

Microvasculopathy May Precede Idiopathic Cerebral Calcifications — Case Report

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Abstract

Cerebral and cerebellar calcifications were discovered by computerized tomography (CT) in a man who presented with a dementing illness characterized by progressive memory loss, irritability, and dystonia. He had no known family. Magnetic resonance imaging showed areas of absent signal corresponding to the calcifications and areas of high-intensity signal on the T2-weighted images without counterpart on the CT. These are postulated to be static liquid pools secondary to endothelial membrane incompetence and leakage of plasma-derived fluid.

Introduction

Radiographic changes thought to be representative of “calcification” of the basal ganglia have been associated with many different conditions. These changes have consisted of areas of hyperdensity that result from the deposition of different minerals, among which calcium seems to be the principal component.¹ Radiologic evidence of mineral deposition in the basal ganglia has been correlated with neurologic syndromes, which include different combinations of impaired mental function, dysarthria, dystonia, rigidity, tremor, choreoathetosis, seizures, and ataxia. Only 1 of these cases has been studied with magnetic resonance imaging (MRI).² More recently, other investigators have described the MRI findings in patients with cerebral calcifications associated with other conditions such as acquired immune deficiency syndrome (AIDS).³ We present the MRI findings of 1 patient who meets the clinical and radiographic criteria for the diagnosis of what has been previously referred to as “Fahr’s disease” (idiopathic calcification of the basal ganglia).

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Case Report

The patient is a forty-six-year-old printer who was referred to us because of progressive deterioration of memory during the five to six years prior to admission. Concomitantly with the memory disturbance he exhibited increasing dysarthria and irritability. He denied any other mental or physical problems. He used no calcium-containing compounds and admitted only to the occasional use of acetaminophen and antacids containing aluminum and magnesium. He had been adopted and knew nothing of his biological family. He had been employed as an offset printer for twenty-four years but without industrial exposure to toxins, chemicals, or metals.

His height was 1.82 m, and he weighed 57.2 kg. A II/VI systolic ejection murmur heard best at the cardiac apex radiated to the left sternal border. He was awake, alert, well oriented, and cooperative but became easily frustrated whenever he was unable to complete tasks during the examination. His speech was dysarthric with special difficulty forming voiced consonants. Language function was otherwise normal. Registration, storage, and recall of both recent and remote events were decreased, and his Wechsler memory quotient was 81. His attention span, as measured by digit retention, was decreased (4 forward, 4 backward with 7 and 6 expected respectively). Judgment was rather concrete (an apple and an orange were similar in that "both were round" and his interpretation of proverbs laced abstraction). Wechsler Adult Intelligence Scale (WAIS) score was 87 (verbal = performance). He did poorest in tasks requiring memorization. The optic fundi were normal. Despite normal posture and normal strength, tone, coordination, and bulk of all his muscles, there was dystonia of the right upper and lower limbs. The former was held in pronation and not swung fully upon walking. The latter became immobile during the swing phase of walking, often causing him to trip. Sensation and coordination were normal. He nimbly executed purposive movements. Muscle stretch and cutaneous reflexes were normally active and symmetrical. The plantar responses were flexor bilaterally.

Values for hematology, serum chemistry, serology, thyroid function tests, vitamin B₁₂ levels, and folate levels were in the normal (N) range. Free serum calcium was 4.8 mg/dL (N=4.5-5.0), and serum ceruloplasmin was 37 mg/100 mL (N=27-338). Parathyroid hormone level was 6 mL Eq/mL (N= < 3-10). Radiologic studies of kidney, abdomen, limbs, and spine disclosed no other ectopic calcifications.

Methods

The patient underwent cranial computerized tomography (CT) with a third-generation high-resolution scanner and, later, MRI with a 0.15 Tesla resistive magnet. The magnetic images were obtained with spin-echo (SE) recovery sequences of echo (TE) and repetition times (TR) of 30 and 1030 msec, respectively, and later with TE = 120 msec and TR = 2120 msec. The first set yielded proton-density images and the second, T2 = weighted images.

