

Letter to the Editor

Atypical parkinsonism and SCA8

We read with great interest the paper by Baba et al. [1] reporting a sporadic case of SCA8 mutation mimicking corticobasal degeneration (CBD). The patient presented in this report featured several clues to the diagnosis of CBD including frankly asymmetrical levodopa unresponsive parkinsonism, apraxia, alien hand sign, dystonia, and a rapid disease progression. Although early prominent ataxia is not typical, this patient fulfills research criteria for CBD with the caveat that there are no fully validated guidelines for clinical diagnosis of this condition. However, after molecular genetic analysis showed a combined 82 CTA/CTG heterozygous expansion at the SCA8 locus, the authors assume that, although pathological confirmation is missing, this is the first SCA8 patient reported in the literature with a phenotype mimicking CBD.

In fact, both CTA and CTG tracts have been shown to be polymorphic implying that CTA/CTG expansions at the SCA8 locus may be rare polymorphisms with a clinical significance that remains to be determined [2]. We have recently completed an ataxia genetic panel in six patients with diagnosis of probable cerebellar multiple system atrophy (MSA-C), according to the Consensus Committee [3] [late onset sporadic ataxia (mean age of onset 53, 47–62, 3 female) with early dysautonomia (orthostatic hypotension and/or urinary incontinence); two had corticospinal tract dysfunction] followed for at least 5 five years at the Movement Disorders Unit, Hospital de Clínicas of the Federal University of Paraná (Curitiba, Brazil). Five of the patients analyzed had normal alleles at the SCA8 locus with 20–25 CTA/CTG repeats, and, to our surprise, one female patient showed an expansion of 76 repeats, in the same range as the one reported in the Baba et al. patient. Of interest, our patient had typical REM sleep behavior disorder, no corticospinal tract dysfunction and no particular feature that could be distinguished from the remaining MSA-C cases.

The authors discuss several atypical phenotypes described in the literature for sporadic and familial SCA8 cases including pure parkinsonism, dystonia, sensory deficits, incontinence, psychiatric symptoms, deafness, oculomotor deficits and amyotrophy [1]. From

a different perspective, however, SCA8 expansions may be present in normal subjects as well as in patients with Lafora disease [3], levodopa responsive Parkinson's disease [4], Alzheimer's disease [5,6], in addition to genetically proven SCA 1, 2, 6 and Friedreich's ataxia [6–8]. Perhaps the most striking of such 'false positive' SCA8 gene testing is the one published recently by Factor et al. [9] describing a pathologically confirmed case of MSA-C with 145 CTA/CTG repeats in the SCA allele, published concomitantly with the paper that motivated this letter [1]. To our knowledge, ours is the second case of MSA with such an expansion with the caveat that pathological confirmation is still pending in our case.

In light of these and other observations, the association between SCA8 repeat expansions and sporadic, heterogeneous phenotypes has become debatable and should be interpreted with caution. Our personal conclusion is that until the relationship between CTA/CTG repeat expansions and a clinical syndrome has become clear, such testing in patients with atypical sporadic phenotypes may become a source of diagnostic confusion. Moreover, clinicopathologic correlation studies as well as objective demonstration of a pathogenic role for SCA8 expansions in atypical cases should be performed before testing for SCA8 is recommended in clinical settings.

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Renato P. Munhoz^{ab*}, Hélio A. Teive^a, Salmo Raskin^c,
André R. Troiano^{ad}

^a*Department of Neurology, Hospital de Clínicas, Federal University of Paraná, Curitiba, PR, Brazil*

^b*Department of Neurology, Pontifical Catholic University of Paraná, Curitiba, PR, Brazil*

^c*Genetika Laboratory, Curitiba, PR, Brazil*

^d*Pacific Parkinson's Research Centre, University of British Columbia, Vancouver Hospital and Health Sciences Centre, Vancouver, BC, Canada*

E-mail address: renatopuppi@yahoo.com

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* Corresponding author. Travessa Lange, 225, 1201, Curitiba, PR 80240-170, Brazil. Tel.: +55 41 3244 4483; fax: +55 41 3244 4483..