Fahr's Disease: A paradoxical appearance of calcification on MRI

G. Riley, R. Henderson
Department of Radiology, Darlington Memorial Hospital, Darlington, UK
garanriley@hotmail.com

Abstract

Fahr's Disease is a rare neurodegenerative disorder characterised by widespread calcification of brain parenchyma. We report a case of Fahr's Disease that demonstrates a specific appearance of calcium on MR imaging that is both unexpected and uncharacteristic. This paradoxical appearance of calcium on MR may appear in any condition in which calcium is a feature and be interpreted incorrectly.

Case Report

A 66 year old female presented with a year's history of reduced hearing and occasional tinnitus particularly involving the left ear. There was no recent head trauma or exposure to loud sounds. She had no other symptoms, took no medications and had no relevant past medical or family history.

On examination, both eardrums appeared healthy. Sounds were more audible via air conduction than bone conduction on both sides (positive Rinne's test). Weber's test, however, revealed asymmetry, and a pure tone audiogram confirmed bilateral sensorineural hearing impairment, worse on the left.

Due to the asymmetric findings, an MR scan of the brain and internal acoustic meatus was performed (sequences included axial T_2 and FIESTA, and coronal T_1 with and without gadolinium contrast). Analysis of the images allowed exclusion of a significant brain tumour or vestibular schwannoma. However, there were abnormal appearances of the basal ganglia and cerebellum bilaterally, characterised by discrete hypo intense signal voids representing mineralisation. Confusingly, these areas of signal void had adjacent hyper intense signal. This was more apparent on the T_1-weighted images (figure 1). The unusual appearances required correlation with CT, which did confirm the presence of symmetric, dense calcification in these regions (figure 2).

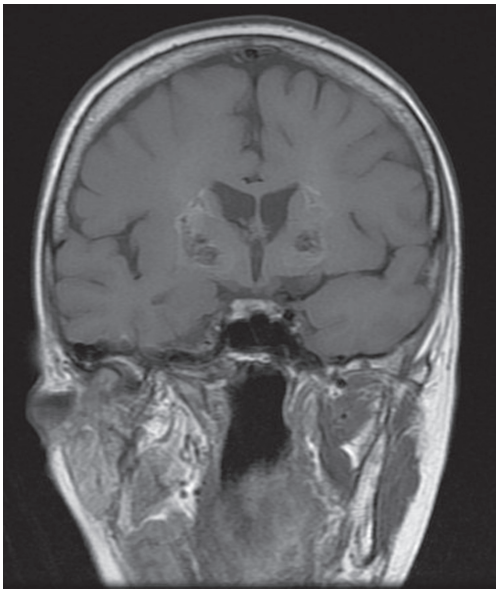

Figure 1.

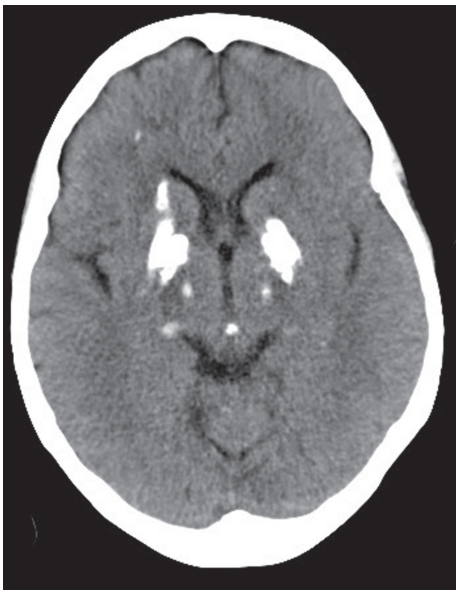

Figure 2.

Further evaluation with laboratory studies ruled out metabolic disorders, including hypoparathyroidism - and a diagnosis of Fahr's Disease (Brain Calcinosis Syndrome) was made.

Discussion

The diagnosis of Fahr's Disease (Brain Calcinosis Syndrome; BCS) is an uncommon one and, for our patient, the particular way in which it appeared on neuroimaging was peculiar and caused some initial confusion.

Brain Calcinosis Syndrome is a neurodegenerative disorder usually defined as "bilateral calcium accumulation in the brain parenchyma, primarily in the basal ganglia".[1] The diagnosis of BCS is typically made in the 4th-6th decade, and there may be progressive neuro-psychiatric and movement disorders. Extra-pyramidal signs and seizures of various types can also occur.[2,3]

There are more than 50 reported clinical conditions that have been associated with BCS.[1] Some of the more common are listed in table 1.

Differential diagnosis (table 1)	
Endocrine	Hypoparathyroidism Pseudohypoparathyroidism
Inflammatory	CMV Toxoplasmosis AIDS encephalopathy
Toxic	Hypoxia in the mature infant Radiation/Chemotherapy CO poisoning
Metabolic	Mitochondrial disorders Cockayne syndrome
Congenital	Tuberous Sclerosis
Idiopathic	Fahr's disease

Table 1.

