An Unusual Cause of Intracranial Calcification in a Pediatric Patient: Idiopathic Basal Ganglia Calcification: Case Report

Pediatrik Bir Hastada İntrakranial Kalsifikasyonun Nadir Bir Nedeni: İdiyopatik Bazal Ganglion Kalsifikasyonu

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ABSTRACT Idiopathic basal ganglia calcification is a neurodegenerative disorder that is characterized by basal ganglia and extrabasal ganglia calcification, and usually inherited in an autosomal dominant pattern. Extensive cerebral calcification may occur as idiopathic disease including familial manifestations (Fahr's disease) or secondary to metabolic disturbances including hypoparathyroidism (Fahr's syndrome). The onset of Fahr syndrome is frequently seen in the fourth and sixth decades of life, though occasional cases have been reported in children. In the present report, we reported an 11-year-old girl with idiopathic basal ganglia calcification who was presented with headache. We also review the pertinent literature on Fahr syndrome. Idiopathic basal ganglia calcification is an uncommon cause of intracerebral calcification in children; however, idiopathic basal ganglia calcification should be suggested as a differential diagnosis in children with bilateral intracranial calcifications.

Key Words: Headache; basal ganglia diseases

ÖZET İdiyopatik bazal ganglion kalsifikasyonu, bazal ganglionun ve ekstrabazal ganglion kalsifikasyonu ile karakterize olan ve genellikle otozomal dominant kalıtılan nörodejeneratif bir hastalıktır. Yaygın serebral kalsifikasyon ailevi belirtileri içeren idiyopatik hastalık (Fahr hastalığı) olarak veya hipoparatiroidiyi içeren ikincil metabolik bozukluklara ikincil (Fahr sendromu) olarak ortaya çıkabilir. Bazı olgular çocuklarda bildirilse de Fahr sendromu başlangıcı sıklıkla yaşamın dördüncü ve altıncı dekadlarında görülmektedir. Bu olguda baş ağrısı ile kendini gösteren idiyopatik bazal ganglion kalsifikasyonlu 11 yaşındaki kız çocuğunu sunuyoruz. Fahr sendromu ile ilgili literatürü de gözden geçiriyoruz. İdiyopatik bazal ganglion kalsifikasyonu çocuklarda intrakraniyal kalsifikasyonun nadir bir sebebidir, bununla birlikte, idiyopatik bazal ganglion kalsifikasyonu iki taraflı intrakraniyal kalsifikasyonu olan çocuklarda ayırıcı tanıda düşünülmelidir.

Anahtar Kelimeler: Baş ağrısı; bazal ganglion hastalıkları

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Idiopathic basal ganglia calcification (BGC) is a neurodegenerative disorder that is characterized by basal ganglia and extrabasal ganglia calcification, and usually inherited in an autosomal dominant pattern.[1,2] Extensive cerebral calcification may occur as idiopathic disease including familial manifestations (Fahr's disease) or secondary to metabolic disturbances including hypoparathyroidism (Fahr's syndrome).[3] The onset of Fahr syndrome is frequently seen in the fourth and sixth decades of life, though occasional cases have been reported in children.[4,5] In the present report, we reported an 11-year-old girl with idiopathic BGC who was presented with headache. We also reviewed the pertinent literature on Fahr syndrome.

CASE REPORT

A healthy 11-year-old girl was admitted to hospital complaining with intermittent headache that did not respond to paracetamol. We found out that she had headache for recent 4 weeks and also had fever for recent 3 days. Her medical history was unremarkable except for rhinosinusitis 3 weeks before admission. She was the 2nd child of a nonconsanguineous couple. The patient had fever and had no change in mental status. Her weight was 39 kg (10-25th percentile) and height was 153 cm (50th percentile), and her head circumference was 55 cm (50-98th percentile). In physical examination pulse rate was 72/min, respiratory rate was 15/min, blood pressure was 100/60 mmHg, and temperature 37.2°. The physical examination yielded purulent secretions in the middle meatus using a nasal speculum and a directed light. Her neurologic examination was normal. The evaluation of the secondary sexual characters revealed breast development of Tanner grade 2, pubic hair Tanner grade 2, and axillary hair Tanner grade 2. The remainder of physical examination was normal. Clinical diagnosis was acute sinusitis. Sinus radiography revealed multiple intracranial calcifications. Laboratory examinations, including complete blood count, peripheral blood smear, erythrocyte sedimentation rate, C-reactive protein, and procalcitonin, lactate level, serum electrolytes including calcium and inorganic phosphorus, liver function tests, the serum thyroid hormones and intact parathyroid hormone assay were all within normal limits. Urine test was normal. All viral serologies (toxoplasmosis, varicella-zoster virus, rubellavirus, cytomegalovirus, and herpes simplex virus) were negative. Bacterial cultures obtained directly from the sinus ostia were negative. Cerebral computed tomography (CT) disclosed bilateral and symmetric extensive calcifications over the basal ganglia, head of caudate nucleus, periventricular white matter and semioval center (Figure 1). The lesion displayed on cranial CT was hyperintense on axial T1- and hypointense on axial T2-weighted magnetic resonance imaging (MRI) of the brain (Figure 2a, 2b). Because headache in our patient was with an acute onset diagnosis of asymptomatic BGC was made clinically and radiologically. Direct cranial graphy of her father was normal but direct cranial graphy of her mother was not taken because she was pregnant. The diagnosis of asymptomatic BGC in our patient was made by clinical and radiologic findings.

