

Characterization and clinical course of prolactinoma in Korean adolescents

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Introduction

Prolactinoma is most common functioning pituitary adenoma (50%). It occurs most frequently among women aged 20 to 50 years. There have been limited studies for prolactinoma in adolescents. Pituitary adenomas are uncommon in childhood and adolescence.

However, there have been limited studies for prolactinoma in adolescents. Pituitary adenomas are uncommon in childhood and adolescence (<3% of childhood supratentorial tumors, 3-6% of all surgically treated adenomas).

The aim of this study is to assess the characteristics of Korean adolescents with prolactinoma and their clinical course.

Patients and methods

This study is a retrospective cohort study. Patients diagnosed with prolactinoma (age < 19 years) in Samsung Medical Center during a 13-year period (2005-2017). Study subjects are total 25 patients (20 female/5 male). The median age is 16.9, ranged from 10.1 to 18.5, divided into two groups according to tumor size and surgery-done (Surgery group, n=14 vs. non-surgery group, n=11). There are 11 microadenomas and 14 macroadenomas. Factors related to tumor size were evaluated.

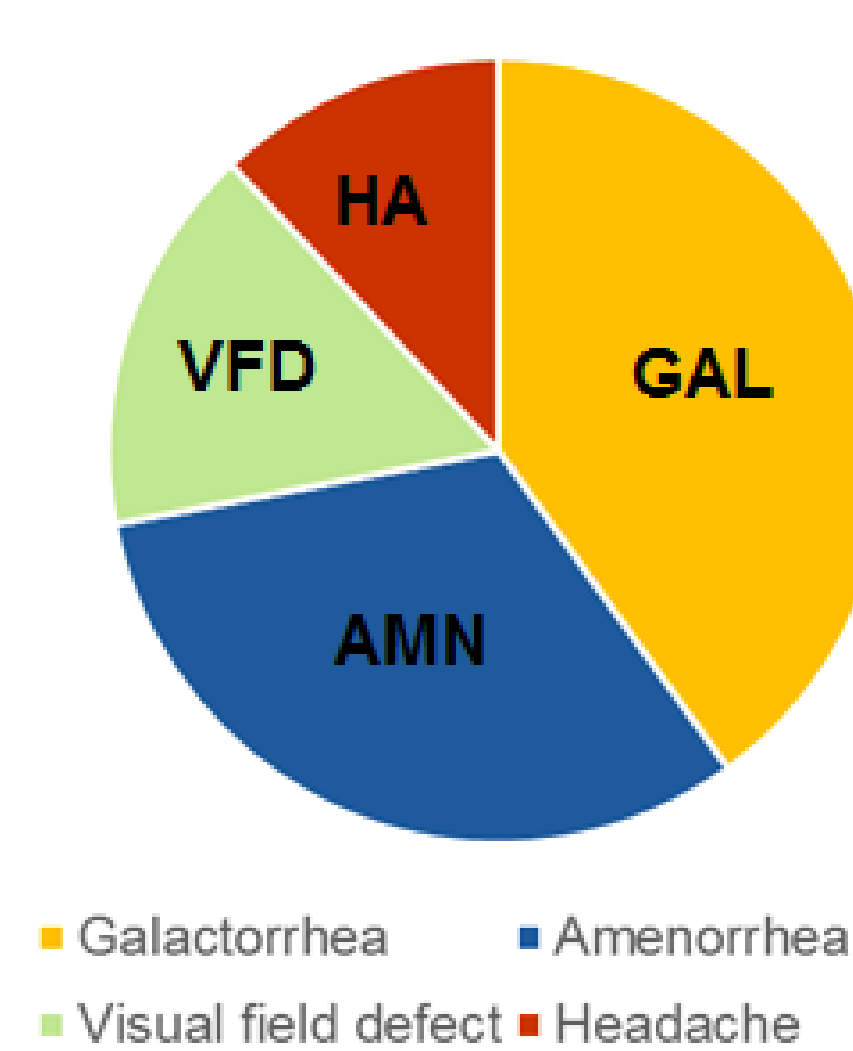
Statistical analysis

The results are presented as the mean (SD) or mean change (SD). For categorical variables, we used Student's t test, and for continuous variables, we used Wilcoxon-Mann-Whitney test.

The relationship of each risk factor with macroprolactinoma was defined by logistic regression analysis. Correlations between macroprolactinoma and other variables were determined by Spearman rank order correlation. All statistical analysis was performed using SPSS Statistics 24 (IBM Corporation, USA).

Results

The most common clinical manifestations are galactorrhea (40%), amenorrhea (36%), visual field defect (16%), and headache (12%). Serum prolactin (PRL) levels at diagnosis are 72 to 10,000 ng/mL. Tumor size at diagnosis is 4 to 74 mm. Mean immediate postoperative decline rate in PRL level is 93.5%. Baseline characteristics of the patients are in Table 1. Mean age at diagnosis is 16.9 (range 16.3-18.0). The follow-up period is 2.0 yr. Mean age at diagnosis did not differ between boys (14.8 ± 3.3 yr; range 10.1-18.2 yr) and girls (16.9 ± 1.3 yr; range 13.4 ~ 18.5 yr) ($p = 0.243$).



Clinical and biochemical presentation of the microadenomas and macroadenomas subgroups are in Table 2. Prolactin level at diagnosis was significantly higher in macroadenoma group (516 vs 114.2 ng/mL, $p < 0.001$). Patient diagnosed to panhypopituitarism is 1 (9%) in microadenoma patients, 10 (71%) in macroadenoma patients ($p = 0.008$). Operation was done in two patients (18%) in microadenomas, twelve (86%) in macroadenomas ($p = 0.003$). Male gender, Prolactin level at diagnosis, and immediate postoperative PRL level were positively correlated with maximal tumor diameter ($r = 0.443$, $p = 0.026$; $r = 0.710$, $p < 0.001$; $r = 0.623$, $p = 0.001$).

