Neurología. 2011;**26(5)**:307-318

NEUROLOGÍA

www.elsevier.es/neurologia

## LETTERS TO THE EDITOR

# A cyanocobalamin def ciency that simulates Creutzfeldt-Jakob disease

## Déf cit de cianocobalamina que simula una enfermedad de Creutzfeldt-Jakob

*Dear Editor:*

Creutzfeldt-Jakob Disease (CJD) is a prionic encephalopathy with a variable combination of dementia, ataxia, myoclonia and pyramidal and extrapyramidal signs. P rionic diseases may present sporadically , within a family group, or be acquired. Sporadic forms of transmissible spongiform encephalopathies (TSE) represent 85% of cases and include sporadic Creutzfeldt-Jakob disease (sCJD) and sporadic fatal insomnia. Familial or genetically determined TSE represent 10-15% of cases and comprise familial Creutzfeldt-Jakob disease (fCJD), familial fatal insomnia and Gerstmann-Scheinker disease. Acquired TSE (< 5% of cases) include kuru, iatrogenic Creutzfeldt-Jakob disease and variant Creutzfeldt-Jakob disease (vCJD). [1] the diagnostic gold standard for prionic diseases is the pathology study . The classic histopathological signs of CJD are the loss of neurons, gliosis and vacuolization (previously referred to as spongiform changes), and it is necessary to detect the scrapie prionic protein ($PrP^{Sc}$).[2] The current WHO criteria used for diagnosing Creutzfeldt-Jakob disease date from 2003.[3]

The medical literature describes clinical cases simulating CJD such s W ernicke's encephalopathy , progressive multifocal leukoencephalopathy, encephalopathy associated with CKGV antibodies, amyloid angiopathy , Hashimoto' s encephalopathy, Gerstmann-Sträussler-Scheinker syndrome, lithium-induced encephalopathy, cerebellar ataxia through anti-Gad antibodies, cerebral gliomatosis, carcinomatous meningitis and rapidly progressive Alzheimer's disease, among others (toxic substances, dietary shortcomings, metabolic, vascular , infectious, autoimmune, neoplastic, psychiatric, neurodegenerative disorders, etc.)[1]. We present a case of rapidly progressive dementia with pyramidal and extrapyramidal symptoms, mutism and ataxia due to a def cit of cyanocobalamine ($B_{12}$) which simulated a potential sCJD.

It involved a 64-year-old female with a history of intercostal zoster and a subsequent status of asthenia with weight loss over 2 years that have not been recorded despite several studies. She came to the clinic due to progressive cognitive impairment over a period of 2 months with loss of attention, disorientation, loss of f uency and she only carried out simple instructions. She presented dystonia in the neck (leftward wry neck) and arms, spastic paraparaesia with pyramidalism and ataxia in her legs. During the f rst few days after admission she progressed to being bedridden and unable to speak.

The electroencephalogram showed slow periodic waves and the cranial NMR shows hyperintensity in the basal nodes, bilateral in the medial and disseminated in the pulvinar thalamus with a diffusion-weighted sequence, as well as hyperintensity in the pyramidal and extrapyramidal route using T1, FLAIR and diffusion-weighted sequences (f gs. 1 and 2). The serology tests for hepatitis and HIV, anti-GAD, anti-Hu/Ma2, anti-neuronal, anti-thyroid antibodies, thyroid hormones and 14-3-3 protein were negative or normal. A def cit of vitamin $B_{12}$ (20 pg/mL, N < 223) was found and she had positive intrinsic anti-factor antibodies and high levels of gastrin. A gastric biopsy was performed and the result showed chronic gastritis in the body and antrum.

Treatment was started with cyanocobalamine with partial progressive remission, more signi f cant on the motor plane albeit also on the cognitive plane. The dystonia in her neck and shoulders disappeared completely with a reduction in the pain caused. She began to walk again although requiring bilateral assistance and with an ataxic gait (lateralizing to the right), as well as slight dissymmetry in the f nger-to-nose manoeuvre. From the cognitive perspective, she continued to show attention de f cit, disorientation in time and space and immediate memory failures. Her nomination improved (6/8 animals), as did her understanding of simple orders and the repetition of sentences. After 3 months of treatment she recovered her baseline situation without any sequelae in both the motor and the cognitive planes, and was able to maintain a normal conversation.

There are several sets of criteria for the clinical diagnosis of CJD such as the WHO criteria in force since 2003 and the Masters criteria.[3,4] The WHO criteria are probably the ones most commonly used [3] (table 1). The sensitivity and specif city f gures for the 14-3-3 protein detection test for diagnosing sCJD vary between 88-97% and 84-100%, respectively.[4] Detection of 14-3-3 may be negative in the early stages of the illness and become positive in subsequent phases; it is most useful when the results coincide with the clinical suspicion, in these cases achieving increases in the verisimilitude ratios in comparison with isolated clinical data.[5,6]

The Masters criteria require progressive dementia with 2 of the following: myoclonias, pyramidal, extrapyramidal or

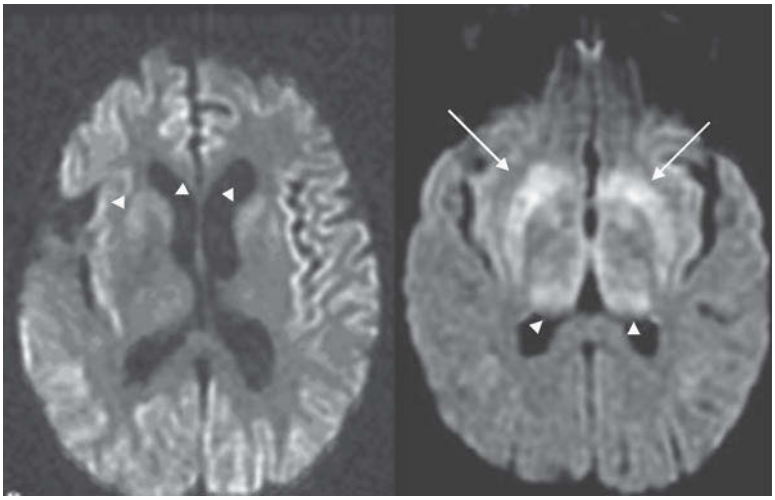

**Figure 1** Cranial NMR of our patient with hyperintensity in the basal nodes, bilateral in the medial and pulvinar thalamus with a diffusion-weighted sequence.

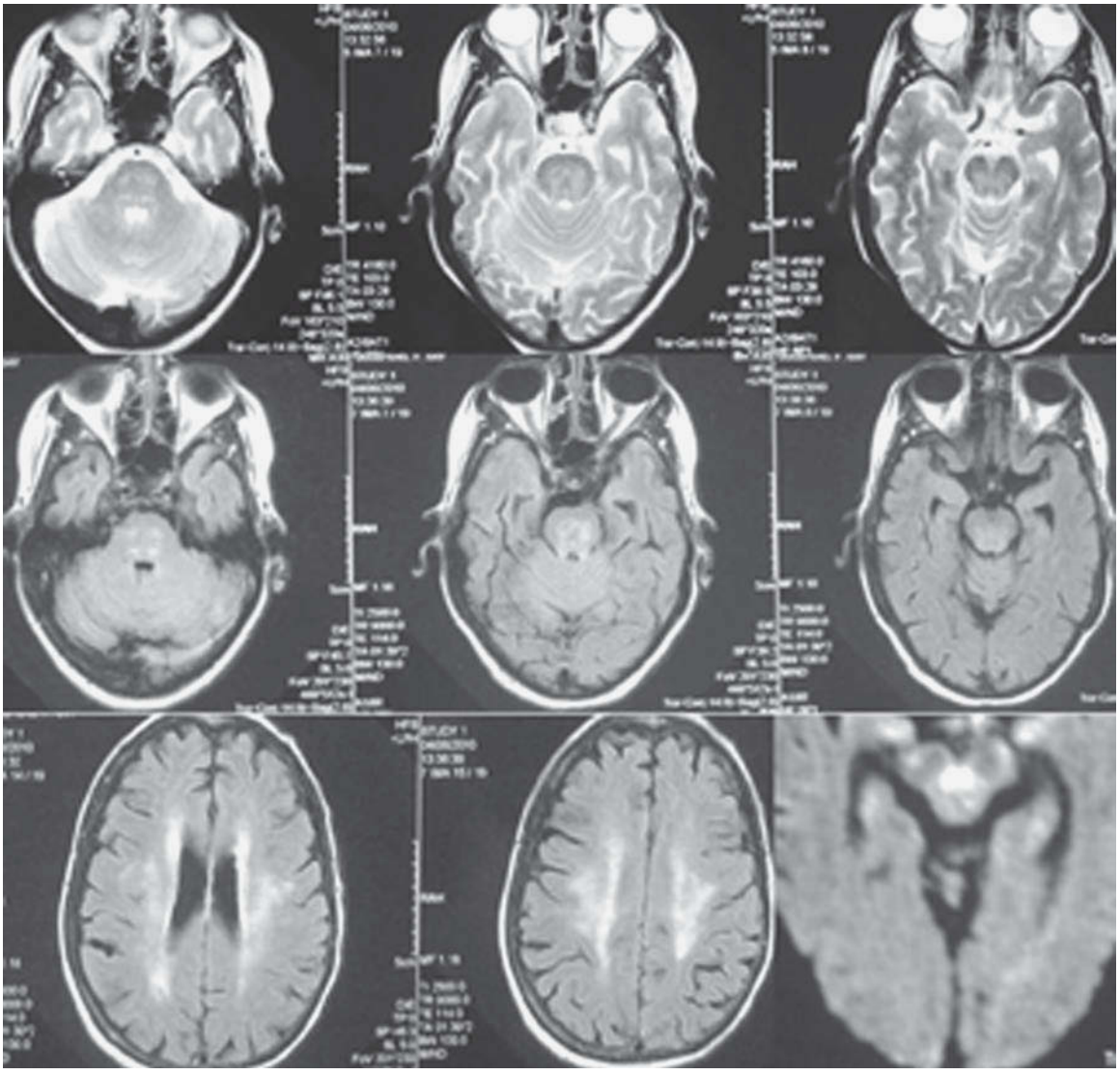

**Figure 2** NMR of our patient with hyperintensity on the pyramidal and extrapyramidal in T2 (top row), FLAIR and diffusion-weighted sequences (lower right row).

**Table 1** 2003 WHO Criteria (sporadic Creutzfeldt-Jakob disease)

*Potential sCJD*

Progressive dementia plus duration of less than 2 years plus other diagnosis suggested by other studies plus 2 or more of the following 4 indications:

1. Myoclonias
2. Visual or cerebellar signs or symptoms
3. Pyramidal or extrapyramidal signs or symptoms
4. Akinetic mutism

*Likely sCJD*

Potential sCJD plus at least one of the following criteria:

1. Periodic EEG complexes with any duration of the condition
2. Protein 14-3-3 in cases with survival less than 2 years

*Definitive CJD*

Confirmation by the pathology laboratory and/or the presence of protease-resistant PrP (immunohistochemistry or Western blot) and/or presence of fibres associated with scrapie (EM)

sCJD: sporadic Creutzfeldt-Jakob disease; EM: electron microscopy; PrP: prionic protein.

cerebellar symptoms and a typical EEG with regular focal epileptiform discharges at approximately 1 Hz or diffuse discharges.[7] The characteristic pattern of sCJD consists in periodic complexes that appear against a diffusely slowed background activity.[3] The sensitivity and specificity values for the diagnosis of sCJD vary between 58-67% and 74-91%, respectively.[5] Although the complexes usually have a generalized distribution, they may be limited in the initial phases to one hemisphere or even to one region.[8] The differential diagnosis of a CJD-type EEG pattern includes a variety of degenerative processes (Alzheimer's disease, dementia with Lewy's bodies), vascular processes (Binswanger's disease, anoxia), infectious processes (multiple abscesses, AIDS-related dementia, sub-acute sclerosing panencephalitis), toxic causes (ketamine, phencyclidine, baclofen, mianserin, metrizamide, lithium) and metabolic triggers (anoxic encephalopathy hyperammonaemia, MELAS). This pattern must also be differentiated from other periodic activities such as periodic lateralized epileptiform discharges and epileptic status.[1,9]

In addition, magnetic resonance imaging of the brain represents one of the greatest advances for the diagnosis of TSE in recent years.The characteristic findings of CJD consist in a signal hyperintensity located in the striate, the cerebral cortex or in both areas. Lesions may be unilateral or bilateral and seem to debut quite early on, even as little as 3 weeks after the onset of the symptoms. The sensitivity and specificity values for the diagnosis of sCJD using FLAIR and DWI sequences vary between 80-100% and 94-100%, respectively.[1] Cyanocobalamine deficit may translate into cognitive changes, affective disorders, combined sub-acute degeneration, peripheral neuropathy and optical atrophy, among others.[10]

In short, our patient met the WHO 2003 criteria for probable sCJD with a progressive dementia lasting less than 2 years, 3 out of 4 of the clinical criteria (cerebellar signs, pyramidal/extrapyramidal signs and symptoms and akinetic mutism) and, in addition, periodic complexes on the EEG.The determination of 14-3-3 was negative, the severe $B_{12}$ deficit and the clinical improvement following treatment changed the diagnosis. The cyanocobalamine deficit secondary to atrophic gastritis due to its clinical behaviour and electroencephalographic findings might occasionally simulate CJD.

## References


1. Jiménez Huete A, Guardado Santervás P, Valentí Soler M. Enfermedades priónicas. In: Molinuevo JL, Peña-Casanova J, editors. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Sociedad Española de Neurología. Barcelona: Thomson Reuters; 2009. p. 193-222.
2. Brown P, Cathala F, Castaigne P, Gajdused DC. Creutzfeldt-Jakob disease: clinical analysis of a consecutive series of 230 neuropathologically verified cases. Ann Neurol. 1986;20:597-602.
3. World Health Organization. WHO manual for surveillance for human spongiform transmissible encephalopathies including variant Creutzfeldt-Jakob disease. Available at: http://whqlibdoc.who.int/publications/2003/9241545887.pdf.
4. Brown P. Transmissible spongiform encephalopathy in the 21st century: neuroscience for the clinical neurologist. Neurology. 2008;70:713-22.
5. Sánchez-Juan P, Sánchez-Valle R, Green A, Ladogana A, Cuadrado-Corrales N, Mitrová E, et al. Influence of timing on CSF test value for Creutzfeldt-Jakob disease diagnosis. J Neurol. 2007;254:901-6.
6. Cuadrado-Corrales N, Jiménez-Huete A, Albo C, Hortigüela R, Vega L, Cerrato L, et al. Impact of the clinical context on the 14-3-3 test for the diagnosis of sporadic CJD. BMC Neurol. 2006;6:25.
7. Masters CL, Harris JO, Gajdusek DC, Gibbs CJ Jr, Bernoulli C, Asher DM. Creuzfeldt-Jakob disease: patterns of worldwide occurrence and the significance of familial and sporadic clustering. Ann Neurol. 1979;5:177–88.
8. Heye N, Cervós-Navarro J. Focal involvement and lateralization in Creutzfeldt-Jakob disease: correlation of clinical, electroencephalographic and neuropathological findings. Eur Neurol. 1992;32:289-92.
9. Au Wj, Gabor Aj, Vijayan N, Markand ON. Periodic lateralized epileptiform complexes (PLEDs) in Creutzfeldt-Jakob disease. Neurology. 1980;30:611-7.
10. Reynolds E. Vitamin B12, folic acid, and the nervous system. Lancet Neurol. 2006;5:949-60.



M. Payán Ortiz,* J. Martinez Simón, P. Guardado Santervás, P. Quiroga Subirana

*Unidad de Neurología Clínica y Diagnóstica, Complejo Hospitalario Torrecárdenas, Almería, Spain*

* Corresponding author.
*E-mail:* payanortiz@hotmail.com (M. Payán Ortiz).