Original Article

High Resolution Ultrasound Guided Needle Aspirate of Parathyroid Lesion; A Preliminary But Accurate Approach to Preoperative Identification and Localization of Parathyroid Adenoma

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Objective: To determine the sensitivity and specificity of high resolution ultrasound guided FNAC as a preliminary but accurate investigation for identification and localization of parathyroid adenoma for minimally invasive surgical road mapping to position the incision directly over the diseased gland.

Material and Methods: This cross sectional study was conducted in Department of Radiology, Omer hospital, Lahore, between September 2012 and September 2013. The study included series of 13 patients, including 5 men and 8 women, ranging between 35 and 70 years (mean, 48.5±13 years). Neck ultrasound for parathyroid glands was performed in the patients presented with non-specific symptoms of hypercalcaemia. Serological analysis included serum calcium, serum PTH, alkaline phosphatase and creatinine. Exact size, location and number of parathyroid adenomas were assessed followed by US-guided FNA.

Results: In 12 out of 13 patients, the position and size of the normal parathyroid gland as well as parathyroid lesions were adequately demonstrated on ultrasound. One patient had ectopic parathyroid adenoma which was confirmed on scintigraphy and excisional biopsy. Two patients had normal appearing parathyroid gland which turned out to be adenomatous on histology. One patient had indeterminate histology of an otherwise hypoechoic parathyroid region reported as adenoma on ultrasound. Remaining 9 patients had large parathyroid adenomas initially picked on ultrasound and later on confirmed on histology through US guided FNA. None of the patients had concomitant thyroid disease or involvement of more than one parathyroid gland. All patients had serum calcium of more than 11mg/dL and elevated serum PTH. On histopathology of FNA, predominant cell type was chief cells arranged in sheets and occasionally small follicles with variably thick connective tissue capsule. Cells with a clearer cystoplasm and occasionally oncocytic cells were also seen.

Conclusion: High resolution ultrasound is a preliminary but sensitive investigation in detecting parathyroid adenomas. When combined with US guided FNA, it becomes a highly specific and accurate modality for preoperative identification and localization of parathyroid adenoma. We highly recommend ultrasound for surgical road mapping of adenomas.

Key words: Ultrasound, fine needle aspiration, parathyroid adenoma, preoperative localization.

Introduction

Excessive secretion of parathyroid hormone (PTH) is a consequence of either a primary parathyroid disease including adenoma or hyperplasia, or secondarily due to renal failure. The development of minimally invasive surgery for parathyroid adenoma has made accurate preoperative identification of the lesion very critical for effective surgical treatment. Four parathyroid glands, two posteriorly placed superior glands and two anteriorly placed inferior glands, usually measures not more than 5 mm in diameter in each location. The parathyroid glands are embedded in thyroid glandular parenchyma; thus supplied by superior and inferior thyroidal arteries.[1]

Noninvasive imaging techniques for the detection of parathyroid adenoma include high resolution sonography, scintigraphy, computed tomography (CT) and magnetic resonance imaging (MRI).[2] Ultrasound (US) and sestamibi scintigraphy (SS) are the most common imaging techniques used for locating parathyroid adenomas. Most of the previous studies support the fact that no additional benefit is gained using both US and scintigraphy for the preoperative localization of parathyroid adenomas. US, in most of the studies, is found to be a reliable tool for identifying and localizing adenoma. Scintigraphy is reserved for the cases when ultrasound findings are inconclusive or to determine the ectopic location of adenomas. CT and MRI are problem solving tools for those cases in which ultrasound as well as scintigraphy cannot

Ascertain the adenomas morphologically.[3]
Invasive diagnostic technique includes needle aspiration, usually done under image guidance. Although not required frequently, tissue diagnosis may help in differentiating glandular hyperplasia from adenoma which is very difficult radiologically. In hyperplasia, all four parathyroid glands are affected, although these are not necessarily enlarged. In adenoma usually only one gland is affected while the other parathyroid glands may become atrophic.4 We aimed to determine the sensitivity and specificity of high resolution ultrasound along sono-guided fine needle aspiration cytology as a preliminary but accurate investigation for identification and localization of parathyroid adenoma for minimally invasive surgical road mapping as ultrasound is used to position the incision directly over the diseased gland, thus reducing the operative time.

Material and Method

This cross sectional study was conducted in Department of Radiology, Omer hospital, Lahore, between September 2012 and September 2013. The study included series of 13 patients, including 5 men and 8 women, ranging between 35 and 70 years (mean, 48.5±13 years). About half of the sample population was above the age of 60 years **(fig. 1).**

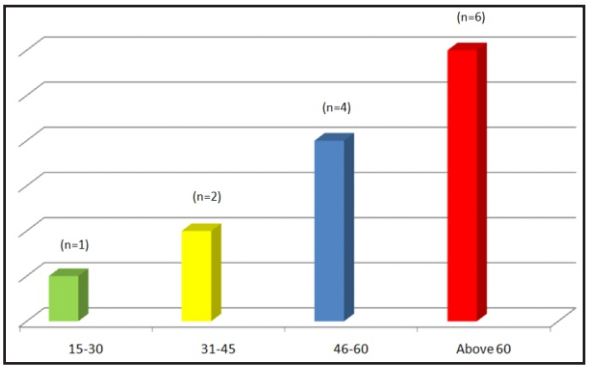


Fig-1: Age distribution in different groups of patients with parathyroid adenoma.

