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Machado Joseph's Disease in a Togolese Family: A Case Report

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Abstract: Spinocerebellar ataxias (SCAs) are rare neurodegenerative disorders of adults characterized by autosomal dominant inheritance. Machado-Joseph disease (MJD) or ASC type 3 is the most common worldwide. We report the first cases of MJD in a Togolese family. We performed a cross-sectional study based on a case of MMJ disease confirmed by genetic testing. We then conducted a family survey to identify suspected familial cases of the disease. The confirmed case was a 46 year old Togolese woman of Ewe ethnicity (south of Togo), hypertensive, who was seen in consultation for speech and walking disorders that had been progressively worsening for 9 years and had been confined to a wheelchair for 3 years. In the family history, we noted similar cases without a precise diagnosis. On examination, we noted cerebellar dysarthria, difficulties in performing calculations, spastic tetraparesis at 4/5, kinetic and static ataxia. Brain magnetic resonance imaging showed cerebral atrophy more marked in the posterior fossa. Genetic analysis revealed the presence of an expanded allele located in the pathological zone at the ASC3 locus, which confirmed the diagnosis. The family investigation allowed us to identify six suspected cases on clinical grounds. This observation confirms the ubiquitous nature of MJD. The existence of a family history of gait disorders in a patient with cerebellar ataxia should raise the possibility of ASC.

Keywords: Spinocerebellar Atrophy, Machado Joseph, Togo, Case Report

1. Introduction

Spinocerebellar ataxias (SCAs) are a heterogeneous group of autosomal dominant neurodegenerative disorders sharing a common feature of cerebellar ataxia. Several ASCs are caused by extensions of repeated cytosine-adenine-guanine trinucleotide within coding regions of unrelated genes, translated into neurotoxic polyglutamine (polyQ) containing proteins [1]. Machado-Joseph disease (MJD) or ASC type 3 (ASC3), whose gene is located on chromosome 14q32.1 [2], is the most common ASC in the world [3, 4].

Globally, SCAs are considered rare disorders, with prevalence estimates varying from 0.3 to 2.0 per 100,000 [5]. Among SCAs, the relative frequency of MJD is higher in countries such as Brazil (69-92%) [6, 7], Portugal (58-74%) [8, 9], Singapore (53%) [10], China (48-49%) [11, 12], the Netherlands (44%) [13], Germany (42%) [14], and Japan (28-63%) [15, 16]. It is relatively less frequent in Canada (24%) [17], United States (21%) [18], Mexico (12%) [19], Australia (12%) [20], and India (5-14%) [21, 22]. In Africa, very few studies have been conducted on ASCs in general and MJD in particular, but the condition has been found in some families in sub-Saharan African (SSA) countries [23-25]. We report the history of MJD in a Togolese family, one of whose members is the first documented case of the disease in Togo, a West African country.

2. Patients

This is a cross-sectional study of a case of MJD confirmed by genetic testing. The clinical observation included information on the history, clinical, paraclinical and evolutionary aspects of the disease. We then conducted a family survey to identify familial cases with clinical expression of the disease.

A 47 year old Togolese patient of Akposso origin (south of Togo) born and residing in Togo, a bank employee, was brought by her brother to a consultation for an umpteenth opinion on walking and language disorders that had been evolving for about nine years. At the beginning, her walking was jerky with difficulties in articulating that appeared at almost the same time. Gradually the problems worsened and six years later she can only walk with the help of a walker. The patient reported frequent nightmares and sleep disturbances that could suggest sleep apnoea syndrome, but also muscle cramps throughout the body, most frequently in the right calf. No cognitive impairment was noted, as the patient continued to work in her profession. She had received several treatments including a lumbar laminectomy for gait disorders without success. Her personal history included presbyopia treated with corrective lenses and hypertension since 2017 treated with amlodipine 5 mg/day. There are reports of similar cases in the paternal family, with the great-grandmother being the first person in whom these disorders had been noted. This led to the grandmother being labelled a witch who had committed a sacrilege, the repercussions of which would continue in the descendants. Numerous consultations with charlatans to ward off the spell were unsuccessful. It was in this context that the patient's brother convinced her to make a final attempt to find a medical cause in order to disprove the thesis of sacrilege that has plagued their family for decades. On examination on 17 November 2018, we noted normal consciousness, cerebellar dysarthria, statokinetic ataxia, difficulties in performing calculations (MMS score is 27/30: calculation 0/3), and tetra pyramidal syndrome with facial diplegia. The examination of the cranial pairs was normal. The rest of the somatic examination was normal. Brain magnetic resonance imaging (MRI) on 17 November 2018 showed more marked brain atrophy in the posterior fossa (figure 1). Standard blood work was normal. Genetic analysis performed on 23 January 2019 revealed the presence of an expanded allele located in the pathological area at the ASC3 locus; this result provides molecular confirmation of the ASC3 diagnosis.

