Reviewer’s report

**Title:** Familial early puberty: presentation and inheritance pattern in 139 families

**Version:** 0  **Date:** 15 Jul 2016

**Reviewer:** Youn Hee Jee

**Reviewer's report:**

Title: Familial early puberty shows predominantly maternal inheritance

Durand et al. studied large series of probands and the families with central precocious puberty (PP) or advanced puberty (AP), which showed prominent maternal inheritance pattern. Although this is an interesting study looking at a big cohort for timing of puberty and its inheritance pattern, there are several major points that need to be addressed.

Major points:

1. **Clarifying Mendelian inheritance mode, de novo, or imprinting**

   The pedigree of each family could be carefully scrutinized to identify accurate inheritance mode. For example, family # 3, #34, #69, #93, #116, #123, and #124 may be considered autosomal recessive inheritance mode. Family # 10, #31, #57, #72 and #121 may have imprinting disorders. The rest of families may have either autosomal inheritance with incomplete penetrance or oligo or polygenic causes of AP/PP. Dividing families into groups with different inheritance modes would help to understand whether each group may have different presentation or severity.

2. **Familial form vs non-familial form**

   The result of comparing familial form vs non-familial form was not presented in result but discussed in discussion. They should appear in result section to show the difference in phenotype and biochemical markers as authors identified.

3. **Difficulty of obtaining timing of puberty in male**

   Presence of pubic hair only without testicular enlargement (in boys) or breast tissue (in girls) would not indicate that the child is in puberty. These subjects should be excluded. Also, since pubertal change is easily noticeable in females (breast development or menarche) and easily
recalled but not in males because enlarging testes may go unnoticed unless pediatric endocrinologist examined and documented, this may have introduced recall bias and resulted in prominent maternal inheritance. The authors may want to clarify whether this was a possibility.

4. Ethnicity is a factor that may affect timing of puberty. Should be included for data analysis.

Minor points:

1. Line 28: The penetrance rate was 33 %. Please specify which phenotype of penetrance was 33%.

2. Line 140: pubic hair only may not be sign of puberty but premature pubarche. Therefore, pubic hair without testicular enlargement should not be included. This will need clarification whether they had biochemical evidence of puberty.

3. Statistical methods were not detailed in method section.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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