Ultrasonographic Appearances of Parathyroid Gland Hyperplasia in Tertiary Hyperparathyroidism

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Background: *Tertiary hyperparathyroidism is due to autonomous hyperfunction of parathyroid gland. Parathyroidectomy are usually performed in patients who are refractory to medical treatment, aiming to decrease serum parathyroid hormone level. Ultrasound plays role in pre-operative detection of the abnormal gland.*
Objective: *The purpose of the study was to describe ultrasonographic appearances of parathyroid gland hyperplasia in tertiary hyperparathyroidism.*
Material and Method: *The study was performed in retrospective design. Patients diagnosed as tertiary hyperparathyroidism with available pre-operative ultrasonography of the neck during May 2009 and Jan 2015, and had pathologic confirming hyperplasia were included into the study. Datas were collected for location, echogenicity, surface, margin, vascularization, cystic change and calcification.*
Results: *There were 28 patients with 58 parathyroid glands found on ultrasound in the study. The size of the gland was ranged from 0.6 to 3.5 cm. The most common ultrasonographic findings found on the study was well-defined hypoechoic lesion with peripheral vascularity.*
Conclusion: *Familiarity of the appearance of the abnormal parathyroid gland could facilitate radiologist to localize the lesion confidently.*

Keywords: *Ultrasonography, Tertiary hyperparathyroidism*

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Tertiary hyperparathyroidism is one of the most common complications in patients with end stage renal disease (ESRD)[1]. It reflects the development of autonomous parathyroidhyperfunction, resulting in excessive secretion of parathyroid hormone (PTH), hypercalcemia and hypophosphatemia. There is a consensus that patients with tertiary hyperparathy roidism should have a bilateral neck exploration with subtotal or total parathyroidectomy and autotrans plantation[1-4]. Ultrasound plays role in pre-operative localization of the abnormally enlarged parathyroid glands and supporting clinical diagnosis[3-10]. To the authors' knowledge, there have not been previous studies describing the ultrasonographic characteristics of parathyroid gland in tertiary hyperparathyroidism in Thai population. The aim of the study was to describe ultrasonographic appearances of parathyroid gland hyperplasia in this condition which could help radiologist confidentially detect the lesion.

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Material and Method

This retrospective study was approved by Ethics committee of Faculty of Medicine, Thammasat University. Informed consent was waived due to the retrospective design.

Study population

The data were obtained from patients who previously had long standing secondary hyperparathyroidism due to chronic renal failure and diagnosed with tertiary hyperparathyroidism. Tertiary hyperparathyroidsm defined as the presence of hypercalcemia (serum calcium >14 mg/dL), hypophosphatemia (serum phosphate <2.5 mg/dL) and very high PTH level (serum PTH level >800 pg/ml). US images were analysed in those patients underwent parathyroidectomy with histologically proven parathyroid hyperplasia during May 2009 and January 2015.

Imaging technique

All of US studies were performed with a PHILIPS iU22 ultrasound machine, using a high resolution linear probe (12 MHz). The patients were

examined under a standard ultrasound neck technique with the patient lying in a supine position and with hyperextended neck.

Data collection and image interpretation

The patients' demographic data including sex, ageand time interval between US and parathyroidec tomy were recorded onto a standard case record form (CRF). Preoperative ultrasonographic findings were reviewed by two experienced neuroradiologists separately on a standard picture achieving and communication system (PACS). Any discrepancies were resolved by consensus between the two neuroradiologists. Surgical pathologic results were used as the gold standard to confirm the presence of parathyroid hyperplasia.

Ultrasonographic morphology of each hyperplastic parathyroid gland was described in terms of: (i) location on the posterior aspect of the thyroid gland (right superior, right middle, right inferior, left superior, left middle or left inferior), (ii) size (measured maximal dimension), and (iii) general characteristics, including echogenicity compared to thyroid gland (hyper-, hypo- or mixed echogenicity), surface (smooth, lobulated or irregular) and margin (well-defined or poor-defined), (iv) internal cystic changes, and (v) presence of intralesional calcification. Patterns of intralesional vascularity were demonstrated by color Doppler ultrasound (CDUS) and recorded as peripheral, central or absent.

Results

There were 61 patients with tertiary hyperparathyroidism who had available preoperative ultrasounds of the parathyroid glands. From this group, only 28 patients underwent parathyroidectomy with pathological confirmation. Time interval between ultrasound and parathyroidectomy ranged from 1 to 9 months (median 3 months). There were 68 parathyroid glands found at surgery and 58 glands were detected on ultrasound (85.3%). The size (maximal dimension) of the hyperplastic glands measured by ultrasound ranged from 0.6 to 3.5 cm (median 1.7 cm). There was at least one abnormally enlarged gland with size more than 1 cm in maximal diameter in each patient.

