

# Evaluation of Preoperative ultrasonographic and biochemical features of patients with aggressive parathyroid disease: Is there any reliable predictive marker?

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## Introduction

Parathyroid cancer (PC) is rare accounting for less than 1 % of all presentations. Tumors that demonstrate these atypical features and do not fulfill criteria for carcinoma can be classified as atypical adenomas (APA). Herein we aimed to evaluate the clinical and biochemical features of the patients with an atypical parathyroid adenoma or carcinoma and compare it with benign parathyroid adenomas

## Methods

➤ Twenty eight patients who were operated for primary hyperparathyroidism and diagnosed with APA or PC were enrolled. Another 102 patients with classical PA were included as the control group. Classic adenomas, APAs and PCs were compared according to preoperative biochemical and ultrasonographic parameters

## Results

➤ Serum Calcium (Ca) was significantly higher in the carcinoma group compared to APA and classical PA groups in post hoc analysis, ( $p < 0.001$  and  $p = 0.010$ , respectively). Serum median parathormone (PTH) was significantly higher in the APA and the carcinoma groups compared to classical PA group ( $p < 0.05$ ). Serum (alkaline phosphatase) ALP and 24-hour urinary Ca excretion were significantly higher in the APA and PC groups compared to classical adenomas ( $p < 0.001$ ). Areas under ROC curve for Ca, PTH, ALP, 24 hour Ca excretion and the adenoma diameter were significant for discrimination of aggressive (APA and PC) from benign disease. Best cut off for Ca, PTH, ALP, 24 hour Ca excretion and the adenoma diameter were 12.45 mg/dl, 265.05 pg/ml, 154.5 IU/l, 348.5mg/day and 21.5 mm, respectively. Multivariate analysis showed that Ca, ALP and isoechoic/cystic appearance were independent predictors for aggressive disease

## Conclusion

➤ Preoperatively high PTH, ALP and urinary Ca levels and large lesions with isoechoic or cystic appearance may be predictive for atypical adenoma or carcinoma that may require more extensive surgery and closer follow up to prevent any lifelong complications.

Table 1: Comparison of the demographic, biochemical and imaging data of the patients in three histological subgroups

	Classic (n=102)	Atypical (n=23)	Carcinoma (n=5)	p-value
Age (years)	51.1±14.0	51.3±13.7	50.4±13.7	0.991†
Gender				0.006‡
Male	20 (20.0%) <sup>a</sup>	11 (47.8%) <sup>a</sup>	3 (60.0%)	
Female	80 (80.0%) <sup>a</sup>	12 (52.2%) <sup>a</sup>	2 (40.0%)	
Ca (mg/dl)	11.3(9.2-14.7) <sup>b</sup>	11.6 (10-16) <sup>c</sup>	16.0(11.6-16.5) <sup>b,c</sup>	0.005¶
P (mg/dl)	2.5 (1.1-4.5)	2.3 (2.5-2.9)	2.1 (1.4-3.5)	0.370¶
PTH (pg/ml)	167.5 (60-900) <sup>a,b</sup>	448.0 (139-735) <sup>a</sup>	520.0 (163-1077) <sup>b</sup>	<0.001¶
ALP (IU/L)	101.0 (27-244) <sup>a,b</sup>	190.0 (66-718) <sup>a</sup>	589.0 (119-1880) <sup>b</sup>	<0.001¶
Urine Ca (mg/day)	370.5 (68-948) <sup>a,b</sup>	500.0 (362.0) <sup>a</sup>	500.0 (483-900) <sup>b</sup>	0.002¶
25-OH-Vit D (ng/ml)	13.47±0.39	12.84±0.47	11.57±0.34	0.072
Adenoma diameter (mm)	14.5 (5-43) <sup>a,b</sup>	22.0 (5-58) <sup>a</sup>	32.0 (15-44) <sup>b</sup>	<0.001¶
USG				<0.001‡
Hypochoic	95 (95.0%) <sup>a,b</sup>	15 (65.2%) <sup>a</sup>	1 (20.0%) <sup>b</sup>	
Isochoic	3 (3.0%) <sup>a,b</sup>	5 (21.7%) <sup>a</sup>	3 (60.0%) <sup>b</sup>	
Cystic	2 (2.0%) <sup>a</sup>	3 (13.0%) <sup>a</sup>	1 (20.0%)	
Positive MIBI	63 (65.6%)	18 (78.3%)	5 (100.0%)	0.158‡
Persistent/Recurrent disease	3 (3.0%) <sup>b</sup>	1 (4.3%) <sup>c</sup>	3 (60.0%) <sup>b,c</sup>	<0.001‡

† One-Way ANOVA, ‡ Chi-square test, ¶ Kruskal Wallis test, a: Classic vs Atypical ( $p < 0.05$ ), b: Classic vs carcinoma ( $p < 0.05$ ), c: Atypical vs carcinoma ( $p = 0.010$ ).

Table 2: Areas under curve for biochemical and ultrasonographic parameters for distinguishing classical adenomas from aggressive disease, best cut off points and diagnostic performances

	AUC	95 % CI	p-value	Cut-off	Sensitivity	Specificity	PPV	NPV
Ca	0.636	0.509-0.762	0.029	>12.45	0.429	0.830	0.414	0.838
PTH	0.787	0.675-0.898	<0.001	>265.05	0.714	0.770	0.465	0.906
ALP	0.843	0.750-0.936	<0.001	>154.5	0.741	0.846	0.588	0.917
Urinary Ca	0.716	0.604-0.829	<0.001	>348.5	0.885	0.478	0.324	0.936
Adenoma diameter	0.715	0.590-0.839	<0.001	>21.5	0.571	0.811	0.471	0.865

AUC: Area Under the Curve, CI: Confidence Interval PPV: Positive predictive value, NPV: Negative predictive value.

