Reviewer's report

Title: Severe and aggressive cognitive SCA17 phenotype in a family with only marginally expanded CAG/CAA repeats in the TATA-box Binding Protein gene: A case report

Version: 2 Date: 25 May 2012

Reviewer: Dagmar Nolte

Reviewer's report:

This manuscript focuses on a case report of an ataxia patient with mild cerebellar signs and symptoms but rapidly decreasing cognitive decline. MRI and PET analysis showed only mild cerebellar atrophy matching the clinical phenotype of distinct motor deficits. Molecular genetic testing revealed a repeat expansion of 43 CAG/CAA codons within the TBP gene. This expansion was also detected in the patient’s mother, who was originally thought to suffer from multiple sclerosis.

The manuscript is well structured and appropriate in length. Clinical findings are presented clearly and in great detail.

Minor Essential Revisions:

(Background) The authors state that „24 subtypes of the autosomal dominantly inherited ataxias are known...“ This statement is misleading, since a minimum of 32 different SCA loci has been described. Among those, the disease causing mutation has been identified for 23-24 SCA types (depends on whether DRPLA is enclosed in counting) [Bird TD. Hereditary Ataxia Overview, GeneReviews 2012, http://www.ncbi.nlm.nih.gov/books/NBK1138/]. And 8 of these (SCA1, 2, 3, 6, 7, 12, 17, and DRPLA) are caused by repeat expansions.

(Discussion) Authors should discuss the “incorrect diagnosis of multiple sclerosis and Parkinson’s disease” (page 9, line 11) in both the maternal grandfather and the patient’s uncle more carefully. Since a parkinsonian phenotype in SCA17 has been well documented for small pathological expansions within the TBP gene [Chen et al. Clin Chim Acta 2010; 411:375-380] this family might be an example for broad phenotypic variation.

Discretionary Revisions:

Abstract, line 10: „Normally, repeats within in this range show... delete “in”

Page 5, line 3: “ Interestingly, he has a very severe cognitive impairment with very rapid...“ delete “very” (twice)

Page 7, line 10: “On the contrary, he was smiling...” write: In contrast, he was...

Page 8, line 20: “farther” (typo)

Page 9, line 1: “Here we report a patient...” please write: Here we report on a...
Page 9, line 2: “…cognitive impairment and very rapid progression,…” delete “very”,
additionally delete it in “Discussion” (page 9, line 17, page 10 lines 2, 4, and 9)

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**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.