Hyperplastic parathyroid glands were more frequent on the right side [(34 glands, 58.6%) compare with the left side (24 glands, 41.3%)] of the posterior thyroid gland. The most common location was inferior aspect of the right lobe (20 glands, 34.6%) followed by superior aspect (9 glands, 15.5%). All parathyroid glands were located in their normal anatomical positions.

All of hyperplastic glands had well-defined margins (Fig. 1) and most (46 glands, 79.3%) showed hypoechogenicity (Fig. 2), followed by mixed-echogenicity (Fig. 3) (10 glands, 17.2%) and hyperechogenicity (Fig. 4) (2 glands, 3.5%). The glands' surfaces were smooth (Fig. 5) in 40 glands (72.5%) and lobulated (Fig. 6) 18 glands (31.4%). None of the hyperplastic glands had irregular surface.

Of 58 glands, 31 glands had CDUS examinations. Peripheral vascularity (Fig. 7, 8) was the most common pattern, presented in 29 of 31 glands

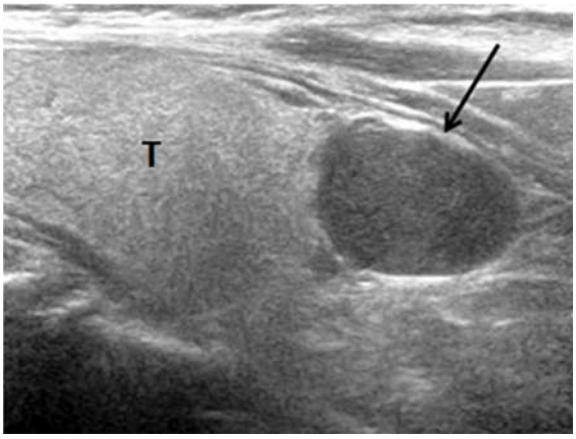

Fig. 1 Longitudinal US scan shows a well-defined hypoechoic nodule (arrow), located inferior to lower pole of left thyroid lobe (T).

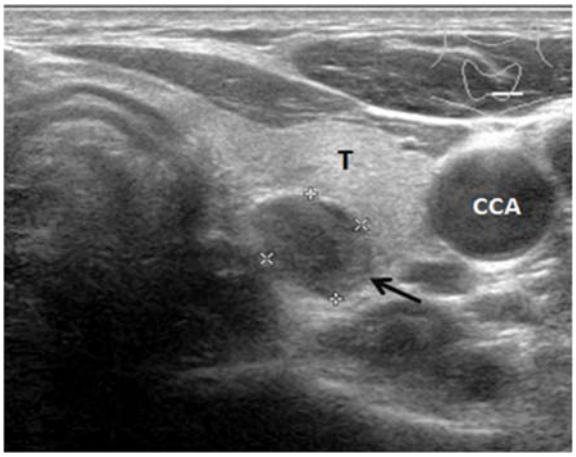

Fig. 2 Transverse US scan shows a well-defined hypoechoic nodule (arrow) at the posterior aspect of left lower pole thyroid (T). CCA refers to common carotid artery.

(93%); no intralesional blood flow was demonstrated in the remaining 2 (7%) glands.

Cystic changes (Fig. 4) were found in 4 of 58 glands (6.9%) and there was internal calcification in 1 of 58 glands (1.7%). The ultrasonographic findings are summarized in Table 1.

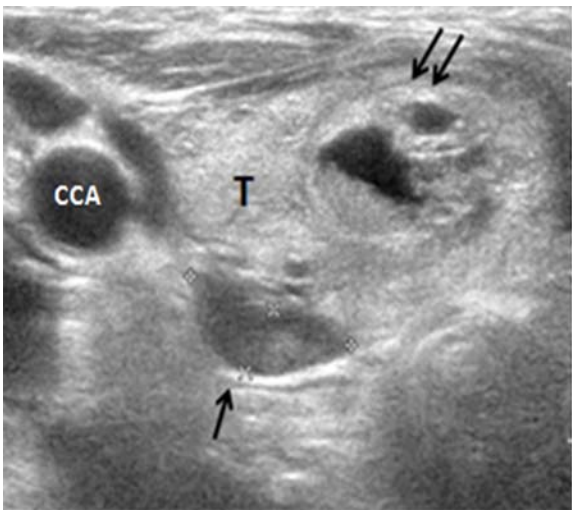

Fig. 3 Transverse US scan shows a well-defined mixed echoic nodule (arrow) located at the posterior aspect of left lower lobe thyroid (T). An adjacent well-defined slightly hypoechoicthyroid nodule with cystic change (double arrows) is also noted. CCA refers to common carotid artery.

