

Bilateral Striopallidodentate Calcinosis: Report of Two Cases and A Review of the Literature

Bilateral Striopallidodentat Kalsifikasyon: İki Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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Abstract: Objectives: Striopallidodentate calcinosis is a relatively rare pathological condition encountered in neurological practice that presents with a range of clinical symptoms. Often this lesion is first detected as an incidental finding on radiological examination.

Patients and Methods: We report two cases of bilateral striopallidodentate calcinosis that presented with headache and paresthesia, and featured similar radiological findings. One patient was a 49-year-old woman who had been operated for thyrotoxicosis due to Grave's disease 18 years ago. The other patient was a 62-year-old man who presented with low-back pain. Both patients' neurological examination were normal.

Results: In both patients, cranial computerized tomography revealed bilateral diffuse calcifications in the cerebellum, basal ganglia, thalamus and white matter. First patient had postoperative hypocalcemia due to hypoparathyroidism and in the other patient there were no abnormal findings on blood biochemistry testing and endocrinologic screening

Conclusion: Bilateral intracerebral calcification is usually detected as an incidental radiological finding. It is important to diagnose the underlying pathology because most causes, such as hypoparathyroidism, are treatable. Asymptomatic patients should be followed carefully because cerebellar symptoms, parkinsonian symptoms,

Özet: Amaç: Striopallidodentat kalsifikasyonlar değişik klinik semptomlarla birlikte olan ve nöroloji pratiğinde nadiren görülen bir durumdur. Bu lezyonlar genellikle radyolojik incelemeler sonucunda rastlantısal olarak farkedilir.

Olgu ve method: Bu yazıda başağrısı ve uyuşmalarla başvuran ve radyolojik bulguları birbirine çok benzeyen iki striopallidodentat kalsinozis vakası sunulmuştur. Birinci vaka 18 sene önce Grave's hastalığına bağlı tirotoksikoz nedeniyle opere edilmiş 49 yaşında kadın hastaydı. Diğer vaka ise bel ağrısı yakınmasıyla başvuran 62 yaşında erkek hastaydı. Her iki hastanın nörolojik muayenesi normaldi.

Bulgular: Her iki vakanın beyin tomografisinde; beyaz cevher, talamus, bazal ganglia ve serebellumda difüz bilateral intrakranial kalsifikasyonlar mevcuttu. İlk vaka hipoparatiroidizme bağlı hipokalsemi ile başvururken diğer vakanın biyokimya ve endokrinolojik incelemeleri normal sınırlar içerisindeydi.

Sonuç: Bilateral intrakranial kalsifikasyonlar genellikle rastlantısal radyolojik bir bulgu olarak görülür. Hipoparatiroidizm gibi birçok etyoloji tedavi edilebildiğinden bu vakaların altında yatan patolojinin iyi ortaya konulması gerekir. Serebellar, parkinson semptomları, ekstrapiramidal ve kognitif bulgular zamanla ortaya çıkabildiğinden asemptomatik vakaların dikkatlice takip edilmeleri gereklidir.

and extrapyramidal and cognitive abnormalities may develop over time.

Key Words: Fahr's disease, hypoparathyroidism, striopallidodentate calcinosis

Anahtar Kelimeler: Fahr hastalığı, hipoparatiroidizm, striopallidodentat kalsifikasyon

INTRODUCTION

Deposition of calcium salts in tissues other than bone is a pathological process. Necrosis or hyalinization often precedes calcification. However there are some conditions in which calcium can be deposited in tissues under physiological conditions. Physiological calcification is often observed in arachnoidal granulations and in the basal ganglia, dentate nuclei, choroid plexus, commissure of habenulae, pineal gland, pituitary gland, ligaments and dura. Examples of pathological conditions for cerebral calcification include: infection, vascular disease and neoplasia of the cerebrum. Multiple symmetric macroscopic calcifications of the basal ganglia are very rare in clinical practice, and they are called "Bilateral Striopallidodentate Calcinosis". These are often incidental findings that prompt medical attention (15). Extensive symmetric calcification of the basal ganglia, cerebellum, cerebral and cerebellar cortices (striato-palido-dentales) is a common finding in patients with hypoparathyroidism or pseudohypoparathyroidism (1,5,7-11). Symmetric bilateral intracranial calcifications who have normal parathyroid glands and normal serum calcium levels is defined as Fahr's disease (2,4,5,7,13,14,16). In this article, we describe the cases of two patients with the rare condition striopallidodentate calcinosis, and also review the relevant literature.

CASE REPORTS

Two patients at our clinic have been diagnosed with bilateral symmetrical striopallidodentate calcinosis in the past 2 years. Each individual underwent a thorough work-up, including measurement of serum calcium (Ca) level and assessment of parathyroid function. Both were evaluated with computerized tomography (CT).

Case 1: A 49-year-old woman presented with the complaints of headache and abnormal sensation in her hands. Eighteen years previously,

she had been operated for thyrotoxicosis due to Grave's disease. She has developed hypocalcemia as a results of the parathyroidectomy for eighteen years. The patient's blood biochemistry findings were normal except for hypocalcemia (Ca 7.6 mg/dL) and elevated serum phosphorus (P 7.1 mg/dL). Cranial CT revealed diffuse calcifications bilaterally in the cerebellum, thalami, basal ganglia and white matter (Figure 1).

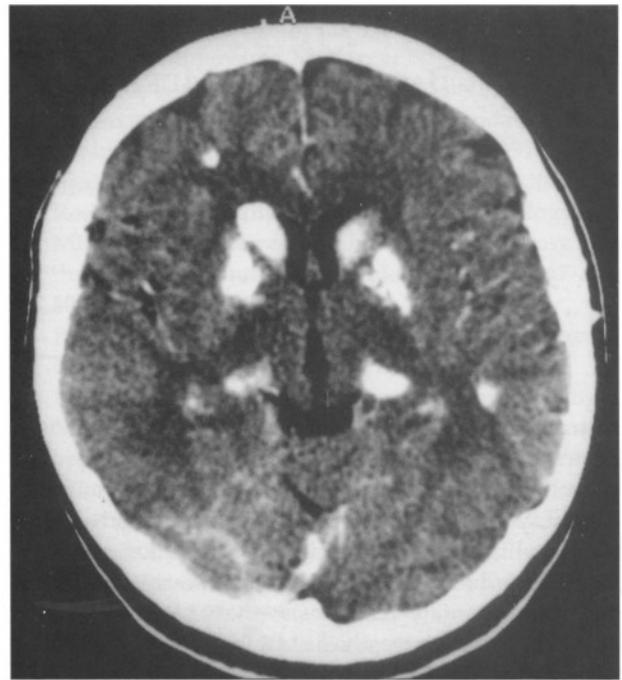


Figure 1a: Cranial computerized tomography of Case 1 with bilateral striopallidodentate calcinosis. This individual had post-parathyroidectomy hypocalcemia. Note the calcifications in the white matter, thalami and basal ganglia.

Case 2: A 62-year-old man presented with the complaints of low-back pain, headache and abnormal sensation around the lips. His neurological examination was unremarkable except for paraspinal muscle spasm and perioral hypoesthesia. There were no abnormal findings on blood biochemistry analysis or endocrinologic screening (Ca 9.8 mg/dL, P 5.06 mg/dL, parathyroid hormone 20.4 pg/ml). Cranial CT



Figure 1b: Computerized tomography of case 1 patient shows bilateral cerebellar calcifications.

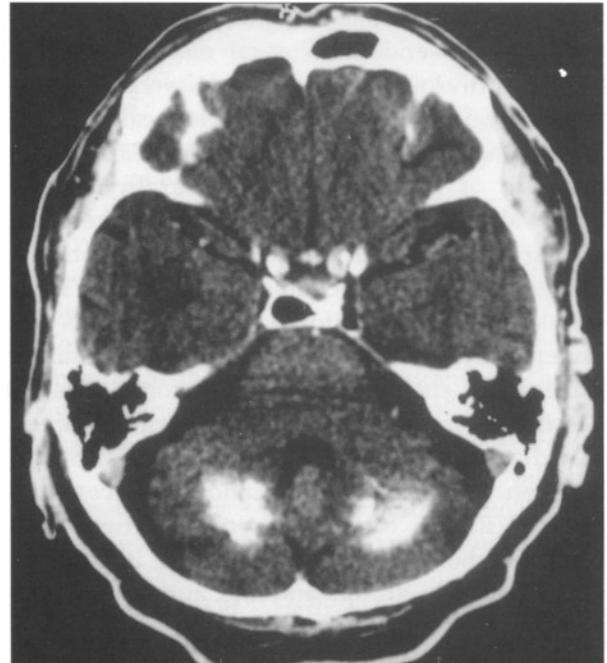


Figure 2b: Computerized tomography of case 2 demonstrates calcifications in both cerebellar hemispheres.

revealed diffuse calcifications bilaterally in the cerebellum, thalami, basal ganglia and white matter, that was consistent with the diagnosis of Fahr's disease (Figure 2).

DISCUSSION

Wider use of new technology is increasing the number of cases of macroscopic bilateral basal ganglia calcifications that are detected. Many asymptomatic patients with these lesions are examined by CT for other medical reasons, and the calcifications are discovered incidentally. Gomille et al. examined 2318 cerebral CT scans of patients presented with any neurological symptoms retrospectively during 1993-1995. They found that 12.5% of the CT showed calcification of the basal ganglia, and that the most frequent site of deposition noted was the globus pallidus (96.4%). In this retrospective study of 2318 cerebral CT the authors observed no correlation between the anatomic sites of calcification and the presenting symptoms (6).

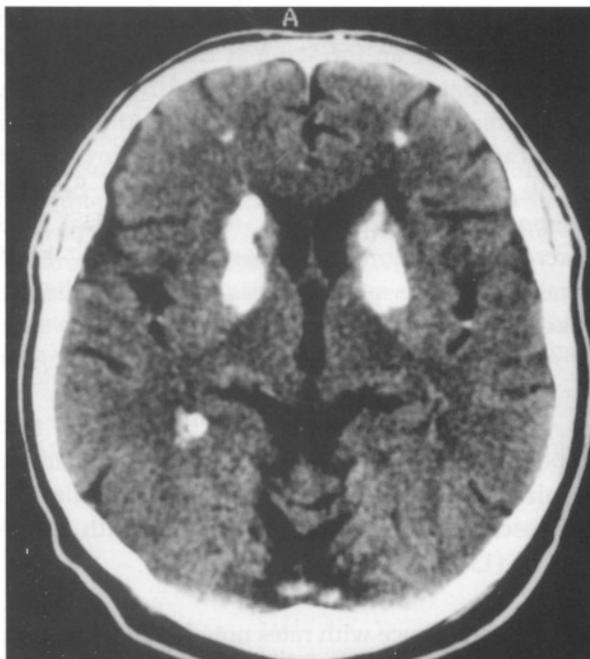


Figure 2a: Cranial computerized tomography of Case 2 with Fahr's disease. Calcifications are evident in the white matter, thalami and basal ganglia.

Multiple microscopic calcifications of the basal ganglia and hippocampus are common incidental findings in the brains of elderly people (2,16). In general, cerebral calcium deposits in this group are thought to be due to vascular changes associated with aging. However, macroscopic bilateral basal ganglia calcifications in any age group are usually associated with neurological and

metabolic diseases. These lesions may be seen in patients with endocrinological diseases, such as hypoparathyroidism or pseudohypoparathyroidism. Some individuals develop calcifications after thyroid or parathyroid surgery. Case 1 is an example of post-surgical hypoparathyroidism. Removal of the parathyroid glands iatrogenically during thyroid surgery led to brain calcification in this patient. Serum calcium and phosphorus levels should be closely monitored in all individuals who undergo thyroid or parathyroid surgery, because in some cases, such as parathyroidectomy, it is not possible to measure parathyroid hormone levels. Kowdley et al. investigated the relationship between intracranial calcification and cognitive deficits in 11 hypoparathyroid patients (9). Neuropsychological testing revealed impairment in 65% of this group, and the authors found a positive correlation between the presence of cognitive deficits and the presence of intracranial calcifications. Keck et al. reported functional disturbances in the brains and cerebella of six patients who had clinical and biochemical signs of parathyroid gland malfunction and symmetrical cerebral calcifications (8). We did not observe any cognitive dysfunction in our patient with post-surgical brain calcifications but this is another important point to consider during further follow-up in this case.

Post-inflammatory brain calcification may occur as a sequela of infections such as tuberculosis, toxoplasmosis, cysticercosis and congenital human immunodeficiency virus. Bilateral cerebral calcifications may also be congenital, as in tuberous sclerosis, Down's syndrome, mitochondrial encephalomyopathies (MELAS/MERRF), Cockayne's syndrome, neurofibromatosis and methemoglobinopathy. Post-anoxic/toxic conditions can also facilitate this type of bilateral deposition. Examples include carbon monoxide poisoning, lead intoxication, chemotherapy and radiotherapy.

There are also idiopathic cases in which no endocrine abnormality or any other cause can be identified. Fahr's disease is an idiopathic familial form of bilateral basal ganglia calcification (2,12). Bamberger was the first to describe bilateral basal ganglia calcifications in 1855. Fahr described the first adult case of bilateral basal ganglia

calcification with its clinical and histological findings in 1930. Fahr's disease, which is also known as bilateral striopallidodentate calcinosis is histopathologically characterized by bilateral extensive calcifications of the globus pallidus, putamen, caudate nucleus, internal capsule, thalamus, and the dentate nucleus of the cerebellum (16).

Plain films of the skull in all types of intracranial calcifications usually show only the highly concentrated calcifications. Computed tomography is more sensitive, and therefore demonstrates even very small quantities of calcium. The findings on CT are distinct and consistent whereas the magnetic resonance images on T₁- and T₂-weighted sequences may vary (15). Interestingly, however, neurological symptoms are more strongly correlated with the hyperintensities on T₂-weighted images than with calcifications on CT. Hyperintense lesions on T₂-weighted images may reflect a slowly progressing metabolic or inflammatory processes that subsequently calcify, causing the neurological deficit (3).

Histologically, in most types of intracranial calcifications the calcium is deposited along the capillaries and in the medial walls of larger arteries and veins (15). Smeyers-Verbeke et al. reported that composition of an intracranial calculus was pure hydroxyapatite in a patient with idiopathic intracranial calcifications (14). They found that the calcification process started with the formation of small round bodies that eventually became cemented to each other to form the final macroscopic stone. Researchers who have investigated the pathogenesis of Fahr's disease speculate that local circulatory disturbances, such as regional ischemia, may be the primary trigger for precipitation of calcium and other minerals (2). In contrast, Pronica et al. postulated that hypoparathyroidism-like changes due to chronic respiratory alkalosis cause the bilateral macroscopic calcifications in patients with Fahr's disease (13).

In accordance with rates noted in the literature, we rarely see cases of macroscopic bilateral intracerebral calcification at our clinic. In the patients we have diagnosed, the most frequent cause is hypoparathyroidism/pseudohypoparathyroidism,

and idiopathic cases are next most frequent. Although our two patients exhibited similar CT findings, the causes of their lesions were different. Hypocalcemia resulting from parathyroidectomy was the etiology in the first case, but even detailed biochemical and endocrinological investigations did not reveal the cause in the second case. As described previously, patients with calcium deposits in these locations may develop cognitive, cerebellar or parkinsonian symptoms. It is very interesting that such large amounts of calcification in the eloquent parts of the brain did not cause significant neurological symptoms in either of these individuals. Such patients must be monitored carefully in the long term, as they may eventually develop cognitive symptoms. Both neurological examinations and biochemical screening are key elements of follow-up.

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