Where a cause is identified it can usually be linked to abnormalities in calcium, phosphorous and parathyroid hormone metabolism - and most often hypoparathyroidism.[2] However, as exemplified by our case, about 80% of patients with BCS have normal biochemical serum markers, and most exhibit none of the typified clinical symptoms or signs.[1] These cases are seen to advance with age and are considered distinct from those associated with abnormal calcium and phosphorous metabolism. They occur either sporadically or as a result of a molecular genetic defect, of which numerous have been identified. The term 'Fahr's Disease' is reserved for those cases of idiopathic or genetic brain calcinosis.

Fahr's disease is usually identified on neuroimaging after appropriate interpretation of brain parenchymal calcification and its distribution. Brain calcifications are best observed on CT though historically plain x-ray imaging was relied upon. More recently Magnetic Resonance (MR) imaging with its increasing usage occasionally detects calcification incidentally – as in this case. The calcification of BCS has been shown to be similar in composition to that found in normal bone and tooth enamel,[4] and one study demonstrated its common biomaterial composition in a cohort of patients with BCS.[5]

Calcification on CT is characterised by areas of highly attenuating substance, with CT numbers (Hounsfield units - HU) in the order of +200 HU to +1000 HU. It is usually easy to identify and can be further scrutinised by selecting: 1) a window level similar to the CT number (i.e. 400); and 2) a wide window width (i.e. 1,800-2,000). Conversely, on MR imaging, calcification, particularly small amounts, can be more difficult to identify than on CT. With most MR sequences calcification is characterised by a signal void, due to the lack of mobile hydrogen nuclei.

The peculiar feature in the described case is the seemingly uncharacteristic appearance of the calcification, particularly on the T_1-weighted MR sequences. There are areas of paradoxical high signal tissue that correspond to the calcified brain parenchyma denoted on the subsequent CT images, instead of areas of pure signal void. Increased signal on T_1 is usually associated with exogenous contrast agent (chelated Gadolinium), denatured blood, melanin, fat or mucin.[6] The explanation offered

for the imaging phenomenon encountered in our presented case is that, in brain parenchyma, calcium may exist in hydrated crystal structures that do contain mobile hydrogen nuclei, and are thus detectable on conventional MR sequences.[6,7,8]

This paradoxical appearance of calcification on MR imaging has the potential to confuse and lead to misdiagnosis. For example, in this clinical context, areas of high signal on T_1-weighted images, with or without calcium, might make the interpreter include haemorrhage or metastases containing melanin, in their list of differentials. Also, if pre-contrast images are not obtained, then calcium deposition could be misinterpreted as areas of contrast enhancement.

In the reported case, the presenting complaint was of sensorineural hearing impairment and is unlikely to be associated with the calcium accumulation in the brain parenchyma. Since a clear biochemical pathogenesis was ruled out, and there were no other apparent symptoms thought to be a consequence of BCS, Fahr's disease was the most likely diagnosis. The subsequent management of our patient focused on symptomatic treatment of the hearing impairment with a hearing aid; and surveillance in the community for neurological and psychiatric occurrences. Genetic counselling of family members should be considered, considering the suggested inheritance patterns.[1,2]

References

1. Yasuhiko B, et al. Heredofamilial Brain Calcinosis Syndrome. Mayo Clinic Proceedings 2005; 80:641-51

2. National Institute of Neurological Disorders an Stroke. NINDS Fahr's Syndrome Information Page (www.ninds.nih.gov/disorders/fahrs/fahrs.htm) 2007

3. Fenelon G, et al. A prospective study of patients with CT-detected pallidal calcifications. Journal of Neurology, Neurosurgery and Psychiatry1993; 56:622-5

4. Smeyers-Verbeke J, et al. The chemical composition of idiopathic nonarteriosclerotic cerebral calcifications. Neurology 1975; 25:48-57.

5. Schoen FJ, et al. Biomaterial-associated calcification: pathology, mechanisms, and strategies for prevention. J Biomed Mater Res 1988; 22(suppl):11-36.

6. Boyko O, et al. Non-heme mechanisms for T1 shortening: pathologic, CT and MR elucidation. American Journal of Neuroradiology 1992; 13:1439-45

7. Tsuchiya K, et al. MRI appearances of calcified regions within intracranial tumours. Neuroradiology 1992; 35:341-4

8. Lecumberri C, et al. Intracranial calcifications on MRI. Radiologia 2006; 48:19-26

9. Avrahami E, et al. MRI demonstartion and CT correlation of the brain in patients with idiopathic intracerebral calcification. Journal of Neurology 1994; 241:381-4

10. Harrington MG, et al. The significance of the incidental finding of basal ganglia calcification on computed tomography. Journal of Neurology, Neurosurgery and Psychiatry 1981; 44:1168-70