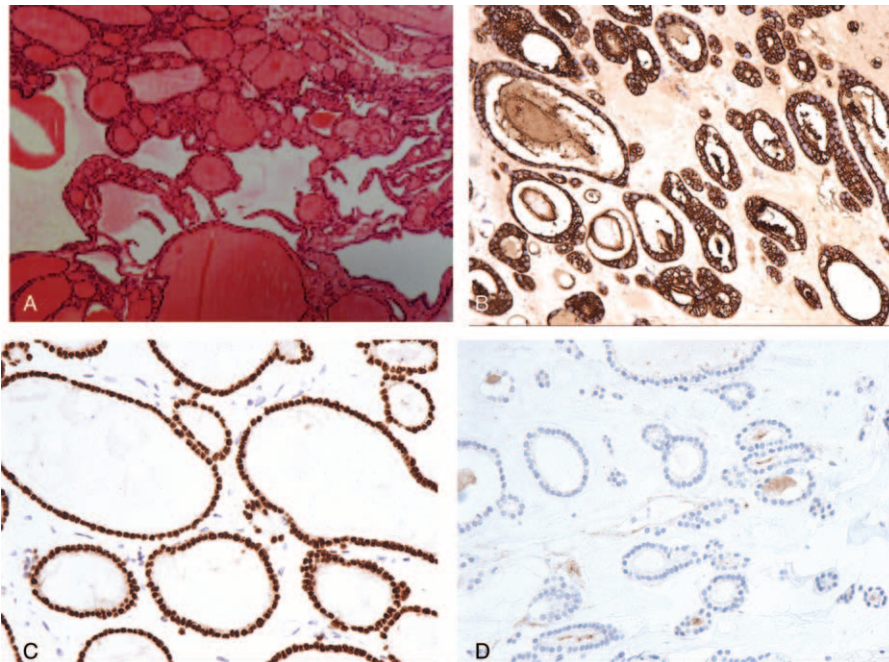


Figure 2. Pathology examination of specimen. (A) Hematoxylin-eosin staining revealed differentiated thyroid tissue (×100). (B–D) Immunoreactivity for TGB and TTF-1, while negativity for and BRAFV66E indicate a benign tissue (×200). TGB=thyroglobulin, TTF-1=thyroid transcription factor-1.