Results

The CT images showed areas of increased attenuation localized in the basal ganglia, cerebellar nuclei, and white matter of the cerebral hemispheres (Figure 1). MR images revealed areas of decreased signal on both proton density and T2-weighted images (Figures 2 and 3).

These corresponded to the regions of calcification seen on CT. Additionally, areas of increased signal were present in the white matter of the cerebral and cerebellar hemispheres. These were adjacent to but not within the regions of calcification.

Discussion

Before the use of computerized tomography (CT), two thirds of the cases of cerebral calcifications were thought to be secondary to abnormalities of calcium metabolism,⁴ most commonly, pseudohypoparathyroidism. Since the introduction of CT, however, it has been possible to find areas of increased radiodensity in the basal ganglia of 0.33-1.5% of all cranial examinations.⁵ Some of these cases have been found to occur in families,^{6,9} and the incidence of abnormalities of calcium metabolism among all these patients varies altogether from 0-5%. Although the name of Fahr has been linked to the familial form of the disorder, this is probably not justified since the patient reported by Fahr¹⁰ had no history suggestive of a familial tendency. Additionally, almost a century earlier, Delacour had already recognized and described this entity.¹¹

Pathologically, the process responsible for mineral deposition in the basal ganglia, cerebral hemispheres, and cerebellum has been a matter of controversy. Some have believed it to

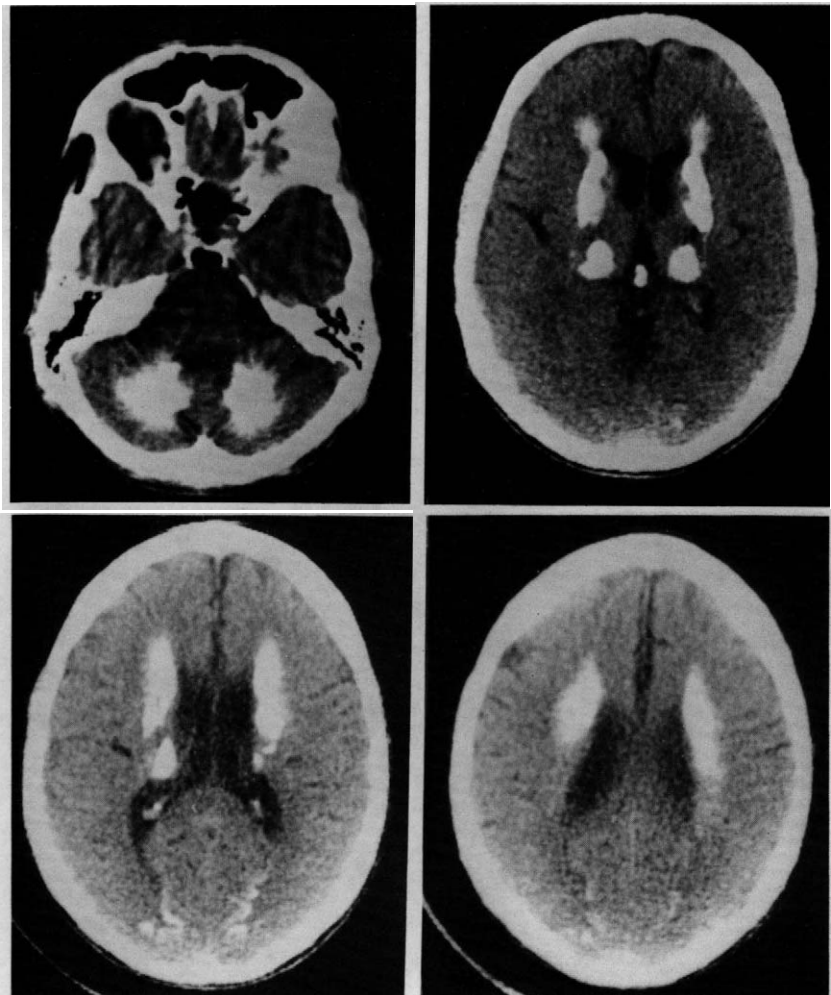


FIG. 1. CT images show extensive areas of increased attenuation on the basal ganglia, cerebellar nuclei, and cerebral white matter.

