Reviewer’s report

Title: Growth Data and Tumour Risk of 32 Chinese children and adolescents with 45, X/46, XY mosaicism

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Reviewer: Ewa Rajpert-De Meyts

Reviewer's report:

Pan et al. performed a retrospective analysis of growth, puberty, genital phenotype, gonadal histology and function of a series of 32 Chinese children and adolescents with 45,X/46,XY mosaicism and variants, who were diagnosed and treated over 13 years in one centre. Although several similar studies have been published, a new larger series from China is of interest for the readers.

The authors focused their description of this series on the growth issues and the risk of germ cell malignancy. The report is very short and is in places difficult to follow. For example, the height data are not listed in Table 1. No information is given concerning the surgery and how the tissue samples were taken? Were there biopsies taken (at what age?) or gonadectomies or both? There is some confusion concerning histology of malignant lesions: in the text and tables the following terms are used: gonadoblastoma, precancerous testicular lesion, carcinoma in situ, without explanation what these terms mean. The discussion does not give much of an insight. Finally, the paper is in general understandable but there are numerous minor errors of spelling and syntax. In many places in the text and tables words are written without spaces. The authors are advised to employ professional language editing service.

Specific comments

1. The first sentence in the paper is not correct: 'The 45, X/46, XY mosaicism is considered to be a rare congenital malformation' - abnormal karyotype is not a 'malformation' (some patients with low percentage aneuploidy do not have malformations).

2. The authors state in the 'Patients' section that they included patients with 'aberration of their Y-chromosome'. I see in Table 1 only one patient with i(Y) in the karyotype. Were there any other aberrations? There is no description how these 'aberrations' were diagnosed. Was a molecular screening for Y-chromosome deletions performed? This information should be added to the method description.
3. The authors stated on page 5 that the pubertal staging was performed according to the criteria of Tanner but cited a paper (ref. 4) which describes pubertal changes in boys. A reference to puberty staging in girls or a general reference to both genders should be added.

4. In the description of immunohistochemistry (page 6) positive and negative controls ought to be mentioned.

5. Table 1 should list the height SDS and info on the tissue source - have there been biopsies or gonadectomies (or both) performed in each patient?

6. Table 1 lists only gonadoblastoma (GB) as pathology, but in Table 2, in the summary of the findings included as the last study, PTL+GB is listed in 7/24 patients. Please explain what it is meant here?

7. The legend to Figure 2 should describe what is the histology of each image, especially that some pictures are pale. I can see that G and H show gonadoblastoma, but it is not clear what is shown in other images, especially A and B. In addition, the legend states that 'negative for OCT3/4 have 'blue nuclear signal' - blue colour is counterstaining and not a 'signal'. Correct to 'lack of red staining' or just remove the phrase.

8. In Figure 3, image A supposedly shows 'normal testicular tissue'. What was the age of the patients who had this specimen. It looks a bit like germ cell neoplasia in situ (GCNIS) previously known as CIS testis. Was this specimen stained for OCT3/4? The last sentence of the figure legend contains errors: 'The nests were encapsulated by granular cells /Sertoli cells'. The nests were not 'encapsulated (there is no capsule) and granular cells = granulosa cells.

9. Table 2 lists among 'Nations' both 'America' (not a nation) and 'USA'. Please explain and correct.

**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.

No
**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

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Not relevant to this manuscript

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