**Peer Review File**

Article information: https://dx.doi.org/10.21037/tp-23-181

**Reviewer A**

Line 27: MRKH usually represents aplasia of not only the upper vagina
Reply: Thank the reviewer for the suggestion, we have modified our text as advised. (See Page 2, line 1-3)
Changes in the text: Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is mainly characterized by congenital aplasia of the uterus and the upper two-thirds of vagina in female with normal secondary sex characteristics and female karyotype (46, XX).

Line 94: maybe better talking about no history of hormone usage instead of contraceptive pills. How about any growth spurt?
Reply: Thank the reviewer for the suggestion, we have modified our text as advised. (See Page 4, line 4)
Changes in the text: She had no history of hormone usage and no growth spurt.

Line 99: what's the implication on mentioning labial fusion?
Reply: Thank the reviewer for the concern. We want to express that the girl has normal female external genitalia, no masculinization manifestation.

Line 111: I would be interested to know if there were any adnexal mass
Reply: Thank the reviewer for the concern. There was no mass in the bilateral adnexal.

Line 155: inappropriate use of 'biased'
Reply: We appreciate the reviewer's careful review of our manuscript. We have corrected this as follows. (See Page 6, line 2-3)
Changes in the text: Transabdominal ultrasound examination is dependent on the experience and skill of the operator; the results may have poor accuracy and insufficient objectivity.

Whereas for the role of MRI in diagnosis, in my opinion it is not absolutely necessary unless in cases where diagnosis is uncertain and there are concerns of a rudimentary horn / uterus with functioning endometrium
Timing of the MRI is important as in prepubertal girls, in which this case where the precocious puberty was supressed by GnRHa, there might be false positive for the MRI. MRI might not be necessary to confirm the diagnosis in all cases of MRKH, only in cases which the diagnosis is uncertain
Reply: We sincerely thank the reviewer for careful reading, we don't think MRI be necessary to confirm the diagnosis in all cases of MRKH, Pelvic MRI examination should be considered for patients only when the diagnosis is uncertain or pelvic ultrasound shows unclear imaging.

Line 156: repetitive for the size of the uterus on the USG, as previously mentioned in the findings already.

Reply: Thank the reviewer for the advice. We have modified our text as advised.
(See Page 6, line 4)
Changes in the text: The size of the uterus "1.6cm× 1.4 cm× 0.5 cm" was deleted.

Line 184-186: Surgical vaginoplasty is usually not recommended as the first line treatment for MRKH, non-surgical vaginal dilation is often suggested as the first line due to lower risk of complications.
Reply: Thank the reviewer for your valuable comment. We are apologized for our carelessness. Based on your comments, we have made the corrections in the manuscript. (See Page 6, line 27-31)
Changes in the text: The treatments for MRKH syndrome include psychological counseling and the correction of anatomical abnormalities. Various different non-surgical vaginal dilation and Surgical vaginoplasties have been suggested for vaginal construction. In relation to the timing of the treatment, vaginal construction can only be performed after sexual maturity and if the patients are willing to be treated.

I think diagnosis of MRKH in a prepubertal girl (even though in this case the girl has ICPP, but puberty has been halted by GnRH agonist) is difficult as the uterus can be underdeveloped. Examination of the vagina might sometimes be difficult, and sometimes might be appropriate to defer the diagnosis of MRKH till the girl has undergone puberty.
Though I agree that multidisciplinary management for girls with MRKH is important for better psychological support.
Reply: We sincerely thank the reviewer for careful reading. In the present case, the girl has ICPP, pelvic ultrasound reexamination during the treatment showed no uterus, the parents initially thought it was a side-effect of GnRHa treatment. Until now, no patient has been reported for CPP children with combined MRKH syndrome who was treated with GnRHa. If MRKH syndrome is diagnosed before GnRHa treatment, the treatment regimen could be fully explained to parents.

Whereas for the role of MRI in diagnosis, in my opinion it is not absolutely necessary unless in cases where diagnosis is uncertain and there are concerns of a rudimentary horn / uterus with functioning endometrium.
Reply: We agree with the reviewer's comments. Pelvic MRI examination should be considered for patients only when the diagnosis is uncertain or pelvic ultrasound shows unclear imaging.
Changes in the text: "A pelvic magnetic resonance imaging examination could help with the diagnosis" was deleted. (Highlight box; paragraph 2)

Indeed, I agree that the development of girls with precocious puberty should be monitored, but I do not think there is any evidence suggesting that the incidence of MRKH or DSD is increased in girls with precocious puberty.
Reply: Thank the reviewer for your insightful comment. We do not mean that the incidence of MRKH or DSD is increased in girls with precocious puberty. As commented by the reviewer, we have corrected the "MRKH syndrome should be considered in children with precocious puberty when an ultrasound examination shows uterus absence or maldevelopment" into

"MRKH syndrome should be considered in girls when an ultrasound examination shows uterus absence or maldevelopment, even in girls with precocious puberty". (See Page 2, line 29-31)
Changes in the text: MRKH syndrome should be considered in girls when an ultrasound examination shows uterus absence or maldevelopment, even in girls with precocious puberty.

