Fahr's Syndrome and Neuropsychiatric Symptoms: Differential Diagnosis in Neuropsychiatry

Síndrome de Fahr e Sintomas Neuropsiquiátricos: Diagnóstico Diferencial em Neuropsiquiatria

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Palavras-chave: Calcinose; Disfunção Cognitiva; Doenças dos Gânglios da Base; Neuropsiquiatria

Dear Editor,

We read with great interest the case report by Ramos-Lopes J *et al*.[1] This interesting case report sparked our interest and drove us to write this brief letter highlighting the importance of secondary causes of neuropsychiatric symptoms when patients present with predominantly behavioral or classical primary 'psychiatric presentations'. Fahr's syndrome or disease, initially described by a German pathologist, is also known as idiopathic basal ganglia calcification, striopallidodentate calcification and calcinosis nucleorum.[2] Despite a somehow confusing nomenclature and the fact that the initial description was not referring to basal ganglia, Fahr's name has come to be invariably associated with bilateral brain calcifications. These may involve several structures including basal ganglia, dentate nucleus, thalamus, cerebral cortex, subcortical white matter and hippocampus.[3]

The variability in distribution of calcifications between individuals might indicate differing pathophysiology. There are several forms: idiopathic, genetic (most frequently involving dominant autosomal *SLC20A2* mutations) and secondary to other medical conditions. Most secondary etiologies include endocrine and metabolic disorders (parathyroid-related dysfunction), infectious and vascular diseases.[2,4] Most brain calcifications are asymptomatic and may be present in as much as 20% of routine brain computed tomography (CT) scans.[3] Although rare, this syndrome is associated with a wide range of neurological and neuropsychiatric symptoms, including schizophrenia-like psychosis (delusions, auditory and visual hallucinations), anxiety, dissociative symptoms, obsessive-spectrum disorders, depressed mood, anhedonia, irritability, deterioration of cognitive status and impaired critical reasoning.[2,4,5] Current diagnostic criteria for the idiopathic form include the presence of bilateral calcifications of the basal ganglia on neuroimaging; progressive neurologic dysfunction and/or neuropsychiatric symptoms; age of onset in the fourth or fifth decade; absence of biochemical abnormalities or other findings suggestive of systemic disorder; absence of infectious, toxic or traumatic cause; positive family history or genetic testing.[2,5] Neurological and psychiatric mental status examination, along with imaging, are the necessary techniques to diagnose this condition. CT is the imaging modality of choice, surpassing magnetic resonance imaging in the detection of calcifications.[2,5] Red flags that should prompt further evaluation are included in Table 1. Currently, there is no specific treatment. Most treatment options are directed at the main symptom clusters using dopamine antagonists, antidepressants and anticonvulsants.[2,4,5] It is essential to consider other medical conditions, even rare ones, when patients present with psychiatric syndromes. The identification of secondary etiologies with potentially correctable abnormalities might allow some symptoms to resolve (such as the correction of phosphate and calcium levels in hypoparathyroidism), thereby preventing disease progression and improving prognosis.

Table 1 – Red flags raising suspicion of psychiatric symptoms associated with brain calcifications and further testing

Red Flags	Further testing
Age of onset (40 – 50)	PTH, calcitonin Calcium, Phosphorus, Magnesium Alkaline phosphatase Vitamin D Heavy metals CSF examination
No previous psychiatric history	
Extrapyramidal symptoms	
History of seizures	
Other miscellaneous neurological symptoms (headache, ataxia, movement disorders, dysarthria, syncope, etc.)	
Previous thyroidectomy	
Symmetrical brain calcification on CT	

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