Neck ultrasound for parathyroid glands was performed in the patients presented with non-specific symptoms of hypercalcaemia including bone pains, fractures, constipation, easy fatigability and nephrolithiasis. The patients' medical records were reviewed prior performing sonography. Serological analysis included serum calcium (normal range 8.9-10.1 mg/dL), serum PTH (normal range 15 - 68.3 pg/ml). In addition, serum alkaline phosphatase (normal range 40-129 IU/L) and creatinine levels (normal range 0.4-1.2 mg/dl) were also included.
Ultrasound was performed by an experienced radiologist using Toshiba Nemio XG ultrasound equipment (SSA 660A; Tokyo, Japan). We used 11 MHz linear array transducer. Patient's thyroid was scanned at upper, middle and lower transverse as well as longitudinal planes in the medial, central and lateral locations through both lobes in search of parathyroid gland. Although, parathyroid gland is often embedded within thyroid gland, it might migrate further afield for which we extended the scan from inferior margin of the submandibular glands down to the supraclavicular fossae. Exact size, location and number of parathyroid adenomas were assessed. This was followed by US-guided fine needle aspiration (FNA) using a 25-gauge needle attached to a 10-ml syringe. Direct smears were fixed in 95% alcohol for Papanicolaou (Pap) staining and air dried.

Results

In 12 out of 13 patients, the position and size of the normal parathyroid gland as well as parathyroid lesions were adequately demonstrated on ultrasound. One patient had ectopic parathyroid adenoma which was not identified on ultrasound and was subsequently confirmed on scintigraphy and excisional biopsy. Two patients had normal appearing parathyroid gland which turned out to be adenomatous on histology. One patient had indeterminate histology of an otherwise hypoechoic parathyroid region reported as adenoma on ultrasound; the likely reason for this was a small sized lesion that was targeted under US guidance. One patient had normal ultrasound features of parathyroid gland and negative cytology as well for adenomatous change. Remaining 8 patients had large parathyroid adenomas initially picked on ultrasound and later on confirmed on histology through US guided FNA. None of the patients in our series had concomitant thyroid disease. Also, we couldn't find the involvement of more than one parathyroid gland by adenoma. Serological analysis was reviewed in all patients which confirmed serum calcium of more than 11mg/dL (normal range 8.9-10.1 mg/dL) and elevated serum PTH more than 70 pg/ml (normal range 15 - 68.3 pg/ml); however, serum alkaline phosphatase and creatinine varied from normal values to higher serum levels according to the severity of the disease. Table 1 demonstrates sonographic, FNAC and serological findings in all 13 patients included in the study.
Normal parathyroid gland, when identified on ultrasound, was 5 mm or less in diameter with isoechoic echopattern of the glandular parenchyma relative to adjacent thyroid gland. The histology of the

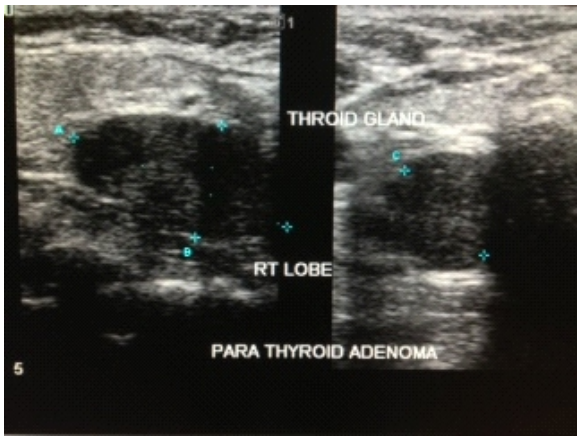
Table-1: Sonographic, FNAC and serological findings in all the patients with parathyroid adenoma.

Sonograpic Features	FNAC	Serum Calcium (Normalrange 8.9-10.1mg/dl)	Serum PTH (Normalrange 15-68.3pg/ml)	Serum alp.ph. (Normalrange 50-150U/l)	Serum CRT (Normalrange 0.5-1.4mg/dl)
Hypoechoic enlarged	Positive	11.5	128	160	1.9
Hypoechoic enlarged	Positve	8	181	187	1.8
Hypoechoic enlarged	Positive	24	170	192	2.0
Normal gland	Positive	37.33	91	174	2.0
Normal visualized	Positive	28	320	207	2.8
Hypoechoic enlarged	Positive	100	98	165	1.7
Normal gland	Negative	100	45	98	1.1
Hypoechoic enlarged	Positive	8	102	167	1.9
Hypoechoic enlarged	Positive	24	225	182	2.4
Hypoechoic enlarged	Positive	37.33	201	161	2.1
Normal gland	Positive	28	119	178	2.2
Normal sized	Negative	100	87	120	1.3
Hypoechoic enlarged	Positive	100	284	190	2.5

Table-2: Sensitivity, specificity, positive and negative predictive values of ultrasound for diagnosing parathyroid adenoma preoperatively.

