Dementia in a patient with Fahr's syndrome

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Abstract

Fahr's disease is characterized by idiopathic calcification of the basal ganglia and other brain regions. Clinically it may be accompanied by extrapyramidal and behavioural disorders. In Fahr's syndrome, the same pathology is due to another well-defined disease. Calcium/phosphate metabolic disorders, e.g. hypoparathyroidism or pseudohyperparathyroidism, may be involved. Here, we report a case of 62-year-old man presenting with severe dementia but only mild movement disorders and mild calcium metabolism abnormalities. Extensive brain calcifications together with unevenly distributed perfusion on single photon emission tomography are documented.

CASE REPORT

INTRODUCTION:

Fahr's disease was first described by Karl Theodor Fahr in 1930 as idiopathic calcifications in basal ganglia (Fahr, 1930). The clinical manifestation includes variable neurological disturbances, most commonly extrapyramidal symptoms. The disease may be sporadic or familial, with the usual onset of symptoms between the age of 30 and 50. Fahr's disease is often differentiated from Fahr's syndrome, in which a well-defined underlying cause (e.g. previous trauma, infection, intoxication, or a mitochondrial or metabolic disorder – most commonly hypoparathyroidism) can be found (Ring and Serra-Mestres, 2002). Sometimes a patient may present with psychiatric symptoms only, with no apparent neurological deficit (Mondrego *et al.* 2005, Weisman *et al.* 2007). In such cases the diagnosis of Fahr's disease/syndrome may be missed if appropriate brain imaging is not performed.

CASE REPORT:

62-year-old man was admitted for suicidal contemplations. In his history, no psychiatric heredity was found. He was divorced, with one healthy son. He had worked as a turner but retired due to his somatic diseases, namely coronary heart disease (history of myocardial infarction), arterial hypertension and chronic obstructive pulmonary disease. In 1982 he was admitted to the department of psychiatry due to a depressive disorder. At that time already, bilateral calcifications were seen on his brain CT scan, in the regions of basal ganglia (namely nucleus caudatus) and thalamus. No laboratory abnormalities in calcium/phosphorus metabolism were found.

Now he was admitted for suicidal contemplations due to his poor financial situation. His financial problems were caused by repeated, ill-judged and high loans from various financial institutions.

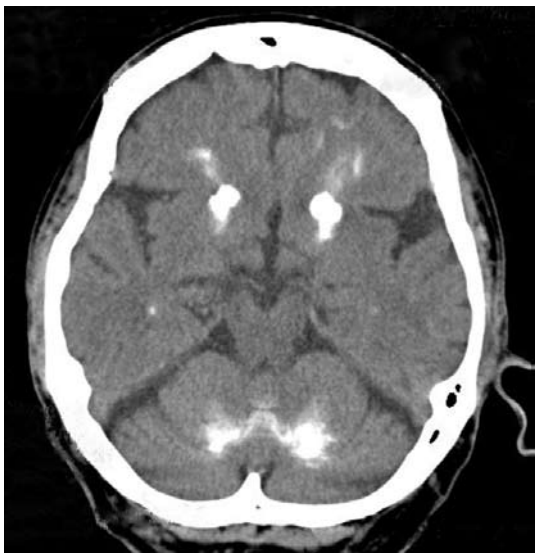

Figure 1. Brain CT scan

On admission, a cognitive deficit and mnestic disorders clinically predominated. The score of the Mini Mental State Examination (MMSE) was 25 (of a maximum 30 points). An organic brain disorder was therefore suspected, and appropriate brain-imaging methods as well as neuropsychological and neurological examinations were instituted.

CT showed extensive bilateral calcifications in the basal ganglia, dorsal thalamic nuclei, cerebellar nuclei, and in the external layers of the frontoparietal white matter, including iuxtacortical U fibers (Fig. 1). Single photon emission tomography (SPECT) showed severe hypoperfusion in the frontoparietal region, and less severe one also in basal ganglia and dorsal thalamus (Fig. 2). Also, cerebral atrophy and mild cerebellar atrophy was found.

Severely decreased intellectual capacity and impaired cognitive functions were clearly demonstrated using a battery of neuropsychological tests.