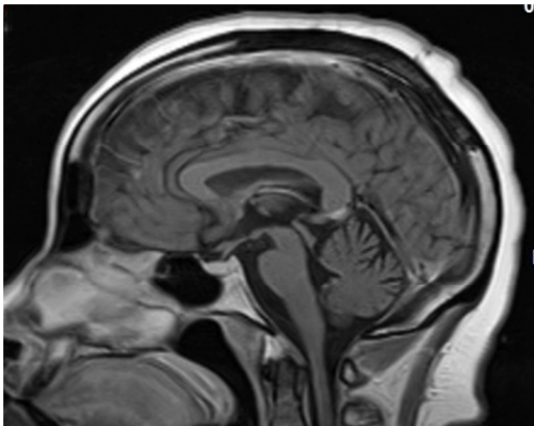

Figure 1. *Brain MRI showing cerebellar atrophy.*

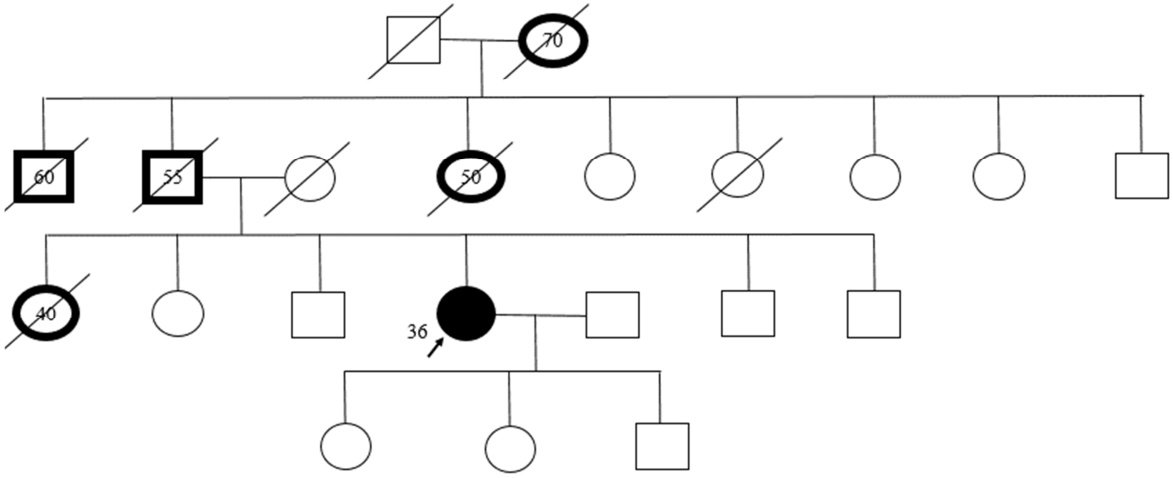

Figure 2. *Pedigree structure of the Togolese family affected with Machado–Joseph disease. Filled symbols designate patient with MJD, and those partially-filled represent patients not observed (affected by history only). Numbers represent the age (years) of onset symptoms.*

The family investigation was carried out by interviewing the patient and her brother. We noted six members of this family, four of whom were women with clinical manifestations of the disease (Figure 2). The common symptomatology was an ataxia probably of cerebellar origin. The age of onset was estimated at 70 years in the first generation, between 50 and 60 years in the second generation and between 36 and 40 years in the last generation. The other members did not want to undergo preclinical genetic testing after discussion with the whole family, including the patient's brother who had pushed her to the consultation and genetic testing. Reasons for refusal included inaccessibility of the test and lack of therapeutic implication to make a preclinical diagnosis.

3. Discussion

We conducted a cross-sectional study of a confirmed case of MJD. The family investigation of this confirmed case was incomplete. Indeed, it was not possible to obtain a detailed clinical description and brain imaging in the suspected family members. Similarly, we were unable to perform separate molecular tests on the confirmed case due to their high cost. This cost constraint contributes to the delay in diagnosis in this family where the diagnosis was only established in a third generation member despite the hereditary nature of this condition being recognised for three decades. Although hereditary, MJD is highly pleiomorphic, not only in the variability of age of onset but also in the heterogeneity of symptoms. In this family, on the basis of clinical arguments including the age of onset of symptoms, we are witnessing the appearance of types II and III of the classification of Coutinho and al. corresponding to the Machado type [26]. The Machado lineage, or G-G-C haplotype, appeared 2000 years ago and is most prevalent in Portugal. The Azores and other families of confirmed or presumed Portuguese ancestry and most likely of Portuguese origin [24]. The presence of MJD in Africa is thought to be linked to Portuguese maritime voyages in the late 15th and 16th centuries, along the Portuguese slave trade routes [26]. The mean age of onset in our study corresponded to the mean age of type III, the second most common type. Our patient had the characteristics of type II, the most common type [26]. MJD is also a late-onset neurogenetic disorder, an incurable condition whose preclinical diagnosis has no therapeutic implications in the light of our current knowledge. The preclinical diagnosis of these neurogenetic conditions is subject to severe psychosocial consequences [27]. All other living family members who have not yet developed the disease are likely to carry the pathological genes, as we have noted cases in this family occurring in later life. Only genetic screening will allow the diagnosis of members carrying the pathological gene.

