Parkinsonism and Related Disorders 20 (2014) 568–569

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Letter to the Editor

Pure ataxia associated with N-methyl-D-aspartate receptor antibodies

Keywords:
Autoimmune
Movement disorders
Anti-NMDA-receptor antibodies
Encephalitis
Ataxia

Dear Sirs

Several movement disorders previously considered idiopathic or degenerative are now recognized as immune-mediated [1]. The N-methyl-D-aspartate receptor antibody (NMDAr) encephalitis has been associated with movement disorders, frequently hyperkinetic, namely chorea, dystonia and ballism. Pure monosymptomatic syndromes occur in less than 5% of the patients [2]. Ataxia is not typical in the setting of anti-NMDAr encephalitis but some cases have been reported [3]. However, in these cases, ataxia was always associated with other typical manifestations of NMDAr syndrome [3].

A 73 year-old missionary priest, caucasian, resident in Mozambique, presented with fever, anorexia and cough lasting for two weeks. He was treated with gentamicin, azithromycin and metronidazole for seven days with complete remission of complaints. Three days after completion of antimicrobials he started a rapidly progressive gait disturbance becoming wheel-chair bound within another three days.

The neurological examination showed a slight bilateral horizontal gaze-evoked nystagmus, bilateral appendicular ataxia of upper and lower limbs, cerebellar ataxic gait and loss of postural reflexes. Changes of mood, behaviour or personality, insomnia, autonomic instability, hypoventilation, hyperkinesias or decreased level of consciousness were absent. Cerebrospinal fluid analysis including DNA search for neurotropic virus by PCR was unremarkable. Brain MRI was normal. The titer of anti-NMDAr antibodies in serum was high (1/1000), while infectious serologies (including Epstein–Barr virus, Varicella zoster virus, Mycoplasma and Human immunodeficiency virus), other autoimmunity studies and search for occult neoplasm (thoracic, abdominal and pelvic CT, upper gastrointestinal endoscopy, colonoscopy, bone scintigraphy and positron emission tomography scan) were negative. Remarkable clinical improvement followed treatment with 1 g of methylprednisolone for 5 days, with complete remission of ataxia within 3 months and reduction of anti-NMDAr titer in serum to 1/320. The patient remains asymptomatic after 18 months.

In previously reported cases of NMDAr encephalitis with dyskinesias, it was proposed that anti-NMDAr antibodies interrupt forebrain corticostriatal input, blocking tonic inhibition of brainstem pattern generators, thus releasing primitive patterns of bulbar and limb movement [4]. Concerning ataxia, several studies have also indicated that impaired glutamate signalling may be involved in the pathophysiology of cerebellar ataxia and antagonists for the NMDA glutamate type receptor, such as phencyclidine and dizocilpine, are known to cause it in humans and experimental animals [5]. Likewise, D-cycloserine, a partial NMDA allosteric agonist, may improve ataxia.

To our knowledge, this is the first report of an association between isolated ataxia and anti-NMDAr antibodies, extending the clinical spectrum of anti-NMDA syndromes. The remission of the severe and rapidly progressive ataxia associated with a marked reduction in the titer of anti-NMDAr supports a pathogenic role of these antibodies in a presumably post-infectious setting. This case also raises the possibility that, in some cases, post-infectious ataxia may be related to the presence of anti-NMDAr antibodies. This hypothesis arises from the fact that our patient had an excellent clinical outcome using only a very short and simple therapeutic regimen, suggesting that a self-limiting course could have happened in the absence of immunotherapy. As the usual clinical course of post-infectious ataxia is self-limiting, at least a subset may be due to a mild form of NMDAr encephalitis. Early recognition of a possible anti-NMDA disorder underling acute/sub-acute ataxia is critically important as immunotherapy can be effective.

Statements

The authors certify that they have no commercial associations that may pose a conflict of interest in connection with the submitted article.

Ethical standard

The work submitted in the manuscript is original and has not been published elsewhere. All people who have a right to be recognised as authors have been included on the list of authors and everyone listed as an author has made an independent material contribution to the manuscript.

References

[1] Panzer J, Dalmau J. Movement disorders in paraneoplastic and autoimmune disease. Curr Opin Neurol 2011 Aug;24(4):346–53.

http://dx.doi.org/10.1016/j.parkreldis.2014.02.015
1353-8020/

[2] Dalmau J, Gleichman AJ, Hughes EG, Rossi JE, Peng X, Lai M, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. Lancet Neurol 2008 Dec;7(12):1091–8.
[3] Baizabal-Carvallo JF, Stocco A, Muscal E, Jankovic J. The spectrum of movement disorders in children with anti-NMDA receptor encephalitis. Mov Disord 2013 Apr;28(4):543–7.
[4] Kleinig TJ, Thompson PD, Matar W, Duggins A, Kimber TE, Morris JG, et al. The distinctive movement disorder of ovarian teratoma-associated encephalitis. Mov Disord 2008 Jul 15;23(9):1256–61.
[5] Tanii Y, Nishikawa T, Hashimoto A, Takahashi K. Stereoselective antagonism by enantiomers of alanine and serine of phencyclidine-induced hyperactivity, stereotypy and ataxia in the rat. J Pharmacol Exp Ther 1994;269(3):1040–8.

Diana Aguiar de Sousa*, Patrícia Pita Lobo, Ana Castro Caldas, Miguel Coelho, Luísa Albuquerque
Department of Neurology,
Hospital de Santa Maria, University of Lisbon,
Avenida Professor Egas Moniz, 1649-035 Lisbon, Portugal

* Corresponding author. Tel.: +351 217957474, +351 965734868; fax: +351 217957474.
E-mail addresses: diana3543@hotmail.com, dianasousa@icloud.com (D. Aguiar de Sousa).

17 November 2013