Table 1**Ectopic thyroids in the abdomen.**

Age/sex	Location/size, cm	Clinical data/endocrine	Preoperational evaluation/diagnosis	Reference
50/F	Pancreas/50 × 40 × 30 mm	Dyspeptic complaint/normal	NA/duodenal ulcer	Eyuboglu, 1999 ^[40]
69/F	Pancreas/70 × 50 × 30 mm	NA/NA	CT/pancreatic cancer	Seelig, 1997 ^[41]
24/F	Porta hepatis/100 × 90 × 80 mm	Incidental occurrence on US/normal	US + CT + FNAC + ¹²³ I scintigraphy/dual ectopia without eutopic thyroid	Ghanem, 2003 ^[34]
30w/M	Porta hepatis/2 mm	Autopsy/NA	NA/trisomy 18	Sekine, 2000 ^[37]
58/F	Porta hepatis/75 mm	Abdominal pain/NA	CT/NA	Jamshidi, 1998 ^[35]
58/F	Porta hepatis/NA	NA/NA	CT/NA	Strohschneider, 1993 ^[36]
76/M	Gallbladder/2 mm	right upper quadrant pain, fever/normal	US/acute cholecystitis	Campora, 2017 ^[5]
51/F	Gallbladder/30 × 20 mm	Recurrent right upper quadrant pain/normal	US/duplicated gall bladder with acute cholecystitis	Kachare, 2013 ^[32]
28/F	Gallbladder wall/small nodule	Chronic calculous cholecystitis/hypothyroidism	NA/chronic calculous cholecystitis	Cassol, 2010 ^[4]
60/F	Gallbladder wall/19 × 17 × 11 mm	Right upper quadrant pain/normal	CT/gallbladder neoplasm	Liang, 2010 ^[3]
62/F	Gallbladder wall/NA	Right upper quadrant pain/normal	NA/biliary colic	Venditti, 2007 ^[31]
68/M	Gallbladder wall/microscopically	Vomiting, right upper quadrant pain/NA	NA/acute cholecystitis	Ihtiyar, 2003 ^[33]
35/F	Gallbladder/7 mm	Abdominal pain/normal	NA/calculous cholecystitis	Harach, 1998 ^[8]
NA/F	Gallbladder wall/microscopically	Right upper quadrant pain/NA	NA/acute cholecystitis	Curtis, 1969 ^[6]
43/F	Retroperitoneal/20 mm	Incidental occurrence on CT/normal	CT + MRI + PET-CT/primary retroperitoneal tumor	Tamaki, 2017 ^[10]
71/F	Liver/57 × 50 mm	Incidental occurrence on US/normal	US + CT + FNAC/ectopic thyroid	Salam, 2012 ^[42]
76/F	Duodenal mesentery/50 mm	Epigastric discomfort/normal	CT/retroperitoneal mass	Kutz, 2012 ^[38]
63/M	Submucosa of duodenum/microscopically	NA/normal	NA/pancreatic cancer	Takahashi, 1991 ^[44]
16/F	Proximal jejunum/microscopically	Epigastric abdominal pain, vomiting/normal	NA/proximal jejuno-jejunal intussusceptions	YA, 2007 ^[7]
56/M	Jejunum mesentery/90 × 50 mm	Mass/ft3, ft4, tt3, tt4, Tg ↑, TSH ↓	US + CT + FNAC/malignant thyroid tumor	Gungor, 2002 ^[39]
63/F	Hilum of spleen/100 × 75 × 50 mm	Dysphagia, vomiting, postprandial pain/normal	barium study/gastric cancer	Çiçek, 1993 ^[43]
57/F	Right adrenal gland/6 × 4 × 6 mm	Incidental occurrence on US/normal	CT + MRI/NA	Yılmaz, 2016 ^[21]
32/F	Right adrenal gland/40 mm	Severe pain in right lumbar side/normal	US + CT/adrenal mass	Casadei, 2015 ^[23]
50/F	Right adrenal gland/30 mm	Right hypochondria pain/NA	CT/nonfunctioning tumor of adrenal gland	Shiraishi, 1999 ^[29]
50/M	Right adrenal gland/tumor ruptured	NA/NA	US + CT/primary tumor of adrenal gland	Shiraishi, 1999 ^[29]
61/F	Right adrenal gland/35 mm	Incidental occurrence on US/normal	CT + MRI/NA	Tsjimura, 1996 ^[30]
50/F	Left adrenal gland/53 mm	Incidental occurrence on CT/normal	CT/NA	Shuno, 2016 ^[27]
49/F	Left adrenal gland/57 × 64 × 57 mm	Incidental occurrence on US/normal	US + CT + MRI/hemorrhagic cyst and degenerative adrenal adenoma	Tada, 2016 ^[22]
51/F	Left adrenal gland/33 mm	Incidental occurrence on CT/normal	CT/NA	Gourmaud, 2014 ^[24]
59/F	Left adrenal gland/50 × 50 mm	Symptomatic obstructive process/normal	CT + MRI + FNAC/NA	Romero, 2013 ^[9]
38/F	Left adrenal gland/52 mm	Lower back pain/normal	CT/adrenal tumor	Romero, 2013 ^[9]
61/F	Left adrenal gland/microscopically	Hyperaldosteronism/normal	CT/functioning adrenal adenoma	Bohinc, 2011 ^[25]
54/F	Left adrenal gland/16 × 12 mm	Hypertension/normal	CT/primary aldosteronism or malignant tumors	Hagiuda, 2006 ^[28]
67/F	Left adrenal gland/25 × 30 × 30 mm	Gastric cancer and gallstones/normal	CT/NA	Takao, 2006 ^[26]

CT=computed tomography, PET=positron emission tomography, TSH=thyroid stimulating hormone.

thyroid transcription factor-1 (TTF-1) and thyroglobulin (TGB) was seen, while BRAFV600E was negative (Fig. 2B–D). On the basis of the morphology and IHC results, ectopic thyroid was diagnosed. Careful evaluation of the thyroid and neck lymph nodes with ultrasound revealed mixed cystic and solid thyroid nodules; as a result, there was a very low chance of malignancy. Thyroid-specific laboratory tests were normal. USG examination of the uterus and bilateral ovaries revealed no lesions. The patient refused to undergo further nuclear scintigraphy to detect ectopic thyroid tissue in other parts of the body. After 2 years of follow-up, she had no signs of relapse according to USG findings, and her thyroid hormone levels were normal. The patient consented to the publication of this case report (Table 1).

