Differential diagnosis among depressive pseudodementia, frontal dementia and subcortical dementia: a case report

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Diagnóstico diferencial entre seudodemencia depresiva, demencia frontal y demencia subcortical: estudio de un caso

Summary

Among the clinical entities that show cognitive impairments it may sometimes be difficult to reach a diagnosis. That is the case with the differential diagnosis among depressive pseudodementia, subcortical dementia without motor symptoms and predominantly frontal-mesial frontotemporal dementia. This current paper presents one clinical case that illustrates such difficulties.

In the first place, clinical, neuropsychological and neuroimaging features as well as common features of these three disorders are described, after which the case, and evolution of the diagnostic process are described.

Key words: *Subcortical dementia. Depression. Neuroimaging. Executive functions.*

Resumen

Entre las entidades clínicas que muestran alteraciones cognitivas a veces puede ser difícil alcanzar un diagnóstico. Tal es el caso con el diagnóstico diferencial entre la seudodemencia depresiva, la demencia subcortical sin síntomas motores y la demencia frontotemporal de predominio frontal-mesial. En el presente artículo se presenta un caso clínico que ilustra estas dificultades.

Primero se describen las características clínicas, neuropsicológicas y de neuroimagen y los rasgos comunes de estos tres trastornos para después presentar el caso y la evolución del proceso diagnóstico.

Palabras clave: *Demencia subcortical. Depresión. Neuroimagen. Funciones ejecutivas.*

INTRODUCTION

This article presents the case of a patient in whom it was difficult to make a differential diagnosis of the picture between three entities because they sometimes present similarities which may make it hard to distinguish between them. The three entities considered were subcortical dementia, frontal-temporal dementia and depressive pseudodementia. They have many common elements, both clinical as well as neuropsychological, that may cause diagnostic doubts, and given the prognostic relevance and therapeutic possibilities of each syndrome, it is especially important to use all the diagnostic tools possible.

The first of these three entities, subcortical dementia, makes up a concept that is especially developed by J. Cummings, who distinguishes between instrumental functions, carried out by the cortex and between those that include language, praxis, memory, etc., and fundamental functions that depend on subcortical structures. These are more primitive phylogenetically and refer to the attentional, motivational and affective functions, whose deterioration accompanied by the conservation of many of the instrumental functions (cortical) constitutes the fundamental clinical picture of subcortical dementia[1].

Subcortical dementia, from the neuropsychological point of view, is characterized by early slowdown in the processing rate as well as by disproportion in the deterioration of the executive functions with relative preservation of the remaining functions (praxes, gnosias, language). Memory is generally characterized by maintenance of the capacity to acquire information, with deterioration of the capacity to recover it as well as by an involvement of the procedural memory. Apathy also frequently appears and associated depressive pictures may sometimes be associated. In fact, subcortical dementia would correspond with alterations in corticosubcortical circuits that join deep structures of the encephalon with the prefrontal cortex. This explains the importance of the executive dysfunctions and the characteristics of the mem-

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ory deficit observed in this entity and would lead us to think that it would be more adequate to speak of a frontosubcortical profile[2]. All this makes the differential diagnosis between subcortical and frontal cortical dementias difficult from the neuropsychological point of view and finally depends on the presence of motor signs.

Three differentiated syndromes have been distinguished from the clinical point of view in regards to frontotemporal dementia: progressive non-fluent dysphasia, semantic dementia and frontal dementia[1]. The latter has the greatest interest for the present case, and within it, in turn, three clinical subsyndomes have been distinguished. These are associated to any of the three known prefrontal syndromes, orbitofrontal, anterior cingulate and dorsolateral[3]. The first one of these subsyndromes would be characterized by disinhibition, distractibility and hyperactivity, the second one by apathy, affective flattening and inhibition and the third by rigidity, oppositionism and stereotypal behaviors and rituals.

We see that behavior disorders, which may sometimes be the only clear signs of the disease during long periods, obtain great importance in this entity[3].

