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Association between estrogen receptor gene polymorphisms and premature thelarche

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Introduction

Premature thelarche (PT) is a benign, non-progressive condition defined as isolated breast development without the activation of the hypothalamic-pituitary axis.[1] While the pathophysiology of PT remains unclear, increased sensitivity to estrogen may cause PT.[2]

Objectives

The aim of this study was to investigate the association between polymorphisms in the estrogen receptor alpha (*ERα)* gene and PT in girls.

Methods

In this case-control study, we examined 96 girls referred for early breast development (before the age of 8 years). The control group included healthy Korean females with normal pubertal progression. Anthropometric and hormonal parameters were measured and *PvuII and XbaI ERα* gene polymorphisms were evaluated by PCR. Out of the 96 girls, all coding exon and exon-intron boundaries of *ERα* were sequenced from the DNA of 46 girls.

Results

Table 1. Clinical and laboratory characteristics of the subjects

Characteristics	Total (n=96)
Age at examination (year)	8.21 ± 0.61
Height SDS	1.09 ± 0.88
Weight SDS	1.10 ± 0.90
BMI SDS	0.85 ± 1.00
Bone age (years)	10.4 ± 0.8
Basal LH (IU/L)	1.1 ± 0.5
Basal FSH (IU/L)	1.9 ± 1.6
Basal E2 (pg/mL)	8.0 ± 4.1
Peak LH (IU/L)	3.3 ± 0.9
Peak FSH (IU/L)	11.8 ± 6.5
Peak E2 (pg/mL)	9.1 ± 4.7

Table 2. Allele frequencies of the ERa polymorphisms form 96 patients and 102 controls.

No.	Location	dbSNP ID	Polymorphism	Group	Allele frequency				*P-value
					1		2		
1	Exon1	rs2077647	152129077 T/C	Patient	62	0.673	30	0.327	0.243
			T=1; C=2	Control	123	0.603	81	0.397	
2	Exon1	rs17847065	152129484 C/A	Patient	90	0.978	2	0.022	0.560
			C=1; A=2	Control	197	0.966	7	0.034	
3	Exon4	rs1801132	152265522 C/G	Patient	51	0.554	41	0.446	0.995
			C=1; G=2	Control	113	0.554	91	0.446	
4	Exon8	rs2228480	152420095 G/A	Patient	80	0.869	12	0.131	0.170
			G=1; A=2	Control	164	0.804	40	0.196	

*Comparison of the allele frequencies between the patient group and the control group The positions of the polymorphisms were defined according to contig NT_025741.15

Table 3. Frequencies of polymorphisms for estrogen receptor α (ERα) P*vu*II and X*ba*I genotypes between girls with premature thelarche (PT) and controls

	PT girls (n=96)	Controls (n=100)	P value
P*vu*II polymorphism			
CC	12 (12.5%)	22 (22.0%)	0.079
TC	51 (53.1%)	41 (41.0%)	0.089
TT	33 (34.3%)	37 (37.0%)	0.520
X*ba*I polymorphism			
GG	2 (2.0%)	4 (4.0%)	0.436
AG	31 (32.3%)	25 (25.0%)	0.259
AA	63 (65.6%)	71 (71.0%)	0.419

Table 4. Association of X*ba*I polymorphism of estrogen receptor α (ERa) with Tanner stage in girls with premature thelarche

Characteristics	AA (n=63)	GG and AG (n=33)	P value*	Odds ratio (95% CI)
Tanner stage (Breast)			0.018	3.073 (1.183-7.979)
Tanner stage 2	52 (82.5%)	20 (60.6%)		
Tanner stage 3	11 (17.5%)	13 (39.4%)		

* The proportion of Tanner stage was compared using the chi square test depending on XbaI polymorphism

There was no significant difference in the distribution of *PvuII* and *XbaI* polymorphisms between patients and controls. However, the carriers of *XbaI* polymorphisms had more advanced Tanner stage than did the non-carriers. Also, four *ERα* gene polymorphisms were previously identified, but these polymorphisms had no clinical significance.

Conclusions

No association was found between the *ERα* gene polymorphisms and PT in girls. However, *XbaI* polymorphisms may contribute to early breast budding. Further studies are needed to validate the role of *ERα* gene polymorphisms in PT.

References

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In relation to this presentation, I declare that there are no conflicts of interest.

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