Reviewer’s report

Title: Desmoid Tumours of the Extremity and Trunk. A retrospective Study of 44 Patients

Version: 0 Date: 10 Jul 2017

Reviewer: Eberhard Stoeckle

Reviewer's report:

Wirth, et al. report outcome in a series of desmoid patients treated surgically through over 34 years. A prognostic factor analysis is performed. Results from this study retrieve already known contradictory data concerning prognosis and treatment options in desmoid fibromatosis (DF). Presented in its actual form, this study does not give new insight into DF. Consequently, I suggest the authors to re-orientate their paper by focusing on the major finding of their study, which is recurrent disease being the major risk of further recurrence, especially when treated by surgery.

I have two major comments:

1. Shorten the manuscript on focusing on your major endpoint

2. Present data more comprehensively, especially avoid the confusion between patient data (44 patients) and procedures (54 treatments). I suggest sticking to patient data.

In the detail:

3. Abstract/Methods/Endpoints. You mention secondary lesions being part of endpoints you looked for. Suppress it as precisely you indicate in the Introduction/First sentence that DF will not metastasize.

4. Shorten and specify the Introduction. It may be unnecessary for the general reader to learn when DF has first been described, what its cause is, or which events characterize the Gardner syndrome. In contrast, clearly distinguish between PAF-associated DF (with a germline APC mutation) and sporadic DF (harboring the CTNNB1 mutation (beta-catenin) in the tumor), which are considered mutually exclusive. Prognosis is quite different between the groups. Then put the basis for the discussion concerning the actual place of surgery in DF by replacing the sentence " In recent years resection of the tumour
and/or radiation were proposed as principal treatment" by "In former years resection of the tumour and/or radiation were proposed as principal treatment."

5. Active observation of DF has been suggested nearly a decade ago. You may cite:

6. Specify patient data. For a better understanding, indicate numbers of patients, not percentages and stick to patient data, not treatments. It may avoid confusing sentences like: "37 patients had primary, 17 recurrent disease". This totals 54 patients. In reality, I guess, 27 patients had primary and 17 recurrent disease. You may put these data into a table.

Suggestion of Table:

<table>
<thead>
<tr>
<th>Age</th>
<th>Mean (range), y</th>
<th>39.4 (14 - 69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>F</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>19</td>
</tr>
<tr>
<td>Tumour size</td>
<td>Mean (range), mm</td>
<td>7.7 (1 - 25)</td>
</tr>
<tr>
<td>Tumour site</td>
<td>n (%) Upper limb</td>
<td>18 (40)</td>
</tr>
<tr>
<td></td>
<td>Lower limb</td>
<td>15 (35)</td>
</tr>
<tr>
<td></td>
<td>Trunk (wall?)</td>
<td>6 (14)</td>
</tr>
<tr>
<td></td>
<td>Pelvis</td>
<td>5 (11)</td>
</tr>
<tr>
<td>Presentation</td>
<td>Primary</td>
<td>27 (61)</td>
</tr>
<tr>
<td></td>
<td>Recurrent</td>
<td>17 (39)</td>
</tr>
<tr>
<td></td>
<td>PAF-associated</td>
<td>X</td>
</tr>
</tbody>
</table>
7. How many patients had PAF-associated DF and how many sporadic?

8. Treatment modalities remain unclear to me, even after several readings of the manuscript:

   a. Surgery: 50 resections and 4 other treatments were given to 44 patients, the latter 4 all in recurrent DF (RecDF). Consequently, 13/17 RecDF were operated, leaving 37 surgeries for 27 primary DF (PrimDF). Right? Consequently 10 patients with PrimDF were operated twice. Why? For recurrence? In Results (Page 6, Alinea 52) you indicate that in a total 10 patients had a recurrence. Ciphers do not fit. Please specify.

   b. Radiotherapy: 21 patients received radiotherapy. How many with PrimDF and RecDF, respectively?

9. Description of R1 resection (Page 5, Alinea 26). Omit the term "capsula" when defining R1 resections, because DF tumors typically are not encapsulated. Prefer "R1 if the margins were contaminated by the tumour".

10. Univariate/multivariate analysis. Replace your sentence "Neither in univariate nor in multivariate analysis margins, radiotherapy, sex, or size of the tumour showed a significant impact on local recurrence." by "In univariate analysis margins, radiotherapy, sex, or size of the tumour did not show a significant impact on local recurrence." Effectively, when variables are insignificant at univariate analysis, they are not included into the multivariate model. Your two significant independent prognostic factors for recurrence were recurrent disease and age. Why did you call recurrent disease a "surgical factor"? Specify also HR and CI for multivariate analysis results.

11. Did you get any information about morbidity or functional outcome, which are important endpoints in a surgical series concerning an indolent (not a "benign") disease?
12. Discussion: begin by commenting first your own findings. It is the high frequency of new recurrences after surgery for recurrence. For a better understanding, indicate in table 1 the number of recurrences by patients, not procedure. This may be followed by the quality of resection debate. Carefully discuss age as a prognostic factor. Effectively, the risk of recurrence also depends on tumor site which is age-dependent. For example, hamstring/popliteal DF occur in young patients (16-18 years) and almost ever recur. In contrast, abdominal wall DF which also occur in young patients < 40 years (women # 36 years) almost never recur. Discuss the place of radiotherapy PrimDF vs RecDF. Avoid discussing colonoscopy (irrelevant) or medical treatments (too seldom in your series), or pediatrics. Contrary to your affirmation of a part location no clear prognostic factors being defined in DF (Page 8, Alinea 5), those have been discussed abundantly in the literature. You may cite Salas S, et al. JCO 2011;29:3553-3558. These authors identified age, size and site as being independent prognostic factors for PFS. There was no difference between resections R0 and R1 in PFS. Conclude that other treatment modalities should be preferred over surgery when DF ultimately recur.

13. Restrain the number of references to 25 or 30.

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.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review
Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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