Reviewer’s report

Title: Isolated brachydactyly type E can be caused by HOXD13 nonsense mutation: case report

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Reviewer: Eva Klopocki

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Jamsheer et al. describe in their manuscript entitled “Isolated brachydactyly type E can be caused by HOXD13 nonsense mutation: case report” a family with two affected (father and daughter) who present with brachydactyly. They compare their findings to the previously published HOXD13 mutations associated with BDE.

Comments:

Major compulsory revisions
1. Case presentation: Previously reported mutations are associated with foot anomalies (“insertional duplication in the first web space” Kan et al 2003) which become apparent only on X rays and are not from the clinical pictures. Therefore the clinical pictures of the father’s feet and the statement “feet of the proband were clinically inconspicuous” are not sufficient to rule out the aforementioned foot anomalie. X-rays of the feet of both proband and her father should be provided in figure 1.

2. Case presentation/figure 1: Description of the phenotype is fragmentary. Female proband and her father show contractures (compare to Johnson et al). Deviations of index and ring finger in the proband. Finger nail of finger V on the left hand of proband’s father appears hypoplastic (figure 1b). Thumbs (left more than right) appear shortened (figure 1b) – X-ray needed for clarification.

3. Case presentation, last paragraph: hypothesis on the pathomechanism? Functional haploinsufficiency as postulated for the truncating mutations in contrast to missense mutations? Give an explanation for the rather mild phenotype.

Minor essential revisions
1. Background: the authors refer to 3 out of 12 annotated HOXD13 mutations which result in premature stop codon. Please give appropriate references. What is the phenotype associated with these mutations?

2. Case presentation: age of the female proband?

3. comment on the recently described nonsense mutation E181X (Brison et al. 2011)

Discretionary revisions
1. Conclusions: this sentence does not read well. I suggest rephrasing.
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