		Fine Needle aspiration		
		Positive Cytology	Negative cytology	
				Positive predictive value
	Detected	8	1	=TP/(TP+FP)
		(TP)	(FP)	=88.9%
				Negative predictive value
Ultrasound Neck		3	1	=TN/(FN+TN)
	Not Detected	(FN)	(TN)	25%
		Sensivetivty	Specificity	
		=TP/(TP+FN)	=TN/(FP+TN)	
		=72.7%	=50%	

normal parathyroid gland demonstrated chief cells, fibrovascular stroma, and adipocytes. Parathyroid adenomas ranged from 10 mm to 40 mm in diameter with hypoechoic, well marginated, solid masses (fig.2). Compact cellularity rendered adenomatous glands hypoechoic relative to the overlying thyroid. A hyperechoic reflective capsule distinguished the adenomas from normal thyroid parenchyma. The smaller adenomas were oval to bean-shaped, but larger ones were multilobulated in most of the cases. Graded compression demonstrated a relatively incompressible gland to differentiate adenoma from surrounding soft tissue. Color and power Doppler showed a characteristic extrathyroidal feeding vessel Entering the parathyroid gland. Internal vascularity of adenoma was seen in a peripheral distribution in a characteristic arc or rim of vascularity. On histopathology, predominant cell type was chief cells arranged in sheets and occasionally small follicles with variably thick connective tissue capsule. Cells with a clearer cystoplasm and occasionally oncocytic cells were also seen.**Fig-2:** Sagittal and transverse sonography of a 47 years old female demonstrates a large hypoechoic right superior parathyroid adenoma deep to the inter-polar region of the right thyroid lobe.



The sensitivity, specificity, positive and negative predictive values are tabulated in table 2. The sensitivity of ultrasound in detecting parathyroid adenoma was 72.7% with positive predictive value of 88.9%.

Discussion

Over the past decade, the surgical treatment of primary hyperparathyroidism has changed from bilateral approach with radical four-gland exploration to unilateral and focused approaches guided by preoperative imaging. Ultrasound and Tc^{99m} sestamibi scintigraphy have assumed dominant roles in preoperative location of solitary adenomas, and focused approaches based on concordant findings from both techniques have cure rates equal to that of the traditional approach. Ultrasound is the most commonly used modality to ascertain preoperatively the location of parathyroid lesions in the neck once serological screening is suggestive of raised serum calcium and serum PTH levels. This allows targeted neck exploration, thus reducing operative time and complications.[5] In equivocal cases, US guided fine-needle aspiration (FNA) for cytology is of certain help, as parathyroid adenoma, hyperplasia and carcinoma may have similar appearances. Similarly, enlarged cervical lymph nodes in central compartment of neck may be confusing with coexistent thyroid disease; however, an echogenic fatty hilum indicates a benign lymph node. Lymph nodes are supplied by small hilar vessels; a polar and peripheral distribution of flow is associated with parathyroid adenomas. Multinodular thyroid gland may limit the detection of parathyroid adenomas. The rare intrathyroid parathyroid gland is very difficult to differentiate from a thyroid nodule. Ectopic parathyroid glands create difficulty particularly in the retrotracheal area.[6] Ultrasound has better sensitivity than scintigraphy, and their combined use is very sensitivity indeed. Sensitivity of parathyroid adenomas detection with ultrasound ranges from 72% to 89%. A meta-analysis by Ruda et al. between 1995 and 2003 for ultrasound detection of adenoma preoperatively was 79% (95% confidence interval, 7780%).[7] These results are concordant with our study. Targeted parathyroidectomy is, therefore, based on preoperative imaging. Prospective study by Rickes et al. including 98 patients for a polar feeding vessel significantly increases specificity for detecting parathyroid adenomas.[8] Sukan et al. evaluated 69 patients with hyperparathyroidism for specificity of MIBI and USG and found it to be 87% and 91% respectively.[9] A study by Stephen et al. of 57 preoperative sonographically guided FNAs in 54 patients found a specificity of 100% and no false-positive findings. The three false-negative FNAs occurred when small glands were sampled.[10] MRI and CT are generally problem solving tools and reserved for failed initial surgery or recurrent hyperparathyroidism due to supernumerary or ectopic parathyroid adenomas.[11]

Conclusion

High resolution ultrasound is a preliminary but sensitive investigation in detecting parathyroid adenomas. When combined with US guided FNA, it becomes a highly specific and accurate modality for preoperative identification and localization of parathyroid adenoma. However, detailed knowledge of cervical anatomy and operator's experience is crucial in the success of diagnosing adenoma. We highly recommend ultrasound for surgical road mapping of adenomas and scintigraphy, CT or MRI may only be helpful when sonography is equivocal.

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