Reviewer's report

Title: Challenges in the management of a patient with Cowden syndrome: case report and literature review

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Reviewer: Rolf Sijmons

Reviewer's report:

The authors present the first patient diagnosed with Cowden syndrome in Latvia and according to the title want to discuss the challenges in the management of this patient. However, these challenges do not come across very strongly. I would suggest presenting them clearer.

What are those challenges in this patient and in Cowden syndrome in general:

- Can we assume a high enough risk to decide for preventive mastectomy, regardless of what lesions are already detected in the breast or should we wait until we see particular types of breast lesions?

- How difficult is it to interpret the imaging results?

- What should the surveillance strategy be for the other organs; in this patient for example the colon and kidneys. (Thyroid and endometrium had been removed)

I suggest that the authors put this in a Discussion section rather than in their Case presentation section.

Additional remarks:

Why was the mutation not tested in the mother but only in the father? No explanation is given. Somatic mosaicism is always a theoretical possibility even if the parents do not show the mutation in blood (e.g. well demonstrated for FAP/APC!). Did the authors consider testing the sisters?

A missense mutation was detected in PTEN. The authors should discuss whether or not this variant has been reported before and whether or not the variant should be consider pathogenic (evolutionary conservation, Grantham scores etc etc). If it is a new variant it should be submitted to an online public PTEN mutation database.

On page 3, I do not understand the sentence: ...To control possible development of breast cancer for patients WITHOUT a family history...

Should the surveillance be radically different from Cowden syndrome patients WITH a family history?

Page 4: Breast cancer surveillance also involves removal of the breast...."This is not correct. Preventive mastectomy is by definition not part of surveillance but
another type of preventive measure.

Page 5: "Clinical geneticist considered" should read "The clinical geneticist considered..."

Page 6: "....proband's father who appeared to be a non-carrier" should be changed, e.g. into

The PTEN variant was not identified in a peripheral blood sample from the father. The mother refused to be tested/....or other explantion why the mother could not be tested.

p.s. if we want to conclude de novo mutation than non-paternity should be proven. It is not uncommon that a father is not the biological father.

The authors should in my opinion briefly mention the nauture of the challenges in the abstract and comment on their interpretation of the PTEN variant detected. If their follow-up after preventive mastectomy is indeed the longest in the literature then this should be mentioned in the abstract as well.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Declaration of competing interests:**

I declare no competing interests