Brain malformations and sellar spine as possible cause of central precocious puberty in a large monocentric study

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Background and Aim

Central precocious puberty (CPP) is defined as the secondary sexual characteristics onset before 8 years of age in females and before 9 in males, due to premature activation of the hypothalamic-pituitary-gonadal axis. The underlying cause remains idiopathic in the great majority; based on the 2009 Consensus, 2% to 7% of girls who have onset of CPP between the ages of 6 and 8 years have unsuspected pathology and only 1% have a tumor such as a gloma or astrocytoma.

Aim of our retrospective study was to assess brain MRI findings and the anthropometric, biochemical, pelvic ultrasound characteristics at presentation of a large monocentric cohort of children with CPP.

Subjects and Methods

CPP Subjects

• 147 children 130 F and 17 M, who received a diagnosis of CPP between July 2005 – June 2019 where enrolled;
• For F mean age of sexual characteristic onset (Tanner stage B2) was 6,5±1,8 yrs;
• Mean age at GnRHa therapy start was 7,1±1,5 yrs (in F 7,6±1,3 yrs and in M 8,0±2,5 yrs).

Study design:

Retrospective monocentric study

Methods:

• Anthropometrics evaluations: height (cm), BMI (kg/m²), puberty (Tanner stage)
• Biochemical evaluations: baseline LH/FSH, peak LH/FSH after GnRHa stimulation, estradiol
• Bone Age (Greulich and Pyle)
• Pelvic ultrasound
• Brain MRIs with particular attention to brain structures and hypothalamic-pituitary region (HP) were analyzed by two experienced neuroradiologists.

Results

Aetiology based on brain MRI (Figures 1 and 2)

• Idiopathic: n=65; 56 F and 9 M
• Hamartomas: n=6, 4 F and 1 M
• Tumors: n=9, 7 F and 2 M
• Acquired injuries: n=16, 14 F and 2 M
• Others: n= 51, 48 F and 3 M (Figure 2)

Figure 1: Distribution of aetiology, according to MRI findings

Figure 2: Principal findings among the “Other” categorized patients

Table 1: Clinical, anthropometric, biochemical and US characteristics of our cohort

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Idiopathic</th>
<th>Hamartomas</th>
<th>Tumors</th>
<th>Acquired Injuries</th>
<th>Others</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antropometric, biochemical parameters</td>
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<tr>
<td>Height (cm)</td>
<td>157,1±0,5</td>
<td>150,5±1,6</td>
<td>158,4±1,6</td>
<td>152,8±0,5</td>
<td>158,9±1,2</td>
<td>158,4±1,2</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>18,9±4,1</td>
<td>18,2±2,2</td>
<td>21,2±2,9</td>
<td>18,5±2,9</td>
<td>17,9±2,8</td>
<td>18,1±2,7</td>
</tr>
<tr>
<td>Age at first menarche</td>
<td>7,8±1,1</td>
<td>7,8±2,6</td>
<td>7,8±3,1</td>
<td>7,8±1,1</td>
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<tr>
<td>Ultrasound (MRI)</td>
<td>51,2±3,1</td>
<td>52,8±4,4</td>
<td>50,8±4,2</td>
<td>53,3±7,1</td>
<td>57,1±11,9</td>
<td>50,3±6,9</td>
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<tr>
<td>Right mammary (cm)</td>
<td>1,5±0,9</td>
<td>1,5±1,5</td>
<td>1,5±1,5</td>
<td>1,4±0,8</td>
<td>2,5±1,9</td>
<td>1,5±1,5</td>
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<tr>
<td>Biochemical evaluations</td>
<td></td>
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<tr>
<td>Baseline FSH (U/L)</td>
<td>5,2±2,1</td>
<td>1,3±2,2</td>
<td>1,3±2,2</td>
<td>1,4±2,2</td>
<td>1,4±2,4</td>
<td>1,3±2,2</td>
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<tr>
<td>Baseline LH (mlU)</td>
<td>1,3±1,3</td>
<td>1,3±1,3</td>
<td>1,3±1,3</td>
<td>1,3±1,3</td>
<td>1,3±1,3</td>
<td>1,3±1,3</td>
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<tr>
<td>Peak FSH (U/L)</td>
<td>10,6±6,6</td>
<td>20±10,2</td>
<td>16,8±8,3</td>
<td>13,5±7,4</td>
<td>15,9±9,2</td>
<td>12,9±5,8</td>
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<tr>
<td>Peak LH (U/L)</td>
<td>9,5±9,5</td>
<td>20,5±10</td>
<td>16,8±10,1</td>
<td>21,8±6,8</td>
<td>19,9±10,6</td>
<td>17,8±11,7</td>
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<td>Estradiol (ng/ml)</td>
<td>29,7±23,8</td>
<td>28,5±20,9</td>
<td>31,6±20,5</td>
<td>39,1±16,6</td>
<td>32,2±18,8</td>
<td>24,4±15,8</td>
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<tr>
<td>Bone age</td>
<td>1,5±1,4</td>
<td>1,5±1,5</td>
<td>1,5±1,5</td>
<td>1,5±0,9</td>
<td>1,5±1,5</td>
<td>1,5±1,5</td>
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<tr>
<td>Bone age in <a href="http://www.boneage.org">www.boneage.org</a></td>
<td>1,5±1,5</td>
<td>1,5±1,5</td>
<td>1,5±1,5</td>
<td>1,5±0,9</td>
<td>1,5±1,5</td>
<td>1,5±1,5</td>
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</tbody>
</table>

There was no significant difference among the analyzed groups in terms of anthropometric measures, biochemical parameters, US findings and bone age, except for a younger age at CPP diagnosis and higher gonadotropins values in hamartomas.

Conclusions

• Brain abnormalities were found in 56% of patients presenting with CPP;
• Midline abnormalities, pineal cyst and sellar spines represent other finding in CPP, either in females and in males;
• In particular, sellar spine, a bony spur protruding from the central portion of the dorsum sellae, may be a not negligible potential cause of CPP due to deformation of the growing pituitary gland.

References

• Cantis-Oradorde J et al.: Prevalence of CNS lesions in girls with CPP, J Pediatr Endocrinol Metab. 2018 Jul 26;31(7):701-710
• Mogensen SS et al. (2012) Pathological and Incidental Findings on Brain MRI in a Single-Center Study of 229 Consecutive Girls with Early or Precocious Puberty. Pediatr OMF. 7(1): e39639