Reviewer’s report

Title: In-depth investigation of the molecular pathogenesis of bladder cancer in a unique young patient with extensive multifocal disease: a case-report

Version: 1 Date: 28 October 2009

Reviewer: Alex Sgambato

Reviewer’s report:

Ms: “In-depth investigation of the molecular pathogenesis of bladder cancer in a unique young patient with extensive multifocal disease: a case-report” by Tahlita CM Zuiverloon.

The Authors analyzed multiple tumors and urine samples of a 26-years old male with multiple recurrences of a bladder cancer. They found that all tumors contained a mutation in FGFR3 and were associated with FGFR3 overexpression. None of the tumors showed overexpression of TP53. Moreover, a deletion was detected on chromosome 9 in the primary tumor which was confirmed by the SNP-array. They also demonstrated that detection of all recurrences was possible by urinary analysis of FGFR3 mutation.

The Authors conclude that the molecular characteristics determine bladder cancer disease course, independently of patient’s age and that FGFR3 mutation analysis on voided urine is a simple non-invasive method for the follow-up of patients with an FGFR3 mutant tumor.

Major Compulsory Revisions

In the Methods-Tissue samples paragraph the Authors state that: “Samples were first deparaffinised and DNA was extracted….”. It is not clear what type of samples were used for DNA extraction: tissue slices? How thick? How many?

In the Methods-FGFR3 and TP53 immunohistochemistry paragraph is described that: “Expression of FGFR3 was scored in a semi-quantitaive scoring system: 0= all tumor cells negative, 1= faint positivity of in some or all cells, 2= weak but extensive positivity and 3= strong positivity /overexpression (regardless of extent). However, this type of scoring is then never used since FGF3 expression was only analyzed in the primary tumor and in the Results section the Authors state that “Molecular analysis of the primary tumor revealed …..overexpression of FGFR3”: however it is not clear what the overexpression is referred to (did they analyze normal tissue?).

The Authors conclude that: “FGFR3 mutation analysis could be a feasible alternative for recurrence detection” of young patients.

The major limitation of the study is that it refers to only one young patients and
that, as the Authors note, FGFR3 mutations are not so frequent in young patients thus limiting the suitability of the proposed method. It would have been of interest to try to define the frequency of FGF3 mutations in a subset of young patients with bladder cancer.

Moreover, the Authors seem to suggest that FGF3 mutations in tumors might characterize young patients with high risk of recurrence. However, as the Authors state: “FGFR3 mutations have been associated with BC tumors of low stage and grade and patients having a favorable prognosis (see ref. 9)”. How to conciliate these points?

Minor Essential Revisions

I would suggest to check the manuscript more carefully for English.

In the Case presentation the Authors state that: “intoxications included a smoking status of 5.5 pack-years”. It might be useful to clarify what is intended for pack since not all readers might know it well.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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