Mini Review Article

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Cerebrall Autosomal Dominant Artheriopathy with Subcortical Infarcts and Leukoencephalopathy

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Introduction

CADASIL is a hereditary cerebrovascular disease that affects small vessels and usually causes recurrent subcortical infarctions with white matter involvement. It is usually closely related to migraine history, in advanced cases a subcortical dementia usually occurs. It is a disease characterized by a picture of progressive deterioration, and in very advanced stages a pseudobulbar paralysis can occur. In 1955 some cases were described that were called hereditary vascular dementia, later in 1977 it was renamed hereditary multi-infarct dementia, in 1991 they came to be referred to as familial arteriopathic leukoencephalopathy [1]. Finally, with the discovery of the gene involved in the disease, it was renamed CADASIL in 1996 by Joutel. As we can see, the pathological discovery of the disease is of recent discovery, thus adopting the various nomenclatures described above.

The disease occurs in all ethnic groups (more in Caucasian Europeans), but the distribution is worldwide. A prevalence of 4 cases per 100,000 inhabitants is estimated [1]. Until 2002 there were at least 500 affected families worldwide. There is a high clinical heterogeneity. An equal proportion between men and women is estimated. The onset of clinical symptoms is usually 45 years old, related to the occurrence of stroke. The onset of cognitive symptoms is estimated in a much wider range, between 40 and 70 years of age. In people over 65 years of age, the prevalence of dementia associated with the disease increases exponentially.

The small vessel arteriopathy that causes the disease usually affects the systemic level (heart, kidney, liver, muscle, skin, etc.). At the level of the central nervous system there is a degeneration and loss of smooth muscle cells in the arterial wall, this is due to the deposition of granular osmiophilic material (GOM) at the extreme basal level of the cells and in the extracellular matrix [2]. These deposits occur in small arteries.

The gene involved is NOTCH3; it is a large gene with 33 exposures that encode a protein of 2,321 amino acids. The study for the identification of this mutation is extremely complex. It is located on chromosome 19p13, in the same locus as hereditary hemiplegic migraine.

Clinical Characteristics

It is possible to say before indicating the clinical characteristics of these patients, the phenotypic expression so variable that it exists. In 80-85% of cases, stroke attacks usually occur, starting between 40 and 50 years of age. In many cases recurrent vascular episodes or lacunar infarctions occur. It is important that the history of vascular risk factors is not collected in the clinical history. These stroke, ischemic in being the vast majority, have high recurrence (in 70% of cases). In 20-35% of cases, migraine also appears, starting between 20 and 40 years of age and this can be classic or with aura, in some cases hemiplegic and may be the only symptom. In 30-50% of cases dementia may appear, increasing to 80% in people over 65 years. This is characterized by presenting a pattern of fronto-subcortical involvement. It is usually indicated that it is produced by the accumulation of multiple silent infarcts. Psychiatric disorders can also occur in 15% of cases, presenting mood alterations (severe depression, mania, psychosis) and behavior disorder.

Stages or phases are usually established, according to heano ae (2007)

1. Stage I (20-40 years): they usually present with migraine (with or without aura) and in the Neuroimaging studies, white lesions appear. In this phase there are also alterations in higher functions such as slight alterations in reasoning, perseverations, distraction, psychomotor slowdown (executive functions), working memory and short-term due to attentional difficulties.
2. Stage II (40-60 years): usually present episodes of stroke or transient ischemic accidents, as well as neuropsychiatric disorder. In neuroimaging studies, coalescent lesions appear in white matter and well defined in nasal nodes. In this phase, there are more significant neuropsychological alterations: highly altered executive functions, decreased attention capacity, impaired memory due to difficulties in information retrieval, slight visuospatial and visuoconstructive abnormalities. Significant reduction of language and hemiparesis, gait disorders, dysarthria, etc.
3. Stage III (> 60 years): subcortical dementia usually appears, and diffuse leukoencephalopathy and multiple well-defined lesions in nasal nodes appear in neuroimaging studies. In this phase

there is also a significant deterioration in all cognitive functions (executive function, attention, memory, visuospatiality, visosocstruction, language, motor functions) and in behavior.

Description of a Clinical Case and Neuropsychological Rehabilitation

The case of a 47-year-old woman, right-handed, with primary education, married, with three children and diagnosed with CADASIL is described here. In 1988 he had the first stroke with clinical expression (left hemiparesis with recovery at two hours). Later in the following years he suffered several ischemic strokes. In the neuroimaging study, there was a marked hyperintensity in periventricular white matter and of the bump, chronic lacunar infarctions, alteration of the white substance in the anterior area of both temporal lobes and small lesions in the anterior half of the corpus callosum. At the neuropsychological level, it showed correct orientation in time, space and person. Marked box office, verbal disinhibition and sudden changes in emotional state. It conserved the production of language and understanding. In summary, a slight or moderate deterioration of the attention and concentration processes, verbal memory, calculation and constructive praxis was established. Significant deterioration of verbal fluency (semantics and phonetics), visual memory (short and long term), and especially motor programming and executive functions.

The Neuropsychological Rehabilitation was carried out through the Guttmann Platform (Guttmann NeuroPersonal Trainer), a cognitive neurostimulation platform that allows to establish an intensive rehabilitation and maintenance program in patients with multiple neurological conditions, fully personalized and aimed at improving the cognitive functions. This platform allows, in a first step, to establish the neuropsychological evaluation of the patient (base level) and with exercises programmed by cognitive functions (memory, attention, executive functions, social cognition, language, etc.) allows them to be assigned to the patient on a specific day. Subsequently, at the end of cognitive stimulation, we report a report with the results.

In the specific case, a 12-month intensive cognitive rehabilitation program was established two days a week in our Neurorehabilitation Unit, belonging to the Rehabilitation Service and the Mental Health Division of the Manresa University Hospital, Althaia Foundation. The patient went weekly to all the proposed sessions. In the analysis of results, by performing a new neuropsychological evaluation, a significant improvement was observed at the level of behavior (decrease in neuropsychiatric disorders) and improvement in verbal fluency as well as attentional functions. Given the results obtained, it was decided to continue with the neurostimulation platform for the maintenance of cognitive functions.

Discussion

As mentioned in the article, the incidence of CADASIL diagnosed worldwide is around 500 families. According to our assessment, we believe that the number of cases could be much higher if the disease was better known and if differential diagnoses could be better adjusted with other pathologies that present with similar symptoms. The improvement in diagnostic accuracy, as well as its early detection, could help, to a large extent, to control and / or improve both behavioral disorders and associated cognitive disorders and reduce the negative impact this produces on the patient and his family. Thus, in the case of a young person with the described clinic, a complete clinical history, a good differential diagnosis is recommended and, in case of minimal suspicion, complete the study with genetic tests to rule out the presence of the gene involved in the disease

In case of confirmation of the diagnosis of CADASIL, A COMPLETE NEUROPSYCHOLOGICAL STUDY SHOULD BE CARRIED OUT AS SOON AS POSSIBLE and initiate a personalized behavioral and cognitive rehabilitation program such as the one offered by the GNPT platform. In addition, a confirmed diagnosis of CADASIL allows the patient and family to be informed of the Risks that it entails and, in some way, could be prevented and / or avoid new cases [3-6].

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