Discussion

Many studies have described ultrasonographic characteristics of hyperplastic parathyroid glands in primary and secondary hyperparathyroidism[12-14] but relatively few have been conducted in patients with tertiary hyperparathyroidism.

The present study has shown that most of the hyperplastic glands in tertiary hyperparathyroidism have well-defined margins and are hypoechogenic, similar to that found in primary and secondary hyperparathyroidism. In primary and secondary hyperparathyroidism, glandular hypoechogenicity correlates with histologically confirmed increase of the cellularity to adipose cells ratio within the gland[14]. Mixed echoic glands were the second most common appearance (17.2%) found in the study. In the present study, the hyperplastic glands had smooth (72.5%) or lobulated (31.4%) surfaces, similar to those reported in secondary hyperparathyroidism[14].

The authors found internal cystic changes about 7% of glands which was higher than previously reported in 1 to 2% of primary hyperparathyroidism[15,16] but is lower than the 11.2% found in secondary hyperparathyroidism[14]. The later may be explained by medical treatment. As tertiary hyperparathyroidism is functionally more severe than secondary hyperparathyroidism. The authors expected to see a high incidenceof cystic changes in tertiary hyperparathyroidism. The discrepancy might be due to small sample size in the present study.

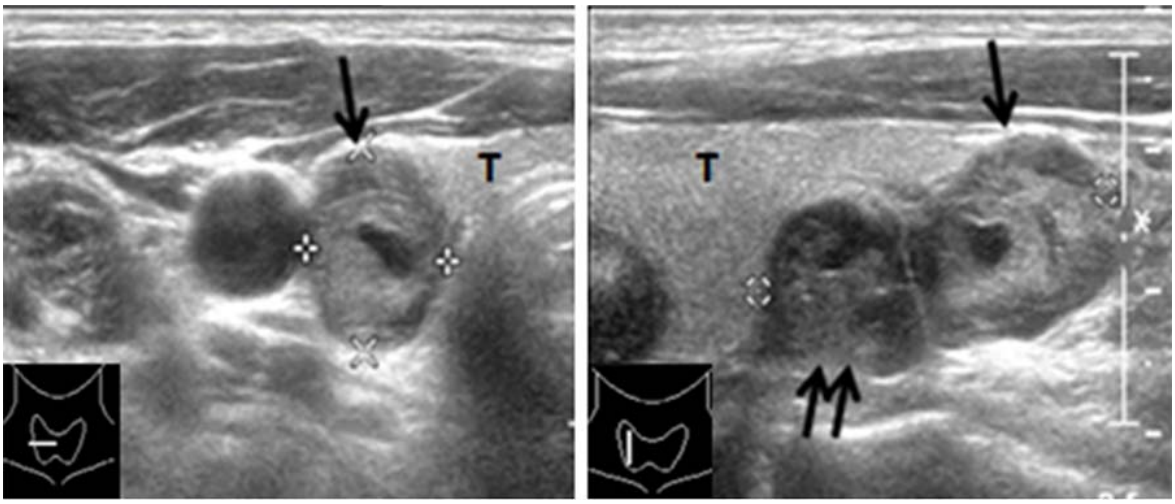

Fig. 4 Grey scale US shows a well-defined hyperechoic nodule (arrow) at posteroinferior to lower pole of the right thyroid lobe (T). Longitudinal US scan demonstrates another well-defined hypoechoic nodule (double arrows) located superior to the first lesion. Internal cystic changes in both nodules are demonstrated.

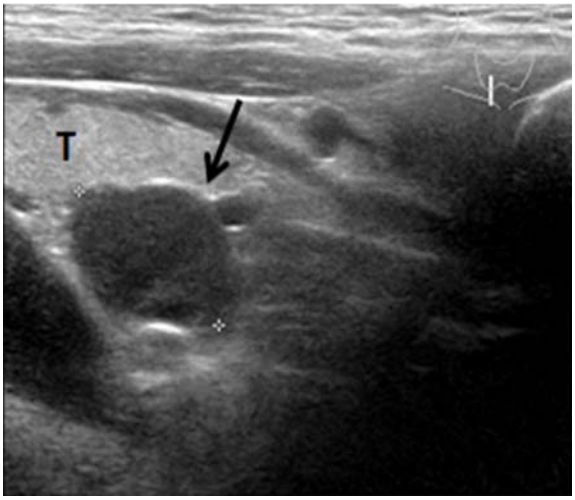

Fig. 5 A well-defined smooth surface hypoechoic nodule (arrow) located posterior to lower pole of right thyroid lobe (T).