Furthermore, executive, attentional function and sometimes language impairments are the most common in these patients. Regarding memory, the findings are generally consistent with executive dysfunctions (as occurred in the case of subcortical dementia) with greater difficulty to recover the information than to acquire and code it, no significant loss of it over time being observed. Mood state disorders are also not rare and, in fact, the disease can often debut as an apparent psychiatric disorder, frequently branded as atypical[3]. In any event, if all these findings are not accompanied by speech impairments, they are not exclusive of the nosological entity as we see in the case of the subcortical dementias and thus they are insufficient for the diagnosis[4].

On the other hand, the studies of morphological neuroimaging are generally normal in the initial stages, the cortical atrophy of frontotemporal predominance only being observable in more advanced phases.

The absence of findings in initial phases or diffuse disorders is also not rare in functional studies[3], although hypometabolism or hypoperufsion that affects the prefrontal cortex is generally observed. In any event, these findings are also not specific and can be observed in extrapyramidal system disorders and in psychiatric disorders such as schizophrenia and, as we will see next, major depression.

Major depression can be manifested with the characteristic of the pseudodementia form. Its presentation is sometimes inconsistent with that which can be expected in a picture of cognitive deterioration, however in other cases, it may be clinically similar to a true dementia, although no neuropathological findings are found in the structural neuroimaging tests or in the EEG, especially if dealing with young patients[5].

Neuropsychological traits in depressive disorders include psychomotor delay, speech slowdown and hypophonia as well as attentional deficiencies and memory impairments that affect the declarative memory more than the procedural one (which would distinguish it from subcortical dementia). Within the declarative memory, these patients perform better in recognition tasks, which is generally attributed to disorders in capacity to group and organize information[6] or to difficulties in the plannings of recovery strategies. This characteristic can be considered suggestive of deficits in the executive function dependent memory processes[7], which are also apparently altered[8].

Regarding the latter, difficulties in the problem solving and in planning capacity, as well as cognitive rigidity with tendency to persist and cognitive inhibition difficulties have been described[9]. Such cognitive dysfunctions also seem to indicate worse prognosis and worse response to treatment with certain antidepressants such as fluoxetine[10] and coincide with the findings, in functional neuroimaging studies, of blood flow reductions in the medial prefrontal cortex, anterior cingulated gyri and basal ganglia[11,12], there being correlation between hypoperfusion or hypometabolism and the scores on the Hamilton scale and the degree of deterioration[13]. Signs typical of cortical disorders such as aphasia, apraxia and agnosia are absent. Thus, the picture has greater similarity with the subcortical demential syndromes[14].

CASE PRESENTATION

This is a 41 year old, single woman with no children. Her family background includes a mother who died at 58 years of age from cerebral vascular disease, and who had been diagnosed of bipolar disorder, which had also been observed in other aunts and a cousin of the patient. The psychomotor development of the patient was normal until she was 16 years old, when she was diagnosed of bipolar disorder after onset of a manic type phase. After that, the course was stable until 2001. She had undergone outpatient treatment with lithium carbonate which was withdrawn due to a picture of insipid nephrogenic diabetes secondary to lithium. Although she presented occasional fluctuations of mood state, she could finish her teaching education studies and had a relatively autonomous life. The support of her father, who was always very attentive of her baseline psychopathological picture, was essential for her daily tasks. He died in August 2001 and the patient was then admitted to a mental patient residence.

At this time, she began to show progressive deterioration, with weight loss of more than 20 kg, and the multiple treatments tested (haloperidol, thioridazine, risperidone, olanzapine, valpromide, clomipramine, lorazepam,

clorazepate, lamotrigine, levodopa) did not improve her course.

Two years later, the patient was transferred to the Hospital Clínico from the residence where she was seen due to deterioration of her general state and fever of one week's evolution.

She was admitted to the Internal Medicine Service, and psychiatric medication was completely withdrawn. She remained there for seven days, where she was treated exclusively with hydroelectrolytic replacement treatment and paracetamol. She was diagnosed of desnutrition, anemia and bipolar disorder on discharge.

On February 9, a request was made for referral to the Psychiatric Service: on examination, it was seen that that the patient was conscious, oriented in time, space and person, calm and collaborator, with an appearance of profound inhibition. She presented absence of spontaneous speech, lack of fluency, with hypophonic speech and marked increase in response latency, but she was coherent at all times and with no alterations of the aphasic character. Alterations in the thought form and content were also not seen. Furthermore, a picture of muscular rigidity with elevation of creatine phosphokinase (CPK) that reached levels of 832 U/I became clear. No alterations were observed at any time in the sensory perceptual area and the patient denied subjective affectation of the mood state.

As reported in the Internal Medicine Service, in the first days of admission, she presented oppositional behavior with refusal to eat, do cleaning chores and dressing, which decreased continuously with the passing of the days. It was considered that she should be transferred to the Acute Psychiatry Unit to perform a study of the picture described and later treatment if necessary. On the Psychiatry floor, brain magnetic resonance imaging (MRI) was requested since a mild enlargement of the sella turcica was observed in a previous CT scan. The report of the MRI showed a hypophysial microadenoma that would not explain the neuropsychiatric symptoms that the patient presents, and no other findings of interest were observed. Furthermore, referral to the Clinical Neurology Service was requested. The examination found signs of frontal release (seeking, suction and grasping) and it was considered that she should be transferred to Neurology, where she remained until the day of discharge in joint study with the referring Psychiatry Service. On discharge, the clinical picture she presented had changed in regards to the time of admission. Negativist behaviors were not seen again and the eagerness expressed at meals was striking. Muscular rigidity abated noticeably, phonological and motor stereotypes (flexoextension of hands and fingers) with psychomotor slowdown becoming clear, the lengthening of response latency time persisting. She presented hypomimic expression, and took short steps, with a slow gait without signs of ataxia.

In the neuropsychological assessment, it was found that the patient presented an important difference between verbal and manipulative performance, in favor of the former (105 and 72 respectively) with a total IQ of 90), difficulties to maintain sustained attentional effort and alterations in the executive functions that made it dif-

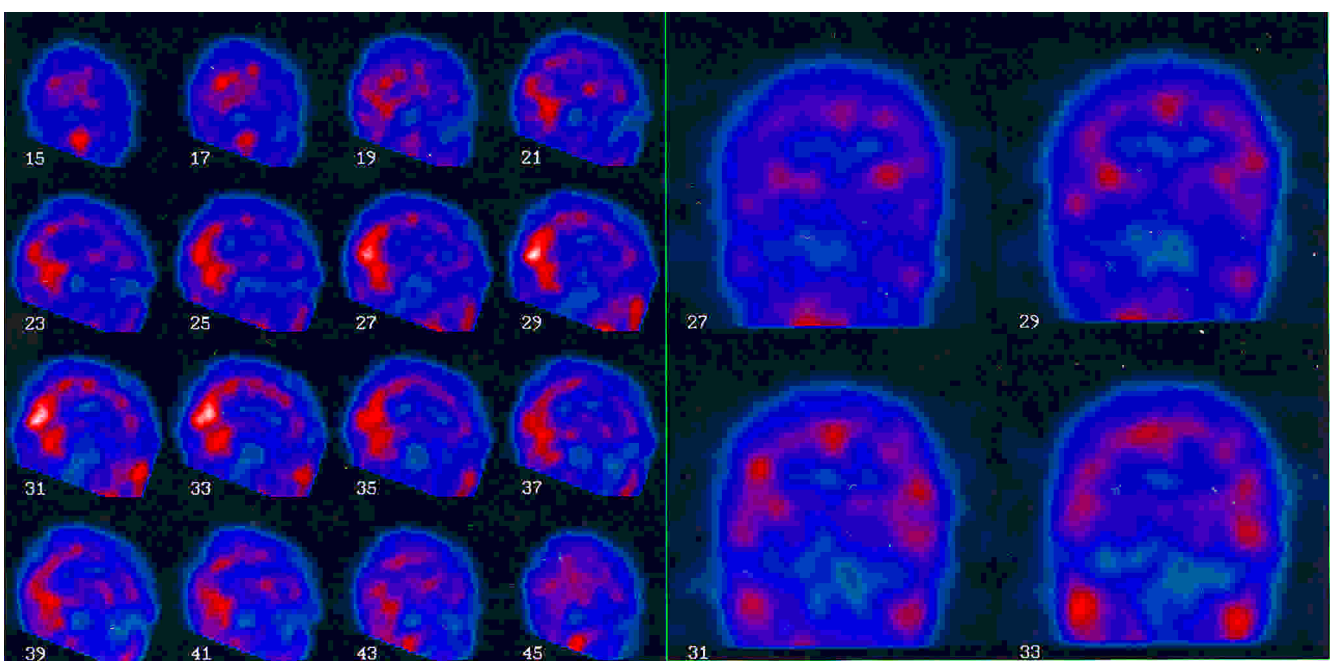

Figure 1. SPECT image that shows hypoperfusion predominating in the frontal region.

ficult to plan and develop effective strategies of problem solution as well as lack of cognitive flexibility with tendency to persistence and little productivity of ideas, there being no spontaneous speech, and she limited herself to responding to the questions asked. Finally, long term memory was affected by difficulties to recover information that may be associated to the executive functioning difficulties.

A SPECT was requested and its images showed a noticeable irregularity in the uptake in cortex (fig. 1) that was principally seen in both frontal lobes with left predominance and in both temporal ones with predominance of the right mesial one. In addition, irregular uptake appeared in the basal ganglia.

CONCLUSION

Diagnostic doubts arise in the present case because both the age as well as clinical history, with family and personal background of bipolar disorder and accelerated deterioration that coincided in time with a traumatic event (the death of her father) make us think about the presence of a depressive state, and the clinical, neuropsychological and structural neuroimaging manifestations do not make it possible to rule out this diagnosis.

However, the severity of the picture, absence of a low mood state component manifested explicitly by the patient as well as importance of the impairments found in the functional neuroimaging study also lead to considering that this picture is probably demential. Among the possible demential pictures, the neuropsychologoical results, characterized by low performance in manipulative skills, executive functions and conserved long term memory impairments, would point the diagnosis either to a frontal type dementia or subcortical type dementia with absence of motor component, discarding the temporoparietal type dementias. Between these two alternatives, neither the symptoms observed nor the neuropsychological profile nor the neuroimaging tests, at least until structural disorders appear, make it possible to unmistakably decide in favor of one or another.

In the present case, the alternative of performing therapeutic trials with antidepressive therapies would be interesting. If they were effective, they would make it possible to rule out the demential picture completely, and in the negative case to opt for the abandonment of the diagnosis of depressive pseudodementia and propose the establishment of pharmacological and neuropsychological treatment as soon as possible for the dementia, until the appearance of structural disorders make it possible to finish the diagnosis.

Finally, we want to stress the importance of being able to use functional neuroimagng studies that can reveal abnormal functioning patterns even when there are no structural abnormalities. In this sense, the combination of neuropsychological tests with neuroimaging tests would be interesting in order to investigate performance patterns, this not being behavioral but physiological, measured by the neuroimaging techniques with the performance of neuropsychological tasks. This type of investigation could help determine diagnostic protocols and specific brain functioning markers that would add additional information to that supplied by the baseline state studies.

ACKNOWLEDGEMENTS

Dr. González Maté and Dr. Cabrera Martín, Medicina Nuclear, Hospital Clínico San Carlos, Madrid.

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