Overall poor grammar, word choices and sentence structure made some parts of the article difficult to understand.
Reply: We sincerely thank the reviewer for careful reading. We revised the whole manuscript carefully to avoid language errors. In addition, we consulted a professor who are good at English to check the grammar and word choices. We believe that the language is now acceptable for the review process.

**Reviewer B**

Although the rarity of the association, it should be clear in the manuscript why this association is important report and publish. I have some suggestions for improvement:

Comments:
1. The authors should elaborate on, whether they consider the two abnormalities linked or just co-incidental in their patient.
Reply: Thank the reviewer for your insightful comment, we have modified our text as advised. (See Page 6, line 10-26)
Changes in the text: "... As the genetic causes of MRKH syndrome and CPP are different, these two diseases seem to be genetically unrelated. Therefore, it is speculated that in the present case, the occurrence of MRKH syndrome and CPP was a coincidence. Although previous study(4) suggested that early stimulated FSH related pathway may contribute to precocious puberty in MRKH syndrome, in our case, FSH was not elevated. More data is needed for further understanding the pathogenetic mechanism for CPP in MRKH syndrome."

2. Writing and clarity could be improved. E.g., the sections on the identification of a uterus, and later no uterus, is not very clearly presented (discussion-part)
Reply: We sincerely thank the reviewer for careful reading, we have modified our text as advised. (See Page6; line3-9)
Changes in the text: In the present case, a pelvic ultrasound before treatment showed that the size of the "uterus" was relatively small according to the ovary volume. However, due to a limited experience of a sonologist, this image was misidentified as a uterus. A pelvic ultrasound re-examination during treatment showed no uterus, and thus pelvic MRI was suggested, but this was refused by the parents twice. A pelvic MRI examination performed after the 3rd ultrasound examination confirmed the diagnosis of MRKH syndrome.

3. Introduction: 2 subtypes, numbers <10 should be spelled out
Reply: Thanks for your careful checks, we have modified our text as advised.
(See Page 3, line17)
Changes in the text: two subtypes.

4. Reference 3. The authors cite a Chinese multicenter study with patients recruited for systematic evaluations and state their mean age at contact, 23 years. This could include patients with previous MRKH-related contacts, and thus an overestimation from population-based data. Normally median age at referral is considered to be 16-19 years (see PMID: 32819397).
Reply: We sincerely thank the reviewer for careful reading. The reference we cited is from department of gynecologm, the study had a retrospective study design, and describes mean age at 'first visit' in 11 centers. Stated mean age seems high compared to the literature in general stating 16-19 years, maybe due to all patients were recruited in tertiary teaching hospitals, which may have caused selection bias. It also shows that the Chinese gynecologists and pediatrician lack an enough understanding of the genital malformations of MRKH syndrome.

5. When stating the setting (hospital name and city), please include the country as well for the international readership
Reply: Thank the reviewer for the suggestion, we added the country and city: Huzhou, China. (See Page 4, line3)
Changes in the text: A 7-year-old girl was admitted to the Huzhou Maternity & Child Health Care Hospital (Huzhou, China).

6. Whole exome sequencing (stated with a negative result) is a comprehensive analysis, and therefore important to detail how it was done. Just briefly regarding bioinformatics and variant filtrering (e.g., which was searched and considered 'relevant to clinical phenotype')
Reply: Thank the reviewer for the suggestion, we added a paragraph to detail how it was done. (See Page 5, line5-13)
Changes in the text: Whole-exome sequencing (WES) and chromosomal microarray analysis (CMA) were performed. Samples were prepared using the IDT xGen Exome Research Panel v1.0 (IDT). Final quantified libraries were seeded onto an Illumina flow cell and sequenced using paired-end 150 cycle chemistry on the NovaSeq 6000 (Illumina). Initial data processing, base calling, alignments to the human genome assembly GRCh37 (hg19) and variant calls were generated by various bioinformatics tools. The mean sequence coverage per base was approximately 100X, and at least 95% of the regions were covered at no leass than 20X. The interpretation of sequence variants was performed according to the American College of Medical Genetics and Genomics (ACMG). WES showed no genetic variation related to clinical phenotype, and no obvious genomic imbalance was detected in the CMA.