Comparison of clinical and laboratory parameters in the surgery and non-surgery groups are in Table 3. Maximal tumor diameter and PRL level at diagnosis were significantly higher in surgery group in comparison with non-surgery group ($p = 0.001$, $p = 0.013$, respectively).

Table 1. Baseline characteristics of the patients

	Median value
Age at diagnosis (median, IQR) (yr)	16.9 (16.3, 18.0)
Height (SD)	0.3 (-1.2, 0.7)
BMI (SD)	0.4 (-0.2, 0.8)
ki-67 index (%)	3.7 (2.0, 5.0)
Maximal tumor diameter (mm)	12.0 (9.0, 21.5)
Nadir PRL level (ng/ml)	9.4 (2.6, 34.5)
PRL at diagnosis (ng/ml)	207.0 (116.6, 1056.5)
Immediate postoperative PRL levels (ng/ml)	25.0 (2.9, 83.0)
Follow-up period (yr)	2.0 (1.0, 3.1)
Cabergoline (CBG) peak (mg/wk)	1.5 (1.0, 2.0)
Cabergoline duration (yr)	1.1 (0.1, 2.2)
Bromocriptin peak (mg/day)	30 (3.4, 105.0)
Bromocriptin duration (yr)	1.9 (1.1, 7.6)
At age of first use with CBG (yr)	17.5 (16.3, 19.6)
At age of op (yr)	17.3 (16.2, 19.6)

Table 2. Clinical and biochemical presentation of the microadenomas and macroadenomas subgroups

	Microadenoma (n=11) (44%)	Macroadenoma (n=14) (56%)	p
Gender (female)	11 (100%)	9 (64%)	0.134
Age at diagnosis	17.1 (16.7, 17.7)	16.8 (14.3, 18.1)	0.727
Height (SD)	0.3 (-0.6, 1.7)	-1.6 (0.1, 0.7)	0.501
BMI (SD)	0.3 (0.1, 0.4)	0.5 (-0.2, 1.3)	0.434
ki-67 index (min/max)	4 (3, 5)	3.7 (1.2, 16.0)	0.727
Maximal tumor diameter (mm)	9 (7, 10)	21 (14.3, 26.3)	0.000
Nadir PRL level	7.5 (0.6, 33.0)	9.7 (4.9, 43.3)	0.373
PRL at diagnosis	114.2 (85.6, 189.5)	516.0 (202.8, 3567.5)	0.000
Panhypopituitarism	1/11 (9%)	10/14 (71%)	0.008
Operation (TSA)	2/11 (18%)	12/14 (86%)	0.003
Sensitivity to DA	5/7 (71%)	6/11 (55%)	0.596
CBG peak (mg/wk) (min/max)	1.0 (0.2, 2.0)	1.0 (0, 1.0)	0.536
CBG duration (yr)	0.3 (0.1, 1.1)	1.8 (0.4, 2.7)	0.081
BRM peak (mg/day)	7.5	52.5 (3.1, 140)	1.000
BRM duration (yr)	0.9	2.1 (1.4, 8.2)	0.333
At age of first use with CBG	18.4 (17.2, 19.6)	16.6 (13.5, 19.5)	0.228

Table 3. Comparison of clinical and laboratory parameters in the surgery and non-surgery groups.

	Non-surgery group (n=11)	Surgery group (n=14)	p
Gender (M/F)	1/10	4/10	0.434
Age at diagnosis	16.9 (16.1, 17.8)	16.9 (15.8, 18.1)	0.727
Height (SD)	0.31 (-0.55, 1.69)	0.06 (-1.83, 0.66)	0.291
BMI (SD)	0.26 (0.02, 0.44)	0.54 (-0.32, 1.37)	0.373
ki-67 index	5.0 (5.0, 5.0)	3.4 (1.9, 4.7)	0.545
Maximal tumor diameter (mm)	9.0 (7, 10)	20.5 (12, 25)	0.001
Nadir PRL level	7.5 (0.2, 33.0)	9.5 (5.1, 43.3)	0.344
Sensitivity to DA	7/8 (88%)	4/10 (40%)	0.101
Panhypopituitarism	1/11 (9%)	10/14 (71%)	0.008
PRL at diagnosis	119 (105, 230)	382 (189, 3568)	0.013
CBG peak (mg/wk)	1.0 (0.75, 2.00)	1.75 (0.88, 2.50)	0.388
CBG duration (yr)	0.25 (0.10, 1.23)	2.00 (0.85, 3.53)	0.059
BRM peak (mg/day)	7.5 (7.5, 7.5)	52.5 (3.1, 140.0)	1.000
BRM duration (yr)	0.9 (0.9, 0.9)	2.1 (1.4, 8.2)	0.333

Conclusions

Macroprolactinoma is more prevalent in adolescents than adults. In adolescents with prolactinoma, girl is more prevalent, boys usually present with mass effect symptoms from macroprolactinoma. Male gender is in higher risk for macroadenoma more than female in adolescents with prolactinoma. Macroprolactinoma usually presents with panhypopituitarism. Given that diagnosis and prognosis may vary depending on the gender, we need to consider a more aggressive treatment in males. In addition, cocktail test for adolescents with prolactinoma is essential and adjustive hormone replacement is important to improve their quality of life.