4. Conclusion

Machado Joseph disease has been found on all continents with very variable frequencies and our observation confirms this ubiquitous character of this disease. The difficult access to neurogenetic testing in sub-Saharan Africa may contribute to the rarity of the reported cases. The existence of a family history of gait disorder in a patient presenting a cerebellar ataxia must lead to the evocation of a spinocerebellar ataxia.

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Kumako, Waklatsi and Apetse followed the patient and designed the manuscript. The other authors participated in the revision of the manuscript.

Consent

Consent was obtained for publication.

References

[1] Bird TD. Overview of hereditary ataxia. 1998 Oct 28 [updated 2019 Jul 25]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. Gene Reviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. PMID: 20301317.

[2] Takiyama Y, Nishizawa M, Tanaka H, Kawashima S, Sakamoto H, Karube Y, Shimazaki H, Soutome M, Endo K, Ohta S, et al. The gene for Machado-Joseph disease maps to human chromosome 14q. Nat Genet. 1993; 4 (3): 300-4. doi: 10.1038/ng0793-300. PMID: 8358439.

[3] Kieling C, Prestes PR, Saraiva-Pereira ML, Jardim LB. Survival estimates for patients with Machado-Joseph disease (SCA3). Clin Genet. 2007; 72 (6): 543-5. doi: 10.1111/j.1399-0004.2007.00910.x. Epub 2007 Sep 25. PMID: 17894834.

[4] Sequeiros J, Coutinho P. Epidemiology and clinical aspects of Machado-Joseph disease. Adv Neurol. 1993; 61: 139-53. PMID: 8421964.

[5] van de Warrenburg BP, Sinke RJ, Verschuuren-Bemelmans CC, Scheffer H, Brunt ER, Ippel PF, Maat-Kievit JA, Dooijes D, Notermans NC, Lindhout D, et al: Spinocerebellar ataxias in the Netherlands: prevalence and age at onset variance analysis. Neurology 2002, 58 (5): 702-708.

[6] Schols L, Bauer P, Schmidt T, Schulte T, Riess O: Autosomal dominant cerebellar ataxias: clinical features, genetics, and pathogenesis. Lancet Neurol 2004, 3 (5): 291-304.

[7] Teive HA, Munhoz RP, Raskin S, Werneck LC: Spinocerebellar ataxia type 6 in Brazil. Arq Neuropsiquiatr 2008, 66 (3B): 691-694.

[8] Jardim LB, Silveira I, Pereira ML, Ferro A, Alonso I, do Ceu Moreira M, Mendonca P, Ferreirinha F, Sequeiros J, Giugliani R: A survey of spinocerebellar ataxia in South Brazil - 66 new cases with Machado-Joseph disease, SCA7, SCA8, or unidentified disease-causing mutations. J Neurol 2001, 248 (10): 870-876.

[9] Vale J, Bugalho P, Silveira I, Sequeiros J, Guimaraes J, Coutinho P: Autosomal dominant cerebellar ataxia: frequency analysis and clinical characterization of 45 families from Portugal. Eur J Neurol 2010, 17 (1): 124-8.

[10] Silveira I, Coutinho P, Maciel P, Gaspar C, Hayes S, Dias A, Guimaraes J, Loureiro L, Sequeiros J, Rouleau GA: Analysis of SCA1, DRPLA, MJD, SCA2, and SCA6 CAG repeats in 48 Portuguese ataxia families. Am J Med Genet 1998, 81 (2): 134-138.

[11] Zhao Y, Tan EK, Law HY, Yoon CS, Wong MC, Ng I: Prevalence and ethnic differences of autosomal-dominant cerebellar ataxia in Singapore. Clin Genet 2002, 62 (6): 478-481.

[12] Tang B, Liu C, Shen L, Dai H, Pan Q, Jing L, Ouyang S, Xia J: Frequency of SCA1, SCA2, SCA3/MJD, SCA6, SCA7, and DRPLA CAG trinucleotide repeat expansion in patients with hereditary spinocerebellar ataxia from Chinese kindreds. Arch Neurol 2000, 57 (4): 540-544.

[13] Jiang H, Tang BS, Xu B, Zhao GH, Shen L, Tang JG, Li QH, Xia K: Frequency analysis of autosomal dominant spinocerebellar ataxias in mainland Chinese patients and clinical and molecular characterization of spinocerebellar ataxia type 6. Chin Med J (Engl) 2005, 18 (10): 837-843.