According to Wechsler Adult Inteligency Scale (WAIS-R) test, his total capacity of intelellective abilities ranged from bottom level of wider average to below-average. Numerically expressed, his result values in the tests include total capacity of intellective abilities (total IQ) of 87; capacity of nonverbal intellect was around 86 and capacity of verbal intellect around 90. Total intellective abilities were thus decreased significantly on the whole – by two standard deviations. Disturbance of multiple types of memory functions was found; namely of immediate mechanical or working memory both for verbal and nonverbal material, but also of visually constructional memory, spatially orientational memory, and of even elementary learning abilities (Fig. 3). Total capacity of memory abilities ranged from bottom level of wider average to below-average. Numerically expressed, the value of memory quotient MQ was 87. Also, in his attention flexibility and concentration and in verbal fluency as well as in visual-motoric and psycho-motoric coordination severe impairments were found. Significant impairment was also seen in Trail Making test part B and in London Tower test; here the patient, with increasing difficulty of the tasks, was gradually losing orientation and was not able to finish them. Executive functions of the patient are thus preserved at a considerably decreased level.

On neurological examination, a symmetrical extrapyramidal syndrome with mild hypokinesis and rigidity was observed. Thus, a combination of extensive brain calcifications with dementia and extrapyramidal symptoms were strongly suggestive of Fahr's syndrome.

As this has sometimes been related to hypoparathyroidism (Ring and Serra-Mestres, 2002), calcium/phosphate metabolism together with parathyroid hormone (PTH) and vitamin D/calcitriol status was evaluated (Table 1). Mild asymptomatic hypocalcemia was repeatedly found, with normal phosphatemia, magnesemia, PTH and vitamin D status. In consistently low calcemia, PTH level may be considered inadequately low (higher values may be expected in response to hypocalcemia). Also calcium urinary excretion was some-

Table 1. Variables relevant to calcium/phosphate/parathyroid hormone status

Variable	Values (... repeatedly measured)
Serum:	
Ca [mmol/L]	1.96 … 2.03 … 1.91 … 2.06 … 2.09 … 2.23 … 2.03
P [mmol/L]	1.28 … 1.01 … 1.10
Mg [mmol/L]	0.78 … 0.90 … 0.87
PTH [pg/mL]	38.5
25(OH)D [nmol/L]	88.9
$1,25(OH)_2D$ [pmol/L]	98.6
Albumin [g/L]	38.9
Arterial blood:	
pH	7.498
pCO_2 [kPa]	3.52
pO_2 [kPa]	14.8
BE [mmol/L]	–1.0
HCO_3^- [mmol/L]	23.6
Urine:	
Ca [mmol/L]	3.93
Creatinine [mmol/L]	7.9
Ca excretion [mmol/L GF]	0.038
Ca/creatinine [ratio in mmol/L]	0.5