represent the deposition of iron and calcium in the walls of the arterioles and venules of the cerebral white matter and nearby deep gray nuclei.^{3,4,6} Extensive postmortem studies of the cerebral calcifications of 1 patient led several investigators to conclude that these were due to a process similar to natural calcification and that, although the capillaries were involved this was only a secondary change.¹² The fact that ferrugination is also prominent has led others to postulate that the accumulation of iron and calcium occurs in response to the extravascular deposition of an acid mucopolysaccharide-alkalic protein complex. Other minerals that have been found in different concentrations in such deposits are copper, aluminum, zinc, cobalt, manganese, magnesium, lead, arsenic, and other trace elements.¹² Whether mineral depositions in the brain are only part of a more generalized process that may also cause mineralization of other parts of the body (such as in the case of Wilson's disease) is unknown at present. No studies of other organs have been reported.

Several theories have been proposed to explain the mechanism of formation of these areas of ferrugination and calcification in the brain. None of them has, however, been proved. Among the explanations offered, previous cerebral anoxia¹³ and vascular disturbances in arterial "boundary zones"¹⁴ are the best known. Increased tissue "avidity" for the deposited mineral, as has been postulated in Wilson's disease,¹⁵ is also a possibility. The concept of some

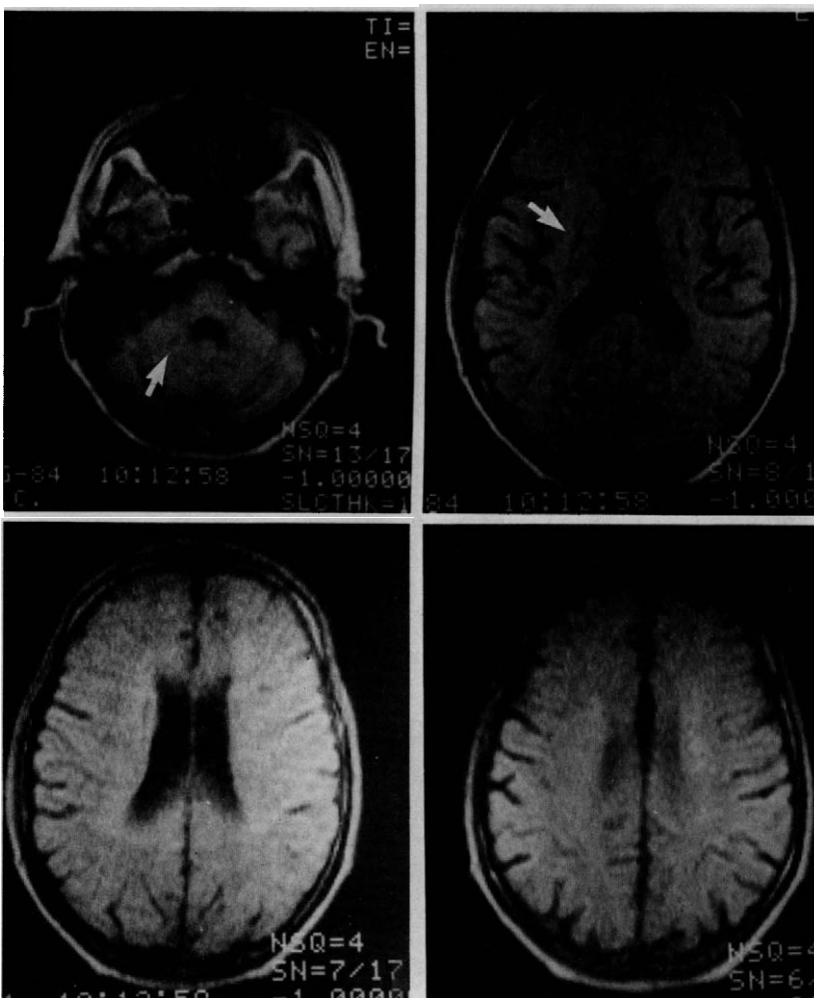


FIG. 2. Proton-density MR images show areas of decreased signal (solid arrows) which correspond to the areas of increased attenuation on CT.

form of microvascular insufficiency being responsible for this abnormal mineralization is a very interesting one since the deposits follow the course of the blood vessels. The results from the recent study of Belman et al³ demonstrate that the penetrating vessels of the basal ganglia are primarily involved by the calcific process. They have suggested that a vasculopathy may be the factor that eventually ends in calcification of the neuropil.

Conclusions

The presence of high-intensity signal on MRI with T2-weighted SE sequences and low-intensity signal on proton-density SE sequences is suggestive of high liquid content (long T1 and T2) such as is seen in edematous states.¹⁴⁻¹⁶ These areas appear distinct from the areas of mineral deposition, which have increased attenuation of CT and long T1 and short T2 on MRI. Perhaps these regions of edematous appearance represent the stage that precedes mineralization. Vascular membrane abnormalities may be responsible for the leakage of plasma-derived fluid, and this, in turn, may damage the neuropil and result in mineral accumulation. Further study of patients with cerebral mineralization using gadolinium-DTPA (diethylenetriaminepentaacetic acid) -enhanced MRI may be helpful in demonstrating abnormalities of the blood-brain barrier. In addition, since the edematous areas may be seen prior to mineral deposition, such a