[14] Schols L, Amoiridis G, Buttner T, Przuntek H, Epplen JT, Riess O: Autosomal dominant cerebellar ataxia: phenotypic differences in genetically defined subtypes? Ann Neurol 1997, 42 (6): 924-932.

[15] Maruyama H, Izumi Y, Morino H, Oda M, Toji H, Nakamura S, Kawakami H: Difference in disease-free survival curve and regional distribution according to subtype of pinocerebellar ataxia: a study of 1,286 Japanese patients. Am J Med Genet 2002, 114 (5): 578-583.

[16] Shibata-Hamaguchi A, Ishida C, Iwasa K, Yamada M: Prevalence of spinocerebellar degenerations in the Hokuriku district in Japan. Neuroepidemiology 2009, 32 (3): 176-183.

[17] Kraft S, Furtado S, Ranawaya R, Parboosingh J, Bleoo S, McElligott K, Bridge P, Spacey S, Das S, Suchowersky O: Adult onset spinocerebellar ataxia in a Canadian movement disorders clinic. Can J Neurol Sci 2005, 32 (4): 450-458.

[18] Moseley ML, Benzow KA, Schut LJ, Bird TD, Gomez CM, Barkhaus PE, Blindauer KA, Labuda M, Pandolfo M, Koob MD, et al: Incidence of dominant spinocerebellar and Friedreich triplet repeats among 361 ataxia families. Neurology 1998, 51 (6): 1666-1671.

[19] Alonso E, Martinez-Ruano L, De Biase I, Mader C, Ochoa A, Yescas P, Gutierrez R, White M, Ruano L, Fragoso-Benitez M, et al: Distinct distribution of autosomal dominant spinocerebellar ataxia in the Mexican population. Mov Disord 2007, 22 (7): 1050-1053.

[20] Storey E, du Sart D, Shaw JH, Lorentzos P, Kelly L, McKinley Gardner RJ, Forrest SM, Biros I, Nicholson GA: Frequency of spinocerebellar ataxia types 1, 2, 3, 6, and 7 in Australian patients with spinocerebellar ataxia. Am J Med Genet 2000, 95 (4): 351-357.

[21] Saleem Q, Choudhry S, Mukerji M, Bashyam L, Padma MV, Chakravarthy A, Maheshwari MC, Jain S, Brahmachari SK: Molecular analysis of autosomal dominant hereditary ataxias in the Indian population: high frequency of SCA2 and evidence for a common founder mutation. Hum Genet 2000, 106 (2): 179-187.

[22] Krishna N, Mohan S, Yashavantha BS, Rammurthy A, Kiran Kumar HB, Mittal U, Tyagi S, Mukerji M, Jain S, Pal PK, et al: SCA1, SCA2 & SCA3/ MJD mutations in ataxia syndromes in southern India. Indian J Med Res 2007, 126 (5): 465-470.

[23] Almaguer-Mederos LE, Sarr L, Abascal JV, Aguilera-Rodríquez R, Martín MA, Khalil MI, Al-Jafari MA, de Jorge López L, Volpini V, Nyan O. Spinocerebellar ataxia type 2 in The Gambia: A case report. J Neurol Sci. 2015; 349 (1-2): 269-71. doi: 10.1016/j.jns.2015.01.027. Epub 2015 Jan 28. PMID: 25649479.

[24] Ogun SA, Martins S, Adebayo PB, Dawodu CO, Sequeiros J, Finkel MF. Machado-Joseph disease in a Nigerian family: mutational origin and review of the literature. Eur J Hum Genet. 2015; 23 (2): 271-3. doi: 10.1038/ejhg.2014.77. Epub 2014 Apr 30. PMID: 24781759; PMCID: PMC4297905.

[25] Ramesar RS, Bardien S, Beighton P, Bryer A. Expanded CAG repeats in spinocerebellar ataxia (SCA1) segregate with distinct haplotypes in South African families. Hum Genet. 1997; 100 (1): 131-7. doi: 10.1007/s004390050478. PMID: 9225982.

[26] Mendonça N, França MC Jr, Gonçalves AF, Januário C. Clinical features of Machado-Joseph disease. Adv Exp Med Biol. 2018; 1049: 255-273. doi: 10.1007/978-3-319-71779-1_13. PMID: 29427108.

[27] Mendes Á, Paneque M, Clarke A, Sequeiros J. Choosing not to know: accounts of non-engagement with pre-symptomatic testing for Machado-Joseph disease. Eur J Hum Genet. 2019; 27 (3): 353-359. doi: 10.1038/s41431-018-0308-y. Epub 2018 Dec 20. PMID: 30573801; PMCID: PMC6460576.