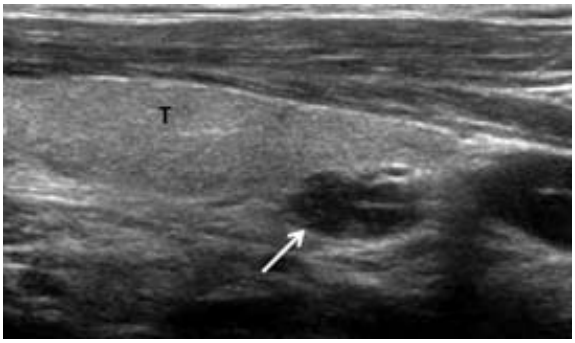

Fig. 6 A well-defined lobulated surface hypoechoic nodule (arrow) at the posterior aspect of right lower lobe thyroid (T).

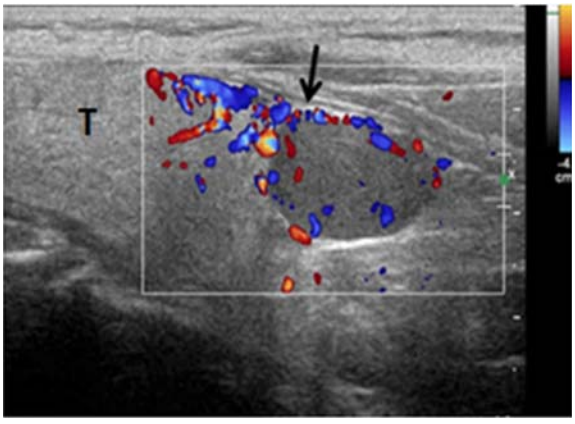

Fig. 7 CDUSs showing a hypoechoic nodule with increased peripheral vascularity (arrow) located just inferior to the thyroid lobe (T).

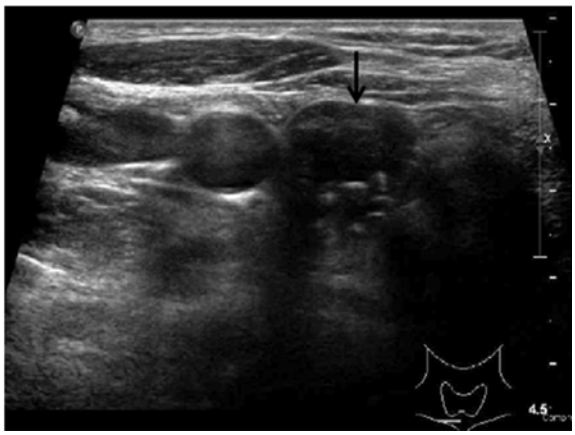

Fig. 8 Grey scale shows a well-defined hypoechoic nodule (arrow) at inferior to lower pole of the right thyroid lobe with internal echoic foci, representing calcification.

Table 1. Summary of the main findings

	Glands	%
Location		
Right superior	9	15
Right mid	5	8.6
Right inferior	20	34.4
Left superior	8	13.8
Left mid	3	5.2
Left inferior	13	22.4
Echogenicity		
Hyperechoic	2	3.5
Hypoechoic	46	79.3
Mixed echoic	10	17.2
Surface		
Smooth	40	72.5
Lobulated	18	31.4
Irregular	0	0
Margin		
Well-defined	58	100
Poor-defined	0	0
Vascularization		
Peripheral	33	57
Central	0	0
Absence	3	5.2
Not done	22	37.8
Others		
Internal cystic change	4	6.9
Intralesional calcification	1	1.7

Internal calcification is reported in both secondary and tertiary hyperparathyroidism (about 1.7%) but is rare in primary hyperparathyroidism[11,15].

The gland size in the present study ranged from 0.6 to 3.5 cm which are higher than those found in secondary hyperparathyroidism (0.5 to 1.6 cm)[7,14]. Larger gland size reflects longer duration of gland hyperactivity.

Increased internal vascularity peripherally found in the study is similar to most studies of primary and secondary hyperparathyroidism and this correlated with enlargement of the arteries supplying the parathyroid glands[11].

The sensitivity of ultrasound to detect hyperplastic parathyroid gland in the study was relatively high (85%, 58 from 68 glands). However, 10 glands were missed, including some ultrasound examination were up to six months prior to surgery. Increased sensitivity could be achieved by repeating US examinations at intervals before parathyroidectomy. The study was limited by its retrospective design. As ultrasound is an operator dependent technique, there mightbe inter-operator differences in collecting and interpreting the information, including unclear marking of gland location, different methods in measuring gland size, and differences in the angle of the color Doppler probe. Furthermore, not all patients underwent CDUS. In the future, study with cohort design, performing ultrasonography prospectively by experience radiologist would be helpful to reduce this bias.

Conclusion

Well-defined hypoechoic lesion with smooth or lobulated margins and peripheral vascularity are the most common and typical ulrasonographic appearance for abnormal parathyroid gland in tertiary hyperparathyroidism. The glandular size found in tertiary hyperparathyroidism are relatively larger than those found in primary and secondary hyperparathy roidism. Familiarity with ultrasound findings help radiologist in detecting the abnormal gland confidently.

What is already known on this topic?

There has been published data of parathyroid gland hyperplasia in tertiary hyperparathyroidism in term of histopathology and gland volume.

There were also published data about ultrasonographic appearances of normal parathyroid gland, parathyroid gland hyperplasia in primary and secondary hyperparathyroidism.

What this study adds?

Ultrasonographic appearances of parathyroid gland hyperplasia in tertiary hyperparathyroidism.

Potential conflicts of interest

None.

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ลักษณะทางคลื่นเสียงความถี่สูงของต่อมพาราไทรอยด์ในผู้ป่วยพาราไทรอยด์ฮอร์โมนเกินแบบตติยภูมิ

วราลี มิ่งขวัญสุข, โชษิตา บุรานนท์, อาวีมาศ วัชรากร

ภูมิหลัง: *ภาวะพาราไทรอยด์ฮอร์โมนสูงแบบตติยภูมิเป็นภาวะที่มีพาราไทรอยด์ฮอร์โมนสูง เนื่องจากต่อมพาราไทรอยด์ กระตุ้นตัวเองให้ทำงานมากผิดปกติ ผู้ป่วยมักได้รับการผ่าตัดเอาต่อมพาราไทรอยด์ออกเพื่อลดระดับพาราไทรอยด์ฮอร์โมน การตรวจด้วยคลื่นเสียงความถี่สูง มีบทบาทในการระบุตำแหน่งต่อมพาราไทรอยด์ที่ผิดปกติ*

วัตถุประสงค์: *เพื่อศึกษาลักษณะทางคลื่นเสียงความถี่สูงของต่อมพาราไทรอยด์ที่พบในผู้ป่วยที่มีภาวะฮอร์โมนพาราไทรอยด์เกินแบบตติยภูมิ*

ผลการศึกษา: *ใช้วิธีเก็บข้อมูลแบบย้อนหลังโดยรวบรวมข้อมูลของผู้ป่วยที่มีภาวะพาราไทรอยด์เกิน แบบตติยภูมิที่ได้รับการตรวจคลื่นเสียงความถี่สูง ในช่วงเดือนพฤษภาคม พ.ศ. 2552 ถึงเดือนมกราคม พ.ศ. 2558 ทั้งนี้ผู้ป่วยทุกคนต้องมีผลยืนยันทางพยาธิวิทยา ลักษณะของคลื่นเสียงความถี่สูงที่ศึกษาได้แก่ตำแหน่ง (location), ความขาวดำของก้อน (echogenicity), ผิวของก้อน (surface), ขอบเขตของก้อน (margin), ลักษณะหลอดเลือดที่มาเลี้ยง (vascularization), ถุงน้ำภายในก้อน (cystic change) และหินปูนภายในก้อน (calcification) ผลที่ได้รับผู้ป่วยจำนวน 28 ราย พบต่อมพาราไทรอยด์ที่ผิดปกติในคลื่นเสียงความถี่สูงจำนวน 58 ต่อมขนาดของต่อมพาราไทรอยด์ ที่พบในคลื่นเสียงความถี่สูงอยู่ระหว่าง 0.6 ถึง 3.5 เซนติเมตร ลักษณะที่พบบ่อยที่สุด ได้แก่ ก้อนสีดำขอบเรียบและมีหลอดเลือดมาเลี้ยงจากรอบนอก (well-defined hypoechoic lesion with peripheral vascularity)*

สรุป: *การทราบลักษณะของต่อมพาราไทรอยด์ที่พบในคลื่นเสียงความถี่สูงดังกล่าวจะช่วยให้รังสีแพทย์มีความมั่นใจในการค้นหาและระบุตำแหน่งของต่อมพาราไทรอยด์ที่ผิดปกติได้ดียิ่งขึ้น*