3. Discussion

The most common reason for ectopic thyroid tissue is an arrest of migration or excessive descent of the thyroid anlage^[3]; thus, it is most often found along the path of thyroid descent (Wölfler area).^[4] Ectopic thyroid tissue in the abdomen is rare and is difficult to explain by abnormal migration as it is distant from the path of embryological development. The most common

interpretation is the heterotopic differentiation of precursor cells from the foregut endoderm,^[5–8] as most intraabdominal organs originate in the endodermal germ layer, which is also the case for the thyroid. An exception is ectopic thyroid tissue in the adrenal gland because the adrenal cortex originates from the mesodermal layer while the medulla originates from the ectodermal layer.^[9] Developmental errors, such as congenital defects in the diaphragm leading to diaphragmatic hernias are also a possible explanation.^[9] In addition, ectopic thyroid tissue could also be explained as a teratoma, which originates from a single germ cell after the first meiotic division, whose histology can show other tissue components, such as skin appendages, cartilage, and bone.^[10] Moreover, pancreas and thyroid gland may demonstrate more interrelationships, as the possible contribution of insulin resistance to thyroid pathology^[11] and autoimmune disease could involve both thyroid and pancreas.^[12]

Another important issue is to rule out metastases from thyroid carcinoma. Distant metastases of differentiated thyroid carcinomas have been found at sites including the pancreas,^[13] porta hepatitis,^[14] liver,^[15] and others.^[16] Therefore, an extensive examination of the neck thyroid gland and neck lymph nodes should be performed. However, ectopic thyroid tissue has also

been reported in patients without histologic evidence of thyroid carcinoma, which is an occult papillary carcinoma. Moreover, malignant transformation of ectopic thyroid tissue could also occur; the estimated incidence of carcinoma arising in a lingual thyroid is less than 1%.^[17] To distinguish benign tissue from malignant tissue, Meyer and Steinberg^[18] proposed morphologic criteria, including microscopic size, round or oval follicles, nonpapillary type, uncrowded nuclei, not enlarged, no stromal proliferation, and no psammoma bodies. In addition, IHC and molecular analysis could provide more information than morphology alone. Mutations in genes regulated by transcription factors, including TTF-1 (Nkx2-1), FOXE1, and PAX-8 could lead to thyroid dysgenesis.^[19] Markers such as BRAFV600E, NRAS/KRAS, galectin-3, and HBME-1 are found in differentiated thyroid carcinoma, but not in benign nonadenomatous follicular epithelium.^[9] In our patient, the morphology met the aforementioned criteria. IHC positivity for TTF-1 and TGB indicated its thyroid nature, and negativity for BRAFV600E also supported a benign finding. Compared with polymerase chain reaction, IHC analysis of BRAFV600E has an 89% sensitivity and 100% specificity.^[20]

Experience with intraabdominal ectopic thyroid tissue in the clinical literature is limited. We reviewed the English literature from 1960 to 2017; a total of 34 cases were reported, including in the adrenal gland (13 cases),^[9,21–30] gallbladder (8 cases),^[3–6, 8,31–33] porta hepatis (4 cases),^[34–37] mesentery (2 cases),^[38,39] pancreas (2 cases),^[40,41] liver (1 case),^[42] spleen (1 case),^[43] retroperitoneum (1 case),^[10] duodenum (1 case),^[44] and jejunum (1 case).^[7] Ectopic thyroid tissues in the ovary (struma ovarii) are more commonly seen, comprising 1% of all ovarian tumors and 2% to 5% of ovarian teratomas.^[45] Thus, our review mainly focuses on those extremely rare entities. Our case is the 3rd found in the pancreatic region.

Of the 34 cases reported, there was a predominance of women (82.4%), which is similar to ectopic thyroid tissue found in other locations. The age at diagnosis varied from 30 weeks of gestation to 76 years of age. According to the reports, ectopic thyroid was mostly asymptomatic; however, nonspecific symptoms, such as weakness, pain, dyspnea, diarrhea, hemorrhage, and other complications, may occur depending on the different anatomic sites. Ectopic thyroid tissue of the gallbladder was usually discovered after cholecystectomy for cholecystitis, while in one case^[3] it was identified preoperatively as a gallbladder neoplasm that caused recurrent right upper quadrant pain without gallstones. Another interesting case^[40] illustrated an ectopic thyroid of 50 × 40 × 30 mm that was pushing up the omentum minus; we presume this might be an explanation of the dyspepsia and duodenal ulcer in the patient. Thyroid hormone levels were normal in the majority of patients, except for 2 cases. In one case,^[39] a patient with a nodular colloid goiter and hyperthyroidism no longer required antithyroid drugs after resection of the abdominal mass, indicating functional ectopic thyroid tissue. In contrast, another patient with a history of hypothyroidism did not experience any changes after resection of the ectopic thyroid.^[4]