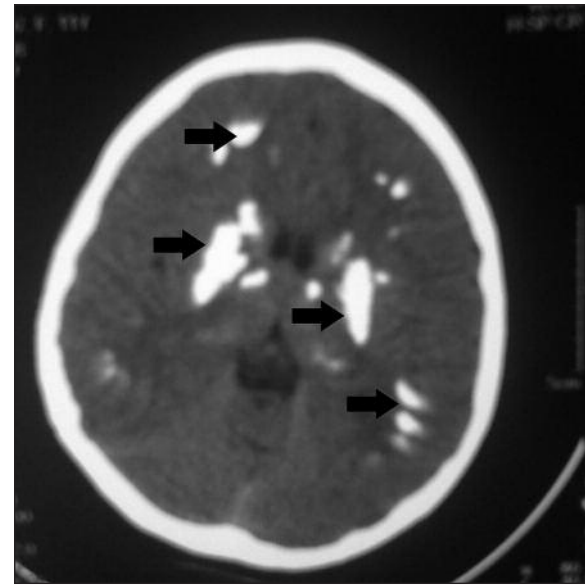

FIGURE 1: A computerized tomography scan showing hyperdensities suggestive of bilateral symmetric calcifications over the basal ganglia, caudate nucleus, periventricular white matter in the patient (see arrows).

DISCUSSION

Bilateral striopallidodentate calcinosis, also known as BGC, is characterized by the accumulation of calcium deposits in different brain regions and is associated with a neurodegenerative clinical phenotype. The changes seen in childhood-onset form of BGC occur in the absence of calcium or parathyroid hormone metabolic disorders, such as hypoparathyroidism or pseudohypoparathyroidism (Basal ganglia calcification, idiopathic, childhood-onset; OMIM#114100). Billard et al. reported 14 cases of childhood-onset encephalopathy with BGC and proposed a 4-group classification based on a review of the literature.[4] Group 1 represented a slowly progressive encephalopathy of presumably autosomal recessive inheritance associated with microcephaly, dwarfism, retinal degeneration or optic atrophy, and symmetrical patchy demyelinization. Group 2 comprised patients with a sporadic, stationary encephalopathy resulting from an unknown prenatal insult. Group 3 was character-

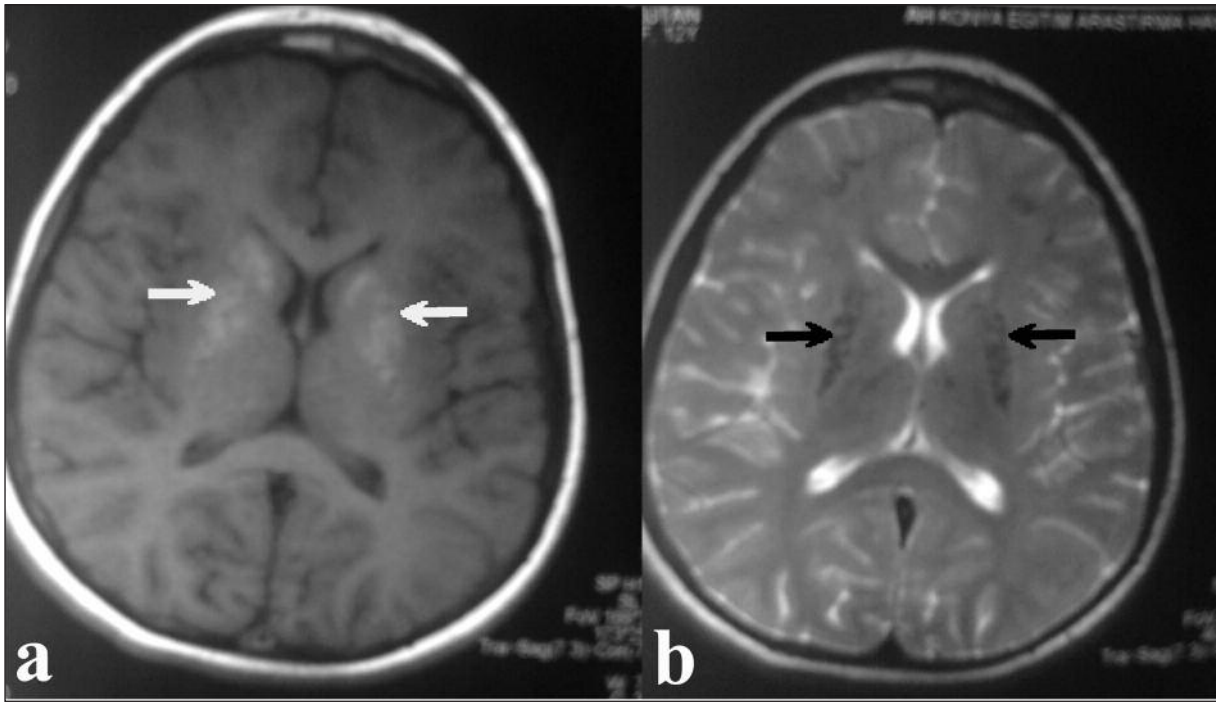

FIGURE 2: a,b : Calcified regions are observed as hyperintense and hypointense on axial T1- and T2- weighted MRI scans, respectively (see arrows).

ized by progressive encephalopathy with chronic spinal fluid lymphocytosis. Group 4 was an autosomal dominant disorder with mild neurologic symptoms in the oldest family members only.

