Fahr-Type Calcification and Neuropsychiatric Symptoms With M-Proteinemia

To the Editor: Bilateral idiopathic calcification of the basal ganglia (ICBG), commonly identified as Fahr's disease, has been documented since the 19th century. This diagnosis has been applied variably to indicate either ICBG or cases of secondary Fahr-type mineralization, and it is referred to generally as basal ganglia calcification (BGC). A small number of studies have indicated a relationship between brain calcification and multiple myeloma (MM), but not monoclonal gammopathy of undetermined significance (MGUS). The following is a case description of this plausible association and its neuropsychiatric manifestations.

Case Report

A 77-year-old man was admitted with an index episode of schizophrenia-like psychosis, including paranoid delusions and auditory hallucinations. He had been diagnosed with M-proteinemia at age 60. Physical examination revealed diminished arm swing, abnormal gait, micrographia, and dysarthria. These neurological symptoms had reportedly worsened over the years. Medical and psychiatric family history were noncontributory.

Recent laboratory investigations revealed new anemia and presence of Bence-Jones proteins of 0.25*g*/liter (reference range: negative), raising concern of progression to MM or similar myeloproliferative disorders. Immunoelectrophoresis showed evidence of IgG of 16.6*g*/liter (reference range: 6.35–14.65*g*/liter) with lambda light chain M-proteinemia. Blood chemistry, ECG, and electroencephalographic examination were normal. The patient declined a bone marrow biopsy. Brain CT scan indicated mild fronto-temporal atrophy and bilateral calcification of the basal ganglia. The Montreal Cognitive Assessment (MoCA)[1] score was 20 out of 30, with notable deficits in attention, recall, and executive function. Neuropsychological assessment battery was consistent with fronto-subcortical dysfunction.

Discussion

The presence of a rigid hypokinetic syndrome, psychotic symptoms, and cognitive impairment was particularly interesting in context of BGC. He had no significant symptoms or history requiring work-up for ruling out unlikely causes for BGC (e.g., hypoparathyroidism, systemic lupus erythematosus, or Wilson's disease), although his monoclonal lambda-chain gammopathy may have contributed to his brain calcification. As described by Isoe et al.,[2] M-proteinemia was believed to have played some part in the development of intracranial calcification leading to dementia in a 66-year-old man. Much support exists to suggest that patients with BGC often present with neurological and psychotic features. Our patient exhibited many of these symptoms and was monitored by the hematology service for his progressive MGUS.

There is evidence to support that almost all cases of MM are preceded by MGUS.[3] What causes MGUS to transform into MM is unknown. Neuropsychiatric manifestations of MM have been described, including secondary mania, which can be one of the first presenting symptoms.[4] By contrast, a search of the literature produced no reports of neuropsychiatric manifestations associated with MGUS. Therefore, this case illustrates the possible onset of psychotic and cognitive symptoms in MGUS preceding any frank evidence of progression to a hematological malignancy.

Tentolouris et al.[5] reported three cases of calcification of the aorta and aortic valve associated with a monoclonal lambda-chain gammopathy. They further indicated that immunologic abnormalities were associated with calcifications. Thus, an immunologic origin of our patient's brain calcification is plausible. Longitudinal assessment is needed of the evolution and progression of neuropsychiatric manifestations over the course of MGUS and perhaps immunologically-induced Fahr-type calcification.

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