Reviewer’s report

Title: Intrafamilial phenotypic heterogeneity in a Taiwanese family with MAPT p.R5H mutation: a case report and literature review

Version: 0 Date: 09 Jul 2017

Reviewer: Caspar Stephani

Reviewer’s report:

Lin et al. present a case of a patient presenting with symptoms of a neurodegenerative disorder out of the spectrum of frontotemporal dementia associated with a very uncommon mutation in exon 1 of the MAPT gene, that, reportedly, has been demonstrated in only 2 Japanese families so far.

This report is - with the exception of some minor elisions - well written supported by a useful set of diagnostic data. Its strength is delineating genotype - phenotype heterogeneity as well as the general complexity of the phenotype of the FTD-spectrum.

I recommend acceptance of the article after some minor revisions. The final form should be corrected for some orthographic omissions, and may be formally revised/resubmitted once.

Minor point:

Please add results of lumbar puncture including markers if dementia if available.

Orthographic:

Abstract:
- You wrote: Overlapped

Please write: overlapping

- You wrote: As mostly reported pathogenic mutations in MAPT occur in exons 9-13, few families are reported outside of this region.

Please write: While most reported pathogenic mutations in MAPT occur in exons 9-13, few families have been reported with mutations outside of this region.

- You wrote: Our findings extended the current knowledge of phenotypic heterogeneity among members of family carrying MAPT p.R5H mutation.
Our findings extend the current knowledge of phenotypic heterogeneity among members of families carrying MAPT p.R5H mutation.

Background:

- You wrote: …..including FTD, corticobasal degeneration (CBD), ALS and persistent depressive disorder (PDD).

- Please write: ….. including symptoms of FTD, corticobasal degeneration (CBD), ALS and persistent depressive disorder (PDD).

Case presentation:

- You wrote: A 63-year-old right-handed man, who has underlying medical conditions of hypertension and hyperlipidemia with well control,…..

- Please write: A 63-year-old right-handed man, with underlying well controlled arterial hypertension and hyperlipidemia ….

- You wrote: … limited eye-of-movement…

- Please write:

- Please transfer the sentence: "Neurological examinations showed a mask face, right-hand apraxia, bradykinesia and rigidity. There was stimulus-sensitive myoclonus on his right hand and forearm." Directly after …. "and he could not perform delicate movements with his right hand."

- You wrote: Among his family, the mother of patient had been diagnosed with ALS at the age of 60 (Figure 2).

- Please write: Among his family, the mother of the patient had been diagnosed with ALS at the age of 60 (Figure 2).

Discussion:

- You wrote: As previously studies have shown that FTD, CBS, PSP, and motor neuron disorders are regarded as a clinically and biologically cohesive spectrum of tauopathy, although the neuronal inclusions exhibit distinct differences isoforms of tau deposition, clinical association of FTD and motor neuron disorders is not an exceptional occurrence, and there was 5% of FTD patients with motor neurons disorders under observation.

- Please write: As previous studies have shown that FTD, CBS, PSP, and motor neuron disorders are regarded as a clinically and biologically cohesive spectrum of tauopathy with
neuronal inclusions exhibiting distinct isoforms of tau, clinical association of FTD and motor neuron disorders occurs in approximately 5% of FTD cases.

- You wrote: ….and mother of the index patient had ALS…

o Please write: … and the mother of the index patient had ALS….

- You wrote: … which symptom had contributed to the delay of proper diagnosis and treatment of FTD.

o Please write: … which contributed to the delay of proper diagnosis and treatment of FTD

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

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5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

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