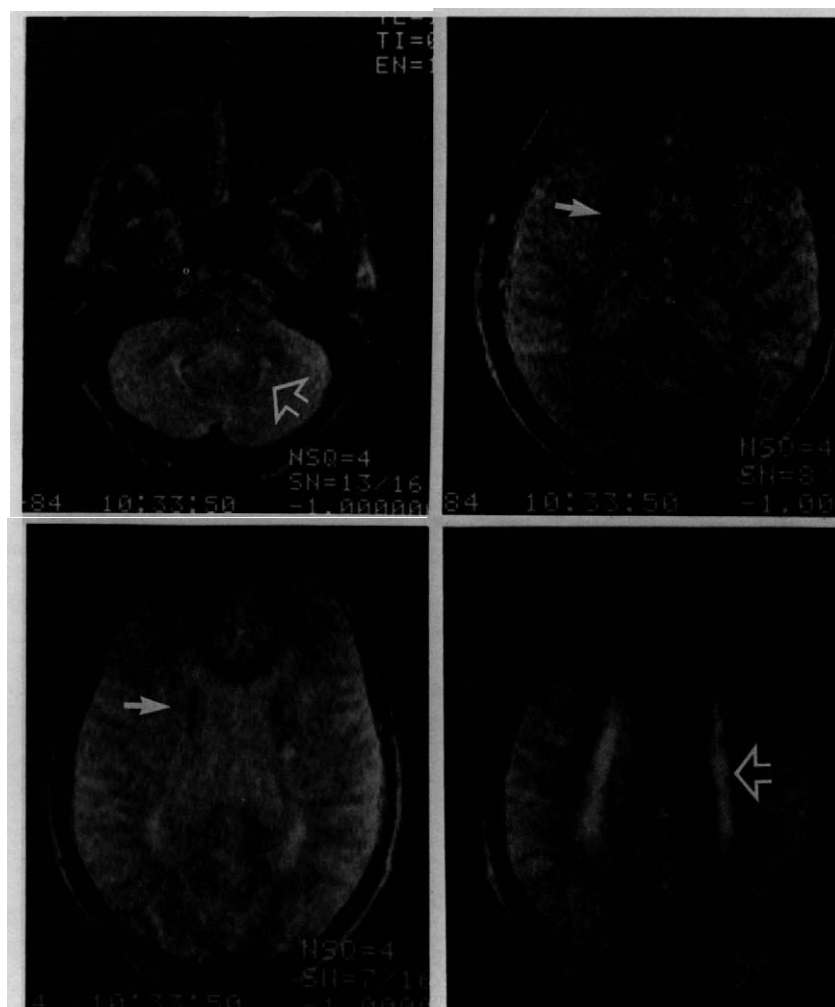


FIG. 3. T2-weighted MR images show areas of decreased signal intensity (solid arrows) corresponding to the areas seen in previous images and periventricular areas of increased signal (open arrows) representing "edematous" tissue.

finding may be useful in screening members of affected families.

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References

- Harrington MG, MacPherson P, McIntosh WB, et al: The significance of the incidental finding of basal ganglia calcification on computerized tomography. *J Neurol Neurosurg Psychiatry* 44:1168-1170, 1981.
- Scotti G, Scialfa G, Tampieri D, et al: MR image in Fahr disease. *J CAT* 9:790-792, 1985.
- Belman AC, Lantos G, Horoupian D, et al: AIDS: calcification of the basal ganglia in infants and children. *Neurol* 36:1192-1199, 1986.
- Lowenthal A, Bruyn GW: Calcification of the striato pallido dentate system. In: *Handbook of Clinical Neurology: Diseases of the Basal Ganglia*, Vol. 6, ed. by Vinken PJ, Bruyn GW. Amsterdam: North Holland Publishing, 1968, pp 703-725.
- Larsen TA, Dunn HG, Jan JE, et al: Dystonia and calcification of the basal ganglia. *Neurology* 35:533-537, 1985.
- Babbitt DP, Taug T, Dobbs J, et al: Idiopathic familial cerebrovascular ferrocalsinosis (Fahr's disease) and review of differential diagnosis of intracranial calcification in children. *Am J Roentgenol* 105:352-358, 1969.
