Rare disease

Fahr's disease: an incidental finding in a patient of tubercular meningitis

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Summary

Fahr's disease, also known as idiopathic basal ganglia calcification, is a rare clinical entity characterised by bilaterally symmetric calcification of the basal ganglia. Most of the patients present with extrapyramidal symptoms, but the natural history, progression and treatment still remain unknown. We report a case of tubercular meningitis diagnosed by a cerebrospinal fluid examination with incidental findings of an extensive basal ganglia calcification on CT. CT of sibling, done to evaluate an episode of seizure, revealed strikingly similar calcification. Both these calcifications were due to Fahr's disease. The patient was treated with antitubercular and antiepileptic drugs. The patient fully recovered clinically and currently is seizure-free on antiepileptic treatment.

BACKGROUND

Fahr's disease is a rare degenerative neurological condition characterised by idiopathic calcification of the basal ganglia. A handful of cases have been reported in literature. Since it is idiopathic and no treatment is available, exclusion of all other causes of intracranial calcification is required before the diagnosis of Fahr's disease is made. Tubercular meningitis, a common disease in developing countries like India, can also be a cause of intracranial calcification and can present as diagnostic dilemma in rare cases.

CASE PRESENTATION

A 34-year-old man presented with complaints of a low-grade fever and headache for 1 month associated with a loss of appetite and weightloss. During the hospital stay, the patient had two episodes of generalised tonic-clonic seizures. The patient had no other neuropsychiatric complaints. There was no history of contact with tuberculosis or a history of tuberculosis. The patient's sibling also had a history of seizure episodes in the past. Upon examination, the patient had neck rigidity and a positive kernig's sign. Fundus examination was normal. The Mini-Mental State Examination score was 30/30. Rest of the neurological and systemic examinations were normal.

INVESTIGATIONS

Haemoglobin level, total and differential leukocyte count, liver function tests, renal function tests and electrolytes of index case were within normal limits. An ECG and a chest skiagram were normal.

The Mantoux test was positive (12×15 mm).

A cerebrospinal fluid (CSF) evaluation by lumbar puncture revealed sugar 40 mg/dl, protein 960 mg/dl, leucocyte count 56 with 94% mononuclear cells. Adenosine deaminase level of CSF was 41 IU/ml, PCR was positive for *Mycobacterium tuberculosis*, and Ziehl Neelsen stain demonstrated acid fast bacilli which confirmed the diagnosis of tubercular meningitis. A CSF examination for serology of

herpes simplex virus, Japanese encephalitis virus and neurosyphilis was negative.

Serum serology for HIV was negative.

A CT head of the patient (figure 1) revealed extensive bilateral symmetrical calcification of the basal ganglia, cerebellum and subcortical white matter.

To evaluate the causes of extensive intracranial calcification, various other investigations were carried out.

Calcium, phosphate, magnesium, vitamin D, parathyroid and calcitonin levels were normal suggesting normal calcium metabolism and parathyroid function.

Thyroid function tests (thyroid stimulating hormone, free triiodothyronine, free thyroxine) of the patient was done to rule out hypothyroidism which was within the normal limit.

To rule out infections like toxoplasma, neurocysticercosis, cytomegalovirus and HIV serology was done which was also negative.

Antinuclear antibodies were negative and the patient had no features suggestive of systemic illnesses like systemic sclerosis and systemic lupus erythematosus.

Since the patient had a family history of seizures in the elder sibling, a CT head of the sibling was done which revealed (figure 2) extensive symmetrical calcification of bilateral caudate nucleus, thalamus, putamen and globus pallidus. This suggested a genetic pattern of inheritance supportive of Fahr's disease.

All the above investigations mentioned in the index case were carried out in the sibling. All of these were within the normal limit.

DIFFERENTIAL DIAGNOSIS

Causes of brain calcification and their characteristic sites are as shown in table 1.

TREATMENT

The patient was treated with antitubercular drugs, steroid and oral antiepileptic drugs. His sibling was also treated with antiepileptics.

Figure 1 CT of the patient showing an extensive symmetrical calcification of bilateral basal ganglia, cerebellum and subcortical white matter.

Figure 2 CT of the sibling showing an extensive calcification of bilateral caudate nucleus, thalamus, putamen and globus pallidus.

Table 1 Causes of brain calcification and their characteristic sites

Lesion	Site of calcifications
Infections	
Tuberculosis	At the site of tuberculoma or tubercular abscess, that is, cortex, basal cisterns and meninges
CMV	Periventricular
HIV	Basal ganglia
HSV	Gyriform in cortex
Toxoplasma	Basal ganglia
Neurocysticercosis	Near cortex, brain stem
Endocrinopathies	
Hypoparathyroidism	Basal ganglia
Hypothyroidism	Rare calcification mostly with hypoparathyroidism
Miscellaneous	
Systemic disease like lupus	Extensive, associated with infarcts
Neoplastic	Anywhere
Fahr's disease or idiopathic calcification	Symmetrical basal ganglia and/or thalamus

HSV, herpes simplex virus; CMV, cytomegalovirus.

OUTCOME AND FOLLOW-UP

After 6 months of a follow-up, both the siblings are free of seizures and other neurological symptoms. They are maintained on antiepileptic drugs only.

DISCUSSION

After excluding other causes by extensive laboratory investigations, intracranial calcifications in our patient had two main differential diagnoses, tubercular meningitis and Fahr's disease.

Intracranial calcifications develop in 20–48% of patients with tubercular meningitis and usually appear 2–3 years after the onset of disease.¹ Calcifications in tuberculosis occur at the site of a tuberculoma or an abscess, that is, cortex, basal cisterns or meninges. Moreover, such symmetrical and bilateral calcifications are not seen in tuberculosis. Also, similar intracranial calcifications were present in the only sibling of index case, who did not have any history suggestive of tuberculosis. So the calcification in our case could not be attributed to tubercular meningitis.

Fahr's disease, also called idiopathic striopallidodentate calcinosis, non-arteriosclerotic cerebral calcification or idiopathic basal ganglia calcification, is a rare clinical entity characterised by bilateral symmetric calcification of the basal ganglia.

The diagnosis requires the following:

1. The presence of bilateral calcification of the basal ganglia;
2. The presence of progressive neurologic dysfunction;
3. The absence of an alternative metabolic, infectious, toxic or traumatic cause;
4. A family history consistent with autosomal dominant inheritance.

The diagnosis of Fahr's disease in our case was made on the basis of a family history, clinical, radiological and laboratory findings.

Our patient lacked extrapyramidal symptoms but generalised tonic clonic seizures were present. We also

diagnosed Fahr's disease incidentally and the patient may develop extrapyramidal symptoms later in the course of the disease. Similar cases with no extrapyramidal symptoms have been reported by Kotan *et al.*²

The disease was first noted by a German neurologist Karl Theodor Fahr in 1930, who reported the case of a 10-year-old boy under the title of 'Idiopathic calcification of the cerebral vessels'.³

The true prevalence of Fahr's disease is unknown, but an incidence of basal ganglia calcifications ranging from 0.24 to 2% has been reported in consecutive radiological studies, showing an evident relationship with an increasing age.^{1 4–6} Tedrus *et al.*⁴ reported an incidence of 0.68% among 3662 cranial CT scans analysed.

Fahr's disease may occur in a sporadic or familial manner. It is believed to have autosomal dominant inheritance, but a few cases may have autosomal recessive inheritance.⁷ Recent studies indicate a focus for Fahr's disease on chromosome 14q.⁸

Typically, the age at the onset of clinical symptoms is 30–60 years. The main neurological manifestations of Fahr's disease include motor disorders such as parkinsonism, dystonia, tics, speech alterations, epilepsy (with a new onset of generalised tonic-clonic seizures) and motor deficits, which are probably due to the involvement of the frontostriatal motor system.⁹

The most common radiological feature of Fahr's disease is the presence of bilateral intracranial calcifications which are usually seen in the globus pallidus, but may also affect the putamen, caudate nucleus, thalamus, dentate nucleus and white matter of the cerebral hemispheres.¹⁰

There is neither a cure for Fahr's disease, nor a standard treatment. The prognosis is variable and is hard to predict.⁸ There are no specific treatments to limit the progression.¹¹ Antipsychotics and antiepileptics help control the symptoms. No treatment recommendation is made for asymptomatic patients.

Learning points

- ▶ Tubercular meningitis can also cause intracranial calcification but only after a latent period of 2–3 years.
- ▶ Fahr's disease is a rare and an idiopathic cause of intracranial calcification.
- ▶ A family history is almost always available in Fahr's disease.
- ▶ Fahr's disease can present even without extrapyramidal symptoms.
- ▶ No cure is available for Fahr's disease, so exclusion of all other causes of intracranial calcification is a must.

Competi interests None.

Patient consent Obtained.

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