Imaging methods have been used in the diagnosis of ectopic thyroid, including high-resolution ultrasound, CT, and magnetic resonance imaging, as well as nuclear scintigraphy. Ultrasounds are excellent as the 1st approach with the color-power-Doppler technique to show hypervascularity. Further unenhanced CT scans could show a characteristic uniform high attenuation^[46] of the ectopic tissue because of the intrinsic iodine content. Reported Hounsfield units were 56 HU in our study, 43 HU in a study by

Liang et al,^[3] 59 HU in a study by Tada et al,^[22] and 20 HU as reported by Takao et al.^[26] Normal thyroid gland measured around 100 HU in our hospital, higher than these ectopic tissues. Notably, most adrenal gland ectopic thyroid tissues were described as cystic lesions,^[22] whereas those around the porta hepatis were usually solid or semisolid masses with cystic components.^[3,34,39,47] Since HU value was average, they were not exactly comparable to normal thyroid gland. All the reported ectopic thyroid tissues exhibited well-defined borders, and some had small calcifications.^[21,24,28,34] After contrast medium administration, the tissues mostly showed inhomogeneous enhancement,^[10,21,34,35,41,42] except for in the study by Liang et al, where they showed no obvious enhancement.^[3] Presentations on magnetic resonance imaging were not uniform, showing low to high signal intensity on either T1WI or T2WI,^[9,10,22,30] depending on the gelatinous colloid material; low signal intensity on T2WI was likely to correspond with highly gelatinous material.^[22] Combining the aforementioned imaging methods with positron emission tomography-CT scan could help to rule out malignancy.

FNAC and core biopsy are suggested for use in preoperative diagnosis, especially for pancreatic neoplasms. Only 3 cases have involved FNAC preoperatively, 2 of which showed typical thyrocytes and follicles,^[34,42] while the other found small, round epithelial cells with slightly hyperchromatic nuclei that indicated malignancy^[39]; however, the final pathology was benign.

Scintigraphy using ¹²³I, ¹³¹I, or ^{99m}Tc-pertechnetate has tissue specificity that could be used to confirm the thyroid nature of the mass, as well as to show ectopic thyroid. However, it may have limitations with regard to nonfunctional ectopic thyroid tissue.^[48] In addition, give the rarity of intraabdominal ectopic thyroid tissue, scintigraphy was usually performed after biopsy or postoperatively to evaluate the presence of ectopic thyroid and demonstrate ectopic thyroid tissue in additional locations. Of the 34 cases, only 6 cases involved whole-body nuclear scintigraphy; in one case,^[34] scintigraphy was performed after FNAC, while in the other cases it was performed postoperatively.^[21,27,32,35,43]

For the symptomatic ectopic thyroid, the choice of treatment depends on the symptoms, size and location of the mass, histological findings, and thyroid function.^[2] Surgical intervention should be applied in cases with severe obstruction, bleeding, ulceration, or suspicion of malignancy. If ectopic thyroid tissue is diagnosed, it is important to confirm the presence of a normally located thyroid gland before removing the ectopic tissue. In one case reported by Ghanem et al,^[34] dual ectopia was discovered at the porta hepatis and lingua, without a gland at the thyroid bed. Only the intraabdominal ectopic thyroid was resected, and the patient received thyroid hormone replacement postoperatively to maintain euthyroidism with suppressed thyroid-stimulating hormone level. The prognosis mainly depends on the coexisting lesion. Patients who underwent simple resection of intraabdominal ectopic thyroid tissue had an uneventful postoperative recovery, without relapse or metastasis.

4. Conclusion

In our case, although ectopic thyroid tissue is benign, it had a tendency to get enlargement and cause compression symptoms. Imaging procedures revealed a retroperitoneal mass with a well-defined border; this showed high attenuation on an unenhanced CT scan and obvious enhancement throughout the 3 phases. In postoperative pathological examination, the thyroid nature could be demonstrated by morphology as well as immunoreactivity for

TGB and thyroid-restricted transcription factors (TTF-1, PAX8, and FOXE1). Negativity for BRAFV66E, NRAS/KRAS, galectin-3, and HBME-1 would also indicate a benign tissue. Polymerase chain reaction could increase the sensitivity of detection. Further detection of other ectopic thyroid tissue using USG and nuclear scintigraphy is suggested in such cases.

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