- Boller F, Boller M, Gilbert J: Familial idiopathic cerebral calcifications. *J Neurol Neurosurg Psychiatry* 40:280-285, 1977.
- Caraceni T, Broggi G, Avanzini G: Familial idiopathic basal ganglia calcification exhibiting "dystonia musculorum deformans" features. *Eur Neurol* 12:351-359, 1974.
- Sala E, Savoildi F: Contributo alla conoscenza delle forme ereditaria della malattia di Fahr. *Nerv Sist* 11:46-73, 1959.
- Fahr T: Idiopathische verkalkung der hirngefasse zentralbl. *Allg Pathol* 50:129-133, 1930.
- Delacour A: Ossification des capillaires du cerveau. *Annales de Medicine et Psychologie* 2:458-461, 1850.
- Smeyers-Verbeke J, Minchott Y, Pelsmaeckers J, et al: The chemical composition of idiopathic nonarteriosclerotic cerebral calcifications. *Neurology* 25:48-57, 1975.
- Alajouanine TM, Contamin F: Crises a types d'epilepsie tonique sous-corticale avec depots calcaires intracerebraux et insuffisance parathyroïdienne, supprimees par le calciferol. *Ann Med Paris* 55:321-359, 1954.
- Norman RM, Ulrich M: The influence of a vascular factor on the distribution of symmetrical cerebral calcifications. *J Neurol Neurosurg Psychiatry* 23:142-147, 1960.
- Uzman LL: On the relationship of urinary copper excretion to aminoacidemia in Wilson's disease. *Am J Med Soc* 226:645, 1953.
- Zambramski JM, Spetzler RF, Kaufman B: MRI: Comparative study of radiofrequency pulse techniques in the evaluation of focal cerebral ischemia. *Neurosurgery* 16:502-510, 1985.