Relationship between US patterns and histological findings in uremic secondary hyperparathyroidism

Poster No.: C-1410
Congress: ECR 2012
Type: Scientific Paper
Authors: M. Ciliberti, M. L. D'andrea, C. Vulpio, G. Fadda, M. Bossola, P. Silvestri, G. Maresca, M. Castagneto, L. Bonomo; Rome/IT
Keywords: Thyroid / Parathyroids, Ultrasound, Comparative studies, Hyperplasia / Hypertrophy, Endocrine disorders, Metabolic disorders
DOI: 10.1594/ecr2012/C-1410

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Purpose

Parathyroidectomy (PTx) is sometimes performed to treat secondary hyperparathyroidism related to long-term dialysis. The role of ultrasonography (US) in patients affected by uremic secondary hyperparathyroidism candidated to parathyroidectomy is still controversial.

Ultrasonography of parathyroid glands (PTGs) has been introduced in the diagnosis of secondary hyperparathyroidism (SHPT) of hemodialysis patients (HDP) since many years [1-7]. Most of the authors believe that US is an indispensable tool for the surgeon to identify the number, the size and the site of the PTGs before surgery and to correctly plan the surgical procedure [8,9]. Others consider the US a procedure of low utility in the pre-operative assessment of SHPT, limiting its use to patients with recurrent disease [10]. Currently, many other non-invasive imaging techniques have become available for the detection of PTGs (Computed Tomography, Magnetic Resonance Imaging, Sesta-MIBI Scintigraphy). Nevertheless, US is largely used in clinical practice since it is non-invasive, easily repeatable and has acceptable sensitivity and specificity (80-95% in primary HPT and 45-80% in SHPT) [11-15]. Indeed, it has been recently suggested that US is not only the most effective method to detect the number and the site of PTGs in patients candidate to parathyroidectomy, but also US patterns of diffuse and nodular hyperplasia (NH) of PTG have been identified and defined [16]. In addition a correlation between the PTG echostructural and vascular patterns and diffuse or nodular hyperplasia has recently been demonstrated [17].

The present study aimed at evaluating US sensitivity and specificity and the relationship between US and histological findings.
Methods and Materials

Population

Before surgery ultrasonographically we detected PTG and examined the US findings of PTGs in 31 HDP of the Hemodialysis Service of the Department of Surgery of the Catholic University of Rome.

Serum concentrations of calcium (Ca), phosphorus (Pi), alkaline phosphatase activities (AlP) and intact parathyroid hormone (iPTH) were measured in each patient. The intact-PTH level was determined by electrochemiluminescence immunoassay [Roche Modular E 170: Roche Diagnostics Ltd. 6343 Rotkreuz Switzerland (normal range 10 to 65 pg/ml)].

US examination

US was performed by a single experienced radiologist (MG) (unaware of clinical data and iPTH levels) using the same ultrasound device and setting (Toshiba Aplio; Toshiba Co Ltd Tokyo Japan) connected to linear multifrequencies high resolution transducers (7.5-15 MHz) on patient in the supine position with slightly hyper-extended neck. The color gain varied dynamically during each study to enhance color signals while avoiding excessive noise. The US scanning (axial and longitudinal scans) included the thyroid region and the areas above and below the thyroid gland in even atypical sites. In our experience the limit of PTG detection is 3 mm and the and intra-observer coefficient of variance of PTG measurement was <3%.

We have defined PTGs the nodules placed posteriorly to the thyroid capsule, with longitudinal diameter parallel to that of the thyroid, with an independent afferent artery and hypoechoic or heterogeneous/nodular echo-structural pattern. All nodular lesions located within the thyroid parenchyma were excluded from the analysis.

The size of all PTGs detected was determined and expressed as the maximal longitudinal diameter (MLD).

The echo-structural pattern scores (Figure 1a-c) were classified as follows: 1) hypoechoic homogeneous or slightly heterogeneous; 2) highly heterogeneous; and 3) nodular. When the PTG showed fibrous bands, notches or calcifications (Figure 2a-b), or a pseudo-cystic change (Figure 3a-d), the US finding was classified as highly heterogeneous.

The echo-vascular patterns scores were classified as follows (Figure 1d-f): 1) non- or hypo- vascularized pattern: absent or very small peripheral or central single spot of blood flow signal; 2) intermediate score: multiple small spots of blood flow signal surrounding < 30% of
PTG circumference and/or < 30% of surface; 3) hypervascularized: multiple high peripheral and central blood flow signal taking >30% of PTG surface and circumference.

Pathology

The size of PTG was assessed in the operating room immediately after resection and the type of glandular hyperplasia of the PTGs was defined by a single experienced pathologist (FG) according to Tominaga et al. [8] as follows: 1) diffuse hyperplasia, 2) early or micro- nodular hyperplasia, 3) macro-nodular or adenoma-like hyperplasia.
Fig. 1: Figure 1 (a-f): Structural [a) hypoechoic; b) heterogeneous, and c) nodular] and Vascular [d) Non or hypo-vascularized; e) Intermediate score; f) Hypervascularized] echo-patterns scores of parathyroid glands.

© Radiology, UCSC Rome - Rome/IT
Fig. 2: Figure 2 (a-b): The figure 2 a shows the heterogeneous (score 2) structural echo-pattern and the corresponding vascular echo-pattern (at the bottom) : is evident the partial calcification of PTG. The figure 2 b shows the nodular (score3) echo pattern and the corresponding vascular flow signal : frequently, in cases of adenoma-like hyperplasia, the intra glandular arterial branches surround the hyperplastic nodule.

© Radiology, UCSC Rome - Rome/IT
**Fig. 3:** Figure 3 (a-d): The figure shows the structural echo patterns and corresponding macroscopic examination of longitudinal section of all four PTGs of the same patient. The US of upper right (a) and left (b) PTGs shows pseudocystic areas corresponding to hemorrhagic necrosis. The inferior right PTG (c) also shows pseudocystic area and considerable nodular (adenoma-like) hyperplasia. The inferior right PTG (d) with initial diffuse hyperplasia appears homogeneously hypoechoic (score 1). Usually, different types of hyperplasia are simultaneously present in the same patient because the growth of the PTGs is asymmetric and asynchronous.

© Radiology, UCSC Rome - Rome/IT
**Results**

Thirty-one parathyroidectomy were performed and 115 PTGs were overall removed: 85% in orthotopic and 15% in ectopic site. US globally detected 66 of the 115 PTG that were removed surgically with 58% of sensitivity and 94% of specificity; excluding 15 ectopic PTGs, the US sensitivity and specificity were 68% and 94% respectively.

The US MLD correlated significantly with histological diameters (regression equation $y=4.1 + 0.6x$; Coefficient of determination $R^2 0.4$ $p<0.0001$) ([Figure 4](#)). In addition, the histological diameter correlated with hyperplasia type (Spearman's coefficient of correlation 0.48 $p<0.0001$) ([Figure 5](#)).

The mean ± SD ultrasound MLD of PTG with diffuse or nodular hyperplasia was 7.1±0.92 mm and 12.1± 0.66 mm respectively. The mean±SD histological maximum longitudinal diameters (mm) of PTGs with diffuse, micro-nodular and macro-nodular / adenoma like hyperplasia were 7.1±3.1, 10±3.5 and 16.8±4.8 respectively. (Anova $p<0.001$; Student-Newman-Keuls test for all pair wise comparisons: $p<0.05$).

The ROC curve analysis showed that the MLD> 9 mm predict the nodular hyperplasia (micro and macro nodular) with 83% of sensitivity and 70% of specificity(Area under the curve 0.78 $p<0.0001$).

A significant correlation was found between the MLD and echo-structural (Spearman's rank correlation coefficient 0.736, $p <0.0001$) and vascular pattern score (Spearman's coefficient 0.710, $p<0.0001$). These two parameters were also correlated (Spearman's coefficient 0.724, $p<0.0001$): as the MLD increases, more advanced echo-patterns prevail. All PTG with evidence of higher ESP and BSP score at ultrasound showed nodular hyperplasia at pathological examination.

The US detected only 33% out of PTGs with diffuse hyperplasia and the small sample of PTGs with diffuse hyperplasia did not allow a statistical comparison between structural and vascular echo patterns and type of PTGs hyperplasia.

The PTGs with initial diffuse hyperplasia are similar to normal glands and are not detectable by US. Conversely, PTGs with advanced stage of growth presents an echogenic capsule distinct from the thyroid’s one and an hypoechoic shape due to hypercellularity and progressive disappearance of the fatty area. These characteristics make them detectable by US. Initially, enlarged PTG assume a spheroid hypoechoic shape and successively become multi-nodular or adenoma-like ([figure 6a-b](#)). In addition, calcifications, lobulations, cystic degeneration, fibrous bands and nothes or true nodules may be found. Simultaneously to PTG growth, the vascular blood supply also increases [18-20].
The iPTH, Calcium serum and alkaline phosphatases activities levels were significantly correlated with the number of PTGs and MLD, structural and vascular echo-patterns of the largest PTG. The iPTH levels and MLD of the largest PTG were significantly correlated (Person's correlation coefficient 0.529 \( p<0.0001 \)).
Fig. 4: Figure 4: Correlation between US maximum longitudinal diameter (MLD) and histological diameters (regression equation $y = 4.1 + 0.6 x$; Coefficient of determination $R^2 0.4$)

© Radiology, UCSC Rome - Rome/IT
**Fig. 5:** Figure 5: Mean (±SD) of histological Maximum longitudinal diameter (MLD=mm) of PTGs with (1) diffuse (7.1±3.1), (2) micro-nodular (10±3.5) and (3) macro-nodular / adenoma-like hyperplasia (16.8±4.8). (Anova p

© Radiology, UCSC Rome - Rome/IT
Fig. 6: Figure 6 (a-b) The figure shows 2 cases of macro-nodular (6a) and adenoma-like (6b) hyperplasia of PTG: US pattern (on the top), macroscopic examination of longitudinal section (in the middle) and histology (bottom). The PTG are entirely occupied by multiple (macro-nodular) or single nodular (adenoma-like) hyperplasia. It is evident the correspondence between the US images and macroscopic and histological examinations.

© Radiology, UCSC Rome - Rome/IT
Conclusion

We showed that the biochemical markers of calcium-phosphorus metabolism, the histological and ultrasound finding are strongly correlated.

The MLD of PTGs evaluated by US was significantly correlated to MLD determined by histology and predictive of nodular hyperplasia. Infact, the ROC curve analysis showed that histological MLD >9 mm accurately predicted the nodular hyperplasia with 83% of sensitivity and 70% of specificity.

The higher echo-structural and vascular pattern score predict the presence of nodular hyperplasia, but the MLD > 9mm predicts the presence of nodular hyperplasia more than any other parameter.

These results suggest that US parameters are indicative and correlated to SHPT degree and represent an important prognostic tool. To this regard, it is well known that the presence of nodular hyperplasia is commonly recognized as the most important cause of medical therapy failure because of down-regulation of vitamin D receptor (VDR) and Calcium Sensing Receptor (CaSR) [21].
References


Personal Information

Residence UCSC Rome

Michela Ciliberti

michela.ciliberti@libero.it