Familial BGC, which has sometimes been erroneously referred to as Fahr disease, is characterized by bilateral BGC and has been associated with a variety of neurologic, cognitive, and psychiatric abnormalities (Basal ganglia calcification, idiopathic, 1; IBGC; OMIM#213600). Brodaty et al. studied a multigenerational family ascertained through 2 sisters in their seventies with radiologic evidence of BGC, dementia, bipolar affective disorder, and parkinsonism.[5] Of the 10 family members with radiologic intracranial calcification, none except the 2 index cases had dementia, bipolar affective disorder, or parkinsonism. Linkage to the IBGC1 locus on 14q was excluded. Brodaty et al. suggested that this family had a form of IBGC in which calcification is inherited independently of neurologic, cognitive, and psychiatric symptoms.[5]

It is not clear whether the central nervous system calcification in BGC is a metastatic deposition, secondary to local disruption of the blood-brain barrier, or is due to a disorder in neuronal calcium metabolism. Despite numerous pathological and biochemical investigations, the etiology of idiopathic BGC remains unknown.[6] BGC is pathologically characterized by calcium deposits within or adjacent to the vessel walls, with no arteriosclerotic changes.[7] Certain diseases with BGC show calcification in other sites of the central nervous system. The most common area of calcification is the globus pallidus. However, additional areas of involvement may include the putamen, caudate, dentate, thalamus, and cerebral white matter. Calcification can also occur in the cerebellum and internal capsule.[8]

Clinical features are important because BGC may be viewed as an incidental finding. Headache, vertigo, movement disorders, paresis, stroke like events, cognitive impairment, psychiatric disorders, pyramidal signals and seizures are the most common manifestations.[8] Symptoms usually develop after 30 years of age, although symptomatic cases during childhood have been described. There is a report of two Fahr syndrome cases that were initially asymptomatic but became symptomatic on long-term follow up.[9] Our patient had only complaint of headache.

Pathological BGC is related with many etiologies that can be classified as inflammatory (cytomegalovirus infection, neurocysticercosis, toxoplasmosis, neurobrucellosis, tuberculosis, HIV infection), tumoral (astrocytomas), hypoxic and vascular (arteriovenous malformations calcified infarct, ischemic encephalophaty), endocrine (hypoparathyroidsm, pseuso and pseudohypoparathyroidism, hyperparathyroidism), toxic (CO and Pb intoxication, hypervitaminosis D, radiotherapy), metabolic and degenerative (senility, mithocondrial encephalopaties, leukodistrophic diseases, idiopathic familial, motor neuron disease, myotonic muscular dystrophy, carbonic anidrase deficit, biopterin deficit) and other (malabsorption, Down syndrome, lupus, tuberous sclerosis, arthrogriposis).[10]

Recognition of the intracranial calcifications in Fahr's syndrome could be made easily by the high resolving capability of CT. Calcifications consist of hydroxyapatite of a nature similar to that found in bones. Other elements include zinc, iron and magnesium.[11] Because of this material composition, they are always hyperdense on CT. On MRI, however, their signal is variable. On T1 weighted images, low signal is due to the low proton density of calcium and other mineral ions present in higher concentration. However, they might present hyperintense signal, due to proteins and mucopolysaccharides binding the mineral ions.[12]

In our case, the patient exhibited bilateral and symmetric extensive calcifications over the basal ganglia, head of caudate nucleus, periventricular white matter and semioval center (as visualized by CT and MRI). Biochemical and somatic features did not suggest a mitochondrial or metabolic disease, or other systemic disorder (parathyroid function was normal, and there was no calcium-related metabolic disorder). The patient had no history of infectious disease, exposure to toxic substances or other significantly traumatic events in her life.

Calcification of the basal ganglia is also observed in ~0.7% of CT scans as an incidental finding. These incidental calcifications are usually benign and without any clearly identifiable etiology, especially in patients aged >60 years. In contrast, patients with familial idiopathic BGC which is synonymous with Fahr disease, typically do not share a benign prognosis.[13] Our patient was detected incidental intracranial calcifications on plain radiography taken for showing evidence of sinusitis and they were confirmed by cranial CT and MRI.

In conclusion, as mentioned above, BGC secondary to other causes in the pediatric patients was rarely reported. Idiopathic BGC is an uncommon cause of intracerebral calcification in children; however, idiopathic BGC should be suggested as a differential diagnosis in children with bilateral intracranial calcifications.

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