Reviewer's report

Title: Transitional Cell Carcinoma of the Upper Urinary Tract Diagnosed via FGFR3 Mutation Detection in Urine: a Case Report

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Reviewer: Makito Miyake

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<Summary>
In the clinical management of the upper urinary tract carcinomas, one of the biggest issues is that these are sometimes hard to detect and diagnose. It is problematic to perform nephroureterectomy without evidence of malignancy. As to urine-based marker, urinary cytology have been widely used for diagnosing of lower and upper urinary tract. The limitation is poor sensitivity, especially in low-grade tumors. FGFR3 mutation is the most promising marker for detecting low-grade urinary tract marker. Unfortunately, there are few reports addressing usefulness of urine-based FGFR3 mutation assay for diagnosing upper urinary tract. In this case report, a right renal pelvic tumor was diagnosed successfully as a malignancy by FGFR3 mutation assay. This article would have high educational value to urologists.

Major Compulsory Revisions
1) The author has to submit images of CT scan, retrograde pyelogram and intravenous pyelogram as Figures. The CT scan image at initial presentation would be essential. We are unable to know conditions of the patient’s right kidney, tumor location and presence or absence of hydronephrosis. The patient had a complete ureteral duplication. The retrograde pyelogram was successful? Was it possible to subject washing fluid of renal pelvic where the tumor was to cytological exam? The author should explain it in more detail and make the patient condition clearer.

2) The urine obtained after right nephron-ureterectomy was subjected to FGFR3 mutation detection assay? This assay seems to be so sensitive enough to detect invisible urothelial cancer. Were the patient proven to be free from tumor? The author should add some description about the follow-up for this patient.

3) In the section of Abstract, it is described that pathology had confirmed the genetic change of FGFR3. The author should add some description about it in detail, such as mutational types and mutational codons. In the section of Case Presentation, the patient’s urine obtained before operation contained genomic DNA carrying FGFR3 mutations in exon 7, 10 and 15. According to previous reports, a single tumor carrying two different FGFR3 mutations is uncommon. A tumor with three different FGFR3 is supposed to be really rare. Some description about it could make this article’s relevance higher.
4) The description about pathological examination is insufficient. That should be described in accordance with 2004 WHO grading criteria and 2002 TNM staging criteria.

Minor Essential Revisions
none

Discretionary Revisions
The author used words “transitional cell carcinoma” and “urothelial cancer” in the section of Background. In this article, the author described a case with a tumor of the urinary tract, so these two are synonyms. It would be better to make terminology consistent.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests'