Adult-Onset Isolated Hemichorea Revealing Iatrogenic Hypoparathyroidism and Bilateral Basal Ganglia Calcification

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Abstract

Isolated hemichorea (HC) in adults has a relatively restricted differential diagnosis including stroke of contralateral basal ganglia nuclei, nonketotic hyperglycemia, and basal ganglia toxoplasmosis in HIV infection. Hypoparathyroidism-related basal ganglia calcification can potentially cause neurological problems, including movement disorders, that are usually bilateral in keeping with bilateral symmetric lesions. We report a patient with video-documented isolated, adult-onset HC due to iatrogenic hypoparathyroidism and bilateral basal ganglia calcification. A 47-year-old woman presented with isolated adult-onset HC of 2 years' duration as the presenting and only neurological feature of hypoparathyroidism and bilateral extensive basal ganglia calcification, 20 years after thyroidectomy-induced hypoparathyroidism. Significant improvement in the unilateral hyperkinesia was noted after correction of hypocalcemia and hypoparathyroidism at 3 months. Isolated HC in adults is a rare presenting feature of hypoparathyroidism with bilateral basal ganglia calcification and is treatable with correction of the underlying metabolic abnormality. In all cases with a movement disorder and brain calcification, hypoparathyroidism should be actively sought as this treatable condition must not be missed.

Keywords: Basal ganglia calcification, chorea, Fahr's, hemichorea, hypoparathyroidism

Video available on: www.annalsofian.org

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Introduction

Basal ganglia calcification (BGC) can be physiological (seen in up to 20% of routine computed tomography [CT] scans)[1] or pathological. Fahr's *'disease'* denotes a primary (sporadic or familial) cause of BGC, an unraveling of the genetic underpinnings of which is underway in recent years.[1] Fahr's *'syndrome'* is the preferred term for secondary causes of BGC, the latter include hypoparathyroidism, which itself

could be either idiopathic/primary or secondary to inadvertent removal of parathyroid glands during thyroid surgery. Chronic hypocalcemia in these cases triggers a metabolic cascade leading to deposition of calcium in the brain, potentially causing neurological problems including movement disorders that are usually bilateral in keeping with symmetrical lesions. We report a case with isolated hemichorea (HC), as the presenting and only feature of bilateral extensive BGC, presenting 20 years after thyroidectomy-induced iatrogenic hypoparathyroidism.

Case Report

A 47-year-old woman presented to us with a 2-year history of progressive involuntary movements of her left body. The movements had begun gradually in her left leg and were initially intermittent, causing slight clumsiness while walking. Over the next several months, they progressively increased, becoming more continuous and also involving the left hand, causing difficulty with daily activities including cooking, cleaning, and handling small objects. More recently, she had noticed slight clumsiness while speaking and eating; she felt her tongue would sometimes move involuntarily. There were no other medical, psychiatric or cognitive issues, no medication use, no history of chorea in childhood or in pregnancy, and negative family history of neurologic disease. A right eye cataract, likely hypocalcemic in etiology, was removed 2 years ago. Examination revealed the left HC-jerky, irregular, nonrhythmic left hand, and leg movements that persisted on walking. Milder chorea was present in the left lower-face and tongue. A neck scar from thyroidectomy performed 20 years ago was evident, as was a mature left eye cataract [Video 1]. The rest of the neurological examination was normal.

Results

Investigations revealed severe hypocalcemia – total calcium of 4.8 mg/dl (normal level: 8.4–10.5 mg/dl), hyperphosphatemia – serum phosphate 6.6 mg/dl (normal level: 2.5–4.7), and a markedly low parathormone level of <3 pg/mL (normal level: 15–65). She was on thyroid supplementation since after thyroid surgery, and thyroid function tests were normal at presentation to us. Other tests such as complete blood counts, ESR, glucose, creatinine, electrolytes, liver function tests, antiphospholipid antibodies, and peripheral blood smear for acanthocytes were normal/negative.

All other biochemical parameters were normal. Workup for Wilson disease and other causes of chorea was negative. Electroencephalogram was normal. Cognitive (mini-mental state examination) and neuropsychological testing results were within normal range. Brain CT scan showed dense, symmetric BGC [Figure 1]. Oral calcium and cholecalciferol supplementation were commenced and resulted in significant improvement in the HC at 2 weeks. At a 3-month follow-up visit, the movements had improved markedly [Video 2].

Discussion

Adult-onset isolated HC without any other neurological features is a distinctive clinical syndrome with a relatively restricted differential diagnosis, given that it usually implies a structural lesion in the contralateral basal ganglia, most commonly in the putamen, caudate, subthalamic nucleus, thalamus, or pallidum.[2] When the movements have a higher amplitude and speed and affect more proximal limb muscles, they are referred to as *hemiballism*, that may accompany the chorea.[2] The most common cause of HC is *acute stroke* of the aforementioned structures, while other lesions can present more subacutely. Nonketotic hyperglycemia is a well-known cause of HC, thought to be due to incomplete infarct/petechial hemorrhage in the contralateral striatum.[2] In HIV, HC due to basal ganglia toxoplasmosis is the second most common movement disorder after parkinsonism.[3] In children, rheumatic chorea can cause HC without visible structural

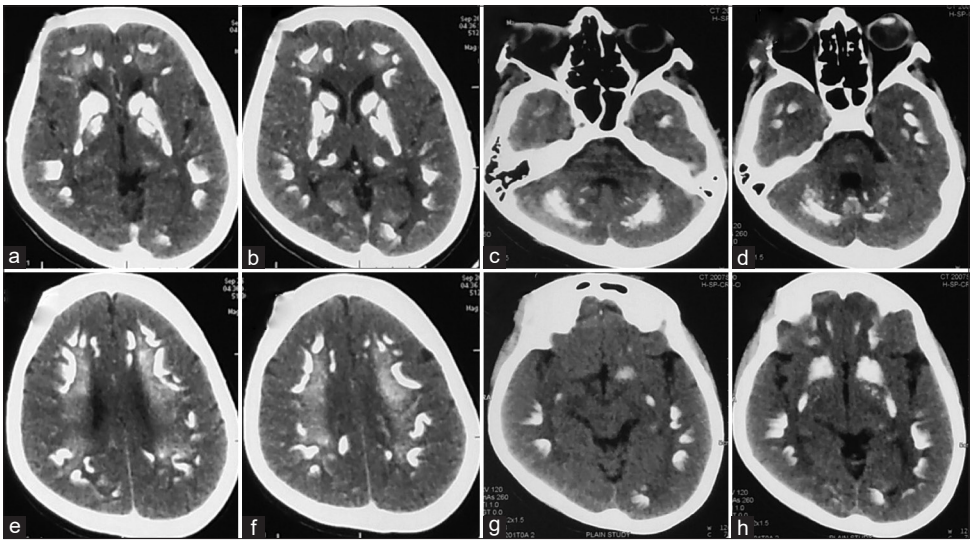

Figure 1: Noncontrast computed tomography brain shows bilateral symmetric, dense calcification in bilateral caudate, putamen and pallidum (a and b), Thalami (b), Dentate nuclei (c and d), pons (d) and generalized subcortical white matter (e-h, also evident in a-d)

abnormality on brain imaging, due to immune-mediated basal ganglia insult. Rarely, HC has been reported with metabolic abnormalities including thyrotoxicosis,[4] systemic lupus erythematosus,[5] or with medication use[6] in isolated case reports and also in pregnancy.

The incidence of permanent hypoparathyroidism after total thyroidectomy is about 1%.[7] In a registry of patients with sporadic/familial (not hypoparathyroidism-related) BGC, movement disorders were the cause of symptoms in 55% of symptomatic patients and of these, parkinsonism accounted for 57%, chorea 19%, tremor 8%, and dystonia 8%.[8] Movement disorders are also common neurological features of hypoparathyroidism-related BGC, and parkinsonism,[9] chorea, dystonia,[10] and paroxysmal dyskinesia/choreoathetosis[11-13] have all been described in various case reports, often in the combination with other features such as psychiatric syndromes, seizures, and cognitive decline. In some cases, the movement disorder was the only feature and/or became apparent several years to decades after thyroid surgery (and inadvertent removal of parathyroid glands), as in the present case. All of these cases, however, had a symmetric movement disorder in keeping with the bilaterality of lesions.

In our patient, the marked unilateral hyperkinesia was the presenting symptom and was clinically isolated with no other neurological features such as psychiatric problems, cognitive decline, seizures, parkinsonism, or other movement disorders as reported above. The striking unilaterality was also considered very unusual for a metabolic disorder especially in the presence of extensive bilateral and symmetric structural basal ganglia lesions. A detailed literature search could find only two reports, worldwide, of isolated HC due to hypoparathyroidism and bilateral BGC, one each due to idiopathic[14] and post-thyroidectomy[15] hypoparathyroidism.[14,15] In one of these individuals,[15] the movements improved after cholecalciferol therapy, as was also the case with our patient. Furthermore, both these historical reports are descriptive and lack video documentation of the movement disorder, as was performed before and after treatment in our case [Videos 1 and 2].

The mechanism for the development of chorea in BGC maybe hypofunction of the indirect pathway from the striatum to pallidum, leading to inappropriate disinhibition of thalamocortical projections.[16] In a case of paroxysmal chorea due to hypocalcemia studied by fluoro-deoxyglucose-positron emission tomography,[17] hypometabolism in the ventral striatum that was present before calcitriol/calcium therapy resolved after the treatment, in parallel with resolution of the clinical episodes.

In summary, we report unilateral chorea as a clinically isolated and presenting feature of iatrogenic hypoparathyroidism and extensive bilateral BGC, with improvement after treatment (despite a delayed presentation) of underlying hypocalcemia and hypoparathyroidism. The case serves as a reminder that both metabolic conditions as well as bilateral symmetric structural lesions can present with a strictly unilateral neurological manifestation, and more importantly that hypoparathyroidism should be actively sought in all patients with any movement disorder and BGC, before considering idiopathic 'Fahr's disease,' as this potentially treatable metabolic condition must not be missed.

Ethical compliance statement

The authors confirm that the approval of an institutional review board was not required for this work. We also confirm that we have read the journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Consent for video

Written, valid, and prior informed consent for the video was obtained from the patient for purposes of publication.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

What is known

1. Isolated hemichorea in adults is usually due to
    a. Stroke (Subthalamic nucleus, pallidum, and thalamus)
    b. Hyperglycemia (Nonketotic)
    c. Basal ganglia Toxoplasmosis (in HIV)
    d. Immune-mediated etiology (e.g. Rheumatic chorea, SLE, and APLA.

What is new

1. Isolated hemichorea may rarely be a presenting feature of hypoparathyroidism with basal ganglia calcification.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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