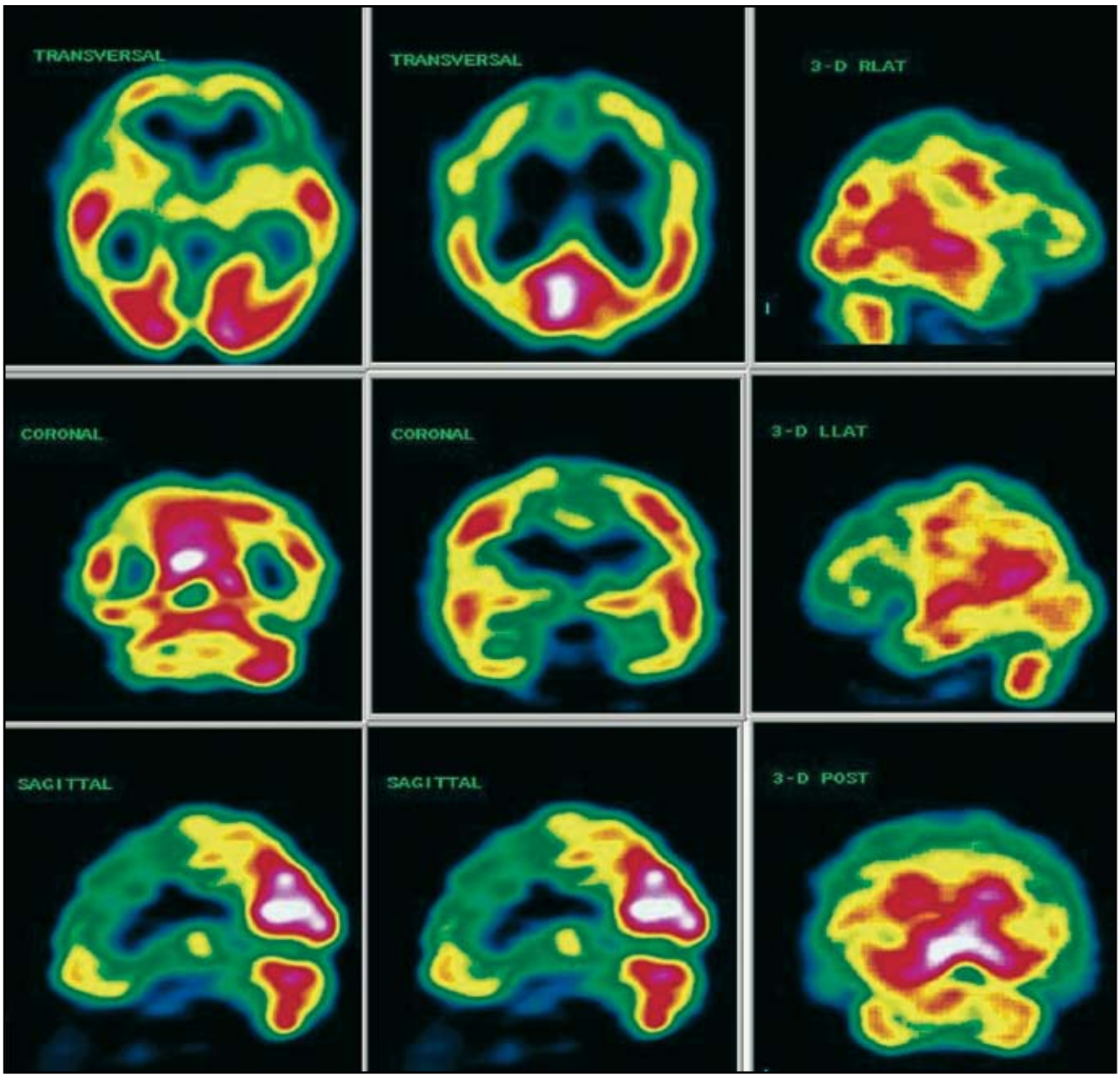

Figure 2. Brain single-photon emission computed tomography (SPECT).

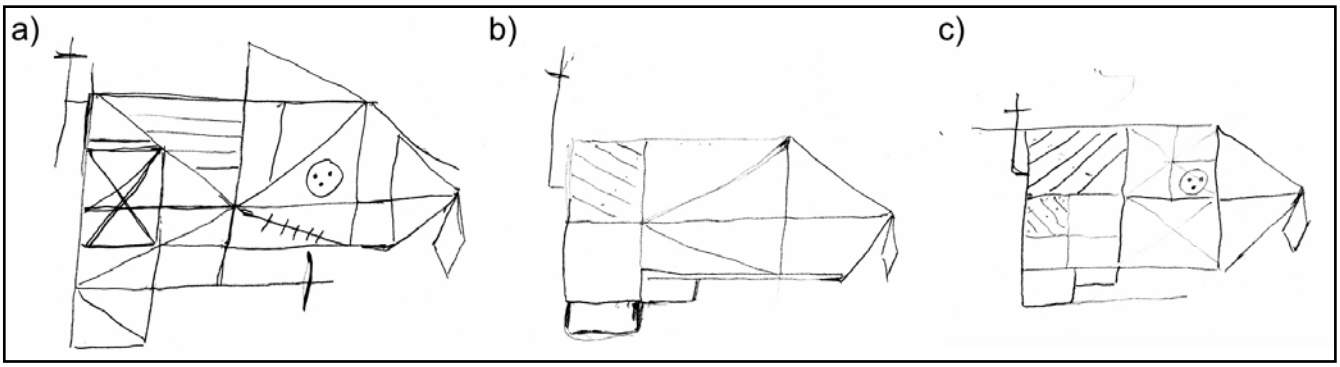

Figure 3. Rey Complex Figure: a) Immediate copy (with original pattern available); b) Copy after 3 minutes (without original pattern available); c) Reproduction after 30 minutes (without original pattern available). The impairment in constructive practice as well as in graphomotorics and short-term visual memory can be demonstrated. The delayed evocation ability was only partially affected.

what higher considering the low calcemia, suggestive of subnormal PTH activity in the kidneys (Peacock *et al*. 1969). Therefore, a mild (subclinical) hypoparathyrodism was postulated.

Consequently, the diagnosis of Fahr's syndrome was made. