



Creutzfeldt-Jakob Disease

Valerio Massimo Magro

ABSTRACT

Creutzfeldt-Jakob disease is the most common human prion pathology. We describe is emblematic of this disease in its form of onset and progression. We have reported the symptoms and the diagnostic possibilities: a 82 years old man accused suddenly confusion, agitation, memory impairment with rapid progression of cognitive decline and psychiatric signs and the appearance of other neurological deficits that led the patient quickly to coma leading to death. The pathological examination clarified the nature of patient's medical and it allowed players to make the diagnosis.

Key words: General practitioner, dementia, Creutzfeldt-Jakob disease

Creutzfeldt-Jakob Hastalığı

ÖZET

Creutzfeldt-Jakob hastalığı en yaygın insan prion patolojidir. Biz bu olgu sunumunda hastalığın başlangıcı ve ilerlemesini sembolik olarak sunduk. Biz hastanın semptom ve tanısal işlemlerini bildirdik. Bunlar; ani gelişen konfüzyon ile gelen 82 yaşında erkek hasta, ajitasyon, kognitif bozulma ile birlikte hafıza bozukluğu, psikiyatrik belirtiler ve ölüme neden olacak koma ya götürecek nörolojik defisitlerin bulunması. Patolojik inceleme ile hastanın tanısı konuldu.

Anahtar kelimeler: Pratisyen hekim, demans, Creutzfeldt-Jakob hastalığı

INTRODUCTION

Creutzfeldt-Jakob disease is a rare cause of dementia evolving fatal even more rarely it is observed on the Italian territory. A case related is observed in a General Practitioner's (GP) study (1).

CASE

Male patient. He was 82 years old. He emigrated young in a country in Eastern Europe in search of work and then he had lived for a long time in Romania. He was back in Italy for few months with plans to live there the rest of his life and he had established residence in Rome (he had a cottage country) for some time. In early February, it occurred the appearance of confusion, agitation, memory

impairment. The patient's general condition seemed fair. His vital signs were as follows: GCS 14 (E4V4M6), blood pressure 130/80 mm Hg, cardiac rhythm activity with a ventricular rate of 70 bpm, body temperature 36.1 ° C, respiratory rate 21 respiratory acts for minute, SpO2 98% on ambient air, HGT 92 mg/dl. Cincinnati Pre-Hospital Stroke Scale was negative. It performed the Mini Mental State Examination (MMNE) with a total score of 23/30. The Geriatric Depression Scale (GDS) and Hachinsky Ischemic Score were not executable. ADL and IADL were not evaluated. Clinical objectivity would not show any significant finding. Biochemical and haematological investigations were normal and chest X-ray did not show pulmonary opacities.

Doctor formed in Medical General Practice, Rome, Italy

Correspondence: Valerio Massimo Magro
Doctor formed in Medical General Practice, Rome, Italy
Correspondence to valerio_magro@hotmail.com

Received: 08.12.2012, Accepted: 27.11.2013

DISCUSSION

The MMSE indicated the presence of a mild cognitive impairment. Dementia, however, has a very diverse etiology, or degenerative primary or secondary (vascular dementia, normotensive hydrocephalia, endocrine and metabolic disorders, poisoning, deficiency states, intracranial infectious-inflammatory expansive processes, etc.). In turn, degenerative disease may be cortical (Alzheimer's disease, fronto-temporal dementia) or sub-cortical (dementia with Lewy bodies, Parkinson's dementia, corticobasal degeneration, etc..) (1). All these forms are characterized by similar symptoms (decline in cognitive performance and/or significant behavioral disturbances), with a highly variable course individually, however. The GP can put the suspected diagnosis through simple questions designed to discover amnesia, apraxia, agnosia, acalculia, depression, etc.. He can also take advantage of quick and easy tools for cognitive (MMSE (2-4), Short Portable Mental Status Questionnaire or SPMSQ (5,6), Hachinsky Ischemic Score (7) and behavioral (the Geriatric Depression Scale or GDS) assessment, also available in some software management of General Practice. Then the management includes some blood tests (complete blood count, blood glucose, electrolytes, renal function, liver and thyroid dose of vitamin B12 and folate) and the use of suitable means of imaging (brain computerized tomography and/or magnetic resonance imaging - MRI). Blood tests were to exclude potentially reversible forms of dementia that have an acute onset mimicking Creutzfeldt-Jakob disease: auto-immune disorders such as infections and metabolic or electrolytes imbalances (8). Then, a diagnosis of "possible Creutzfeldt-Jakob disease" must take into account the differentiation with other diseases such as Alzheimer's disease, vascular dementia and dementia with Lewy bodies (9). The clinical characteristics of the patient (acute onset of symptoms and characteristics, absence of a previous diagnosis of Parkinson's disease) tended to exclude other forms of dementia such as Alzheimer's disease, vascular dementia and Parkinson-dementia), while it was more difficult the exclusion of dementia with Lewy bodies (10) or Hashimoto's encephalopathy (although thyroid function was normal and there was the absence of antibodies anti-TPO) (11,12). For these reasons it was decided to prescribe to the patient an EEG and a brain MRI (13-15).

The subsequent rapid progression of the patient's medical and cognitive impairment (GCS 11 E3V3M5; MMSE 16) prevented them from completing the diagnostic process,

unfortunately. At the end of February, the patient appeared agitated, with a marked spatial and temporal disorientation, aphasia, reported unspecified visual disturbances and myoclonus. It was impossible to organize the implementation of RM and we predisposed hospitalization. At the beginning of March, the patient showed a state of progressively worsening dementia, aphasia, decreased level of alertness, sporadic myoclonus spread. The degree of drowsiness was increasing over time until reaching the coma. The EEG showed triphasic periodic complexes in the terminal phase. The exitus occurred at about 3 months after onset of symptoms.

Then it was asked to review neuropathological brain tissue, on the left half of cerebellum and on the brainstem, fixed in formalin. The same parts of the right cerebral hemisphere were frozen and stored at 80 °C. The macroscopic examination highlighted the left cerebral hemisphere with normal configuration, with smooth and transparent leptomeninges and cortical convolutions within normal limits. We found no areas of discoloration or softening. There were no signs of uncal or the cingulate gyrus herniation. The blood vessels examined showed a normal configuration and mild atherosclerosis. After coronal section it was highlighted the presence of mild atrophy at the level of the cerebral cortex. The ventricular system did not appear neither deformed nor dilated. The semi-oval center was normal, while hippocampus and amygdala showed mild atrophy. Thalamus and basal ganglia appeared microscopically safe. The cross sections of the brain stem revealed no significant lesions. The locus coeruleus and substantia nigra showed normal pigmentation. The cerebellum showed no significant atrophy. It was examined frontal, temporal, parietal, occipital, striatum, pons, medulla oblongata and cerebellum histological sections, finding evidence of spongiform degeneration and neuronal loss with proliferation and activation of glial cells, and presence of sparse amyloid plaques. The research of the prion protein (PrP^{Sc}) with Western Blot of brain tissue gave positive results, confirming the diagnosis of transmissible spongiform encephalopathy.

The electrophoretic migration patterns and the pattern of glycosylation of the protein were consistent with the diagnosis of Creutzfeldt-Jakob disease (classical form). Immunohistochemical examinations were also carried out using the protein beta amyloid and phosphorylated tau protein (Alzheimer's disease), alpha-synuclein (dementia with Lewy bodies), the prion protein (PrP), with positive results for beta amyloid and phosphorylated tau protein,

the color of which showed the presence of neurofibrillary degeneration at the level of the entorhinal cortex associated with rare neurofibrillary tangles in temporo-occipital cortex (stage II-III according to Braak classification). Then the final diagnosis was formalized as "Creutzfeldt-Jakob disease (classical form) with the presence of early lesions of Alzheimer's disease". Creutzfeldt-Jakob disease is a rare spongiform encephalopathy. The key pathogenic event is the formation and accumulation, at the cerebral level, of a characteristic amyloid protein called PrPsc (sc from scrapie, where it was isolated for the first time) (16).

Its major symptoms are represented by rapidly progressive dementia, myoclonic jerks, visual disturbances, ataxia, pyramidal and extrapyramidal signs. Only in a more advanced stage of disease it can be demonstrated the typical changes in EEG (EEG abnormalities, characteristic of disease, are periodic triphasic complex spike-waves at 1-2 cycles per second, but they are not constant throughout the clinical phase) and magnetic resonance imaging (signs of atrophy, symmetrical changes in signal intensity at the level of putamen and caudate nucleus in T2-weighted images, easily identifiable by the FLAIR technique) (17,18). The clinical criteria that they put the suspected "possible" and "probable" diagnosis of the disease remains, in conclusion, fundamental because, as we have seen, the histopathological and immunohistochemical criteria are currently too late and they may have diagnostic value only after the death of the subject. However, such procedures are essential, not only for diagnostic definition, but for also epidemiological evaluation of the disease in the country: only the close cooperation between the various healthcare professionals (GPs, neurologists, geriatricians, pathologists) and the authorities same health makes it possible to define the true extent of the phenomenon in Italy (19).

REFERENCES

- Vergani C, Lucchi T. *Note pratiche di diagnosi e terapia per l'anziano*. Seconda edizione: 49-65. Elsevier. 2008
- Soubelet A, Salthouse TA. *Correlates of level and change in the Mini-Mental State Examination*. *Psychol Assess* 2011; 23(4): 811-8
- Pangman VC, Sloan J, Guse L. *An examination of psychometric properties of the mini-mental state examination and the standardized mini-mental state examination: implications for clinical practice*. *Appl Nurs Res* 2000;13(4):209-13
- Dellasega C, Morris D. *The MMSE to assess the cognitive state of elders*. *Mini-Mental State Examination*. *J Neurosci Nurs* 1993; 25(3):147-52
- Erkinjuntti T, Sulkava R, Wikström J, Autio L. *Short Portable Mental Status Questionnaire as a screening test for dementia and delirium among the elderly*. *J Am Geriatr Soc* 1987; 35(5):412-6
- Pfeiffer E. *A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients*. *J Am Geriatr Soc* 1975 Oct;23(10):433-41
- Hachinski V, Oveisgharan S, Romney AK, Shankle WR. *Optimizing the Hachinski Ischemic Scale*. *Arch Neurol* 2012;69(2):169-75.
- Chitravas N, Jung RS, Kofskey DM, Blevins JE, Gambetti P, Leigh RJ, Cohen ML. *Treatable neurological disorders misdiagnosed as Creutzfeldt-Jakob disease*. *Ann Neurol*. 2011;70(3):437-44.
- Van Everbroeck B, Dobbeleir I, De Waele M, De Deyn P, Martin JJ, Cras P. *Differential diagnosis of 201 possible Creutzfeldt-Jakob disease patients*. *J Neurol* 2004;251(3):298-304.
- Tschampa HJ, Neumann M, Zerr I, et al. *Patients with Alzheimer's disease and dementia with Lewy bodies mistaken for Creutzfeldt-Jakob disease*. *J Neurol Neurosurg Psychiatry* 2001;71(1):33-9.
- Seipelt M, Zerr I, Nau R, et al. *Hashimoto's encephalitis as a differential diagnosis of Creutzfeldt-Jakob disease*. *J Neurol Neurosurg Psychiatry* 1999;66(2):172-6.
- Castillo P, Woodruff B, Caselli R, et al. *Steroid-Responsive Encephalopathy Associated With Autoimmune Thyroiditis*. *Arch Neurol* 2006;63:197-202
- Gençer AG, Pelin Z, Küçükali Cİ, Topçuoğlu OB, Yılmaz N. *Creutzfeldt-Jakob disease*. *Psychogeriatrics* 2011;11(2):119-24.
- Zerr I, Kallenberg K, Summers DM, et al. *Updated clinical diagnostic criteria for sporadic Creutzfeldt-Jakob disease*. *Brain* 2009;132(Pt 10):2659-68.
- Schröter A, Zerr I, Helkel K, et al. *Magnetic Resonance Imaging in the Clinical Diagnosis of Creutzfeldt-Jakob Disease*. *Arch Neurol* 2000;57: 1751-7
- Sideri G, Pasquinelli S. *Le malattie prioniche:1-12*. Aracne Editrice 2008
- Peruzza S, Zanusso G, Bissoli E, et al. *Sporadic Creutzfeldt-Jakob disease*. *G Gerontol*. 2004; 52: 60-7
- Gozke E, Erdal N, Unal M. *Creutzfeldt-Jacob Disease: a case report*. *Cases J* 2008 9;1(1):146
- Circolare del Ministero della Sanità - Dipartimento Professioni Sanitarie, delle risorse umane e tecnologiche in sanità e dell'assistenza sanitaria di competenza statale No. 900.2/16.AG/1755. *Linee Guida e norme di sicurezza da osservare in caso di riscontro autoptico su soggetti con probabile malattia di Creutzfeldt-Jakob o sindromi correlate (Sindrome di Gerstmann-Straussler-Scheinker, Insomnia Fatale Familiare)*. 2 dicembre 1996