Symmetrical and bilateral basal ganglia calcification. Case series and literature review

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Abstract

Introduction: Symmetric, bilateral basal ganglia calcification is rare finding that sometimes occurs asymptotically. Its prevalence increases with age, and the most affected site is the globus pallidus. **Report of cases:** A series of seven cases with clinical and imaging diagnosis of basal ganglia calcification, recorded during the 2012 to 2016 period at the Department of Internal Medicine of the Hospital Civil de Guadalajara "Fray Antonio Alcalde, is presented. Most common clinical presentation was with altered alertness, headache and seizures. There was one case with movement disorders; there were no cases identified with dementia or tetany. **Conclusion:** Ganglia calcification can be associated with age-related neurodegenerative changes, but it can be an initial manifestation of a variety of systemic pathologies, including disorders of the calcium metabolism, intoxication by different agents, and autoimmune and genetic diseases. Correlation of typical imaging findings with clinical manifestations and laboratory results should be established to reach a definitive judgment.

KEY WORDS: Basal ganglia calcification. Fahr's syndrome. Hypoparathyroidism. MELAS syndrome.

Introduction

Basal ganglia calcification is an unspecific finding observed in 1 % of all performed cranial tomographies;¹ for its study, it is classified as physiological and pathological. The former is associated with aging, and the latter with metabolic or autoimmune disorders or primary neurodegenerative diseases, especially in young patients. Most common causes include disorders of the calcium metabolism, especially hypoparathyroidism and pseudohypoparathyroidism.² However it can also be found associated with exposure to certain toxic substances (lead, carbon monoxide), with intracranial radiation and genetic neurodegenerative conditions. Idiopathic basal ganglia calcification or Fahr's disease is a rare condition that can have a specific inheritance pattern or occur sporadically.

In this investigation, seven cases that were admitted to the Hospital Civil de Guadalajara Fray Antonio Alcalde internal medicine department within a period of 4 years, with diagnosis established by imaging, are described.

Methods

Medical records of patients with a basal ganglia calcification diagnosis established by findings on a cranial computed axial tomography, attended to between 2012 and 2016, were reviewed. The following inclusion criteria were considered:

- Computed axial tomography findings consistent with basal ganglia calcification.
- Availability of etiologic diagnosis by paraclinical tests.

Cases with incomplete studies at admission and therefore with inconclusive diagnosis were excluded.

Results

The patients with basal ganglia calcification imaging diagnosis by computed axial tomography were 7, two with concomitant cerebellar and subcortical calcification; 3 of all 7 were males; average age at presentation was 38 years.

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Table 1. Clinical presentation, tomographic findings, laboratory tests and etiologic diagnosis in 7 patients with basal ganglia calcification

Case	Gender	Age	Basal ganglia calcification	Cerebellar calcification	Subcortical calcification	Clinical presentation	Findings	Etiologic diagnosis
1	M	51	Present	Present	Present	Alertness state alteration, headache, seizures, hemiparesis	Hyperlactemia, diabetes mellitus, hypoacusis, muscle biopsy with ragged red fibers in Gomori trichome staining	MELAS
2	M	46	Present	Absent	Absent	Alertness state alteration, seizures	Calcium 3.6 mg/dL (8.5-10.1), Phosphate 8.3 mg/dL (2.4-4.5), PTH 126 pg/mL (4.6-58.1)	Pseudohypoparathyroidism
3	M	62	Present	Present	Present	Seizures, bilateral cataract	Calcium 6.1 mg/dL (8.5-10.1), Phosphate 5 mg/dL (2.4-4.5) PTH 1 pg/mL (4.6-58.1)	Hypoparathyroidism
4	F	34	Present	Absent	Absent	Hemiparesis and vertigo	Normal calcium and phosphate Normal PTH	Fahr
5	F	17	Present	Absent	Absent	Alertness state alteration	Positive antinuclear antibodies	Systemic Lupus Erythematosus
6	F	20	Present	Absent	Absent	Seizures	Hyperlactemia, diabetes mellitus, hypoacusis, muscle biopsy with ragged red fibers in Gomori trichome staining	MELAS
7	F	42	Present	Absent	Absent	Alertness state alteration	Hyperlactemia, diabetes mellitus, hypoacusis, muscle biopsy with ragged red fibers in Gomori trichome staining	MELAS

Most common clinical manifestations were alertness state alteration, headache and seizures. Clinical manifestations, tomographic findings, laboratory tests and etiologic diagnosis are described in table 1. In table 2, most common radiological and clinical alterations are detailed. Finally, table 3 lists the main causes of basal ganglia calcification. There was one case with movement disorder; no one had dementia or tetany, which are differential diagnoses according to the etiology.

Discussion

Together with the cerebellum, the motor thalamus and frontal cortex constitute a complex system that guarantees organization and execution of normal patterns of movement.³

Table 2. Most common radiological and clinical alterations in 7 patients with basal ganglia calcification

	n	%
Cerebellar calcifications	2	28
Subcortical calcifications	3	2
Alertness state alteration	4	57
Seizures	4	57
Headache	1	14
Motor disorders	2	28
Parkinsonism	1	14

Symmetric and bilateral calcification has been described in association with different disorders: toxic (by carbon monoxide or lead), of the calcium

Table 3. Main causes of basal ganglia calcification

Etiology	Example	Etiology	Example
Idiopathic	– Aging – Fahr's disease	Toxic	– Carbon monoxide – Lead – Mineralizing microangiopathy – Anticonvulsant treatment
Metabolic	– Hypoparathyroidism – Pseudohypoparathyroidism	Miscellaneous	– Systemic lupus erythematosus – Chemotherapy/radiotherapy
Hereditary	– Mitochondrial diseases (MELAS/MERRF) – Aicardi-Goutières syndrome – Cockayne Syndrome – Down syndrome

Figure 1. Case 1. MELAS syndrome. Bilateral calcifications in basal ganglia and parieto-occipital hypodensity consistent with stroke-like by magnetic resonance imaging.

metabolism (hypoparathyroidism, hyperparathyroidism, pseudohypoparathyroidism), anoxic-ischemic encephalopathy, autoimmune diseases (systemic lupus erythematosus) and genetic neurodegenerative conditions (MELAS syndrome, Cockayne disease, Hallervorden-Spatz disease). When there is no identifiable cause it is called Fahr's disease.^{4,5}

Calcified ganglia are generally incidentally detected in a computed tomography.⁶ Physiological intracranial calcifications are observed in approximately 0.3 to 1.5 % of cases, are incidentally identified by neuroimaging and are usually asymptomatic. In a cases series of 2012, Abdelrahman retrospectively reviewed 1040 cranial tomographies, with 552 corresponding to males; he found basal ganglia calcification in 1.25 % (0.72 % in males and 1.85 % in females; OR = 2.57 [0.72-9.98]; RR = 2.55 [0.79-8.21]; p = 0.1).^{6,7}

Being part of the aforementioned entities, most cases exhibit symptoms that range from movement disorders (parkinsonism, chorea, athetosis), alertness state alterations, headache and seizures to syndromes such as upper motor neuron and neuropsychiatric syndromes.^{8,9}

The cause whereby the described patients had basal ganglia calcification was different in each one; according to initial history and physical examination, the specific protocol was followed to arrive to definitive diagnosis.

MELAS syndrome is caused by different mitochondrial DNA point mutations of maternal inheritance; the most common (in 80 to 85 %) is the one in tRNA A3243G position of maternal DNA. First description of MELAS syndrome was made by Pavlakis et al. in 1984, who defined it as one of the multi-systemic mitochondrial syndromes related to stroke before 40 years of age, encephalopathy characterized by focal or generalized seizures, lactic acidosis and ragged red fibers in muscle biopsy. Diabetes mellitus, as well as bilateral hypoacusis are common findings. Approximately 30 % of patients with MELAS exhibit basal ganglia calcification.¹⁰⁻¹²

An example of MELAS syndrome can be appreciated in figure 1.

Hypoparathyroidism is an endocrine deficiency characterized by low calcium serum levels, elevated phosphorus levels and absence or inappropriately low

Figure 2. Case 3. Pseudohypoparathyroidism. Bilateral, symmetric calcifications in basal ganglia and cerebellar hemispheres.

Figure 3. Case 3. Hypoparathyroidism. Bilateral, symmetric calcifications in basal ganglia, as well as subcortical.

serum levels of parathyroid hormone (PTH). It can be accompanied by seizures secondary to low calcium levels or to symmetrical and bilateral calcification of different brain structures, such as basal, subcortical or cerebellar ganglia.¹³

Pseudohypoparathyroidism is a rare heterogeneous hereditary disorder, characterized by hypocalcemia-hyperphosphatemia with elevated plasma PTH in the absence of renal damage. It was first described by Albright; in some case series, extra-skeletal calcifications have been identified in up to 84 % of patients, including those of basal ganglia.¹³⁻¹⁵

Pseudohypoparathyroidism and hypoparathyroidism tomographic findings examples can be seen in figures 2 and 3.

Fahr's disease consists of symmetric calcifications, mainly localized in basal ganglia and the cerebellum, which is associated with varied neurological disorders, with the most common including extrapyramidal-type movement disorders (with predominance of parkinsonism, although choreoathetosis, dystonia, tremor, orofacial dyskinesia and paroxysmal chorea is also found), dementia and psychiatric alterations; in few occasions, sensory disturbances are associated. The pathophysiological mechanism resides in the deposit of calcium and other minerals at the globus pallidus, putamen,

corona radiata, thalamus, cerebellar dentate nuclei and hemispheric and cerebellar white matter; these calcium deposits are formed surrounding a polysaccharide nest that is primarily produced on arteriole and capillary walls. For its diagnosis, demonstrating affected first-line relatives is necessary, as well as ruling out the aforementioned disorders.^{16,17}

Systemic lupus erythematosus is a common autoimmune condition that affects young women, and occurs with joint, pleuropulmonary, cutaneous, hematological, renal and neurological symptoms. As for its association with basal ganglia calcification, the pathophysiological mechanism is not fully understood, although different theories try to explain its onset.^{18,19}

Diagnostic algorithm

Laboratory tests should include calcium, phosphorus and PTH levels to rule out parathyroid disorder.

If observed together with hypodensity suggesting stroke, especially in young patients, serum lactate and cerebrospinal fluid should be included, as well as muscle biopsy with Gomori trichome staining looking for ragged red fibers in order to rule out mitochondrial disease. In young patients with multiple organ involvement, antinuclear antibodies should be requested to rule out neurolupus; if results are negative, it can be classified as idiopathic disorder.

Conclusion

Bilateral and symmetrical basal ganglia calcification is a rare finding that sometimes causes no symptoms. Its prevalence increases with age, and the most affected site is the globus pallidus. Most common causes reported in the world literature are Fahr's disease and calcium metabolism disorders; however, differential diagnosis is broad. A correlation of typical imaging findings with clinical manifestations and laboratory results should be established in order to arrive to a definitive diagnosis.

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