

To whom should central nervous system imaging be performed in girls with central precocious puberty (CPP)?

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INTRODUCTION AND OBJECTIVE

Organic etiologies are more likely in girls with central precocious puberty (CPP) who are <6 years of age and/or girls with neurological findings. However it is not known whether other clinical and hormonal features suggest organic causes. The aim of this study is to define new indicators of organic etiology in girls with CPP.

SUBJECT AND METHODS

The medical records of 286 girls who had GnRHa therapy due to CPP in the last 20 years were evaluated retrospectively. Chronological age, bone age, height, pubertal stage, gonadotropin and serum estradiol levels, peak stimulated LH level and findings of CNS imaging at the time of diagnosis were recorded. Pubertal stages were classified as early (Tanner 2 and 3) and advanced (Tanner 4). The cut-off for hormonal values to differentiate organic from idiopathic CPP were determined using ROC curves.

RESULTS

- Organic CPP was present in 6.3% (18/286) of cases.
- Pubertal findings began before age 6 in 88.9% (16/18) of the girls with organic CPP (Table 1).
- Girls with organic CPP were diagnosed at an earlier age, bone ages were more advanced, bone age-corrected height-SDSs were lower and sex steroid levels and peak LH levels in GnRH tests were higher than girls with idiopathic CPP (Table 2).
- Basal E₂ and peak LH levels of organic CPP patients with early stages of puberty were similar to those of idiopathic CPP with advanced pubertal stages (Table 3).
- Cut-off points that differentiate organic vs idiopathic CPP at early pubertal stages was 38.1 pg/ml for basal E_2 (100% sensitivity, 80.4% specifity, AUC:0.945, p<0.001), and 13.6 IU/L for peak LH (100% sensitivity, 66.4% specifity, AUC:0.844, p<0.001).
- No statistically significant cut-off point was found for basal E_2 and peak stimulated LH that differentiate those with organic vs idiopathic CPP at advanced stages of puberty.

POSTER NUMBER: P2-P224

SESSION NAME: Pituitary, neuroendocrinology and puberty 5

Table 1. Age of onset of pubertal findings in girls with organic vs idiopathic CPP

	Age at onset of pubertal findings				
	0-2 yrs	2-6 yrs	6-8 yrs		
	n(%)	n (%)	n (%)		
Idiopathic CPP		36 (72)	232 (99.1)		
Organic CPP	2 (100)	14 (28)	2 (0.9)		
Total	2 (100)	50 (100)	234 (100)		

Table 2. Clinical and hormonal characteristics of patients with organic vs idiopathic CPP

	Girls			
	Organic (n=18)	Idiopathic (n=268)	P value	
Chronological age at diagnosis (CA) (yrs)	4.7±1.2	7.9±0.9	< 0.001	
Age at initiation of symptoms (yrs)	4.0±1.2	6.9±0.9	< 0.001	
Height-SDS	1.8±1.0	1.5±0.8	0.384	
Height-SDS for BA	-2.3±0.8	-0.7±0.7	< 0.001	
Pubertal stage			0.582	
T2	6 (33.3%)	95 (35.5%)		
T3	10 (55.6%)	140 (52.2%)		
T4	2 (11.1%)	33 (12.3%)		
Bone age (BA) (yrs)	8.3±1.1	10.1±0.8	< 0.001	
BA advancement (BA-CA) (yrs)	3.6±1.2	2.2±0.9	< 0.001	
Basal FSH (IU/L)	3.7±1.1	4.3±1.6	0.525	
Basal LH (IU/L)	1.5±0.9	1.4±1.0	0.422	
Basal E ₂ (pg/ml)	65.2±22.4	28.6±14.6	< 0.001	
Peak stimulated LH (IU/L)	17.2±3.6	12.7±4.3	< 0.001	
Early menarche history (<10 years of age)	0	53 (18.5)	< 0.001	
in family				

Table 3. The comparison of hormone levels with respect to pubertal stages between idiopathic vs organic cases

	Early pubertal stages			Advanced pubertal stages		
	(T2&T3)			(T4)		
Hormone levels	Idiopathic	Organic	P value	Idiopathic	Organic	P value
	(n:235)	(n:16)		(n:33)	(n:2)	
Basal E ₂ (pg/ml)	29.1±9.5	62.4±19.8	< 0.001	64.6±17.6	87.6±4.8	< 0.001
Peak stimulated LH (IU/L)	12.2±3.7	16.8±3.2	< 0.001	16.6±4.8	20.8±0.6	< 0.001

CONCLUSION

CNS imaging should be prioritized for those with an estradiol level above 38 pg/ml and/or a peak LH level above 13.6 IU /L in early pubertal stages. It is not possible to differentiate organic vs idiopathic causes with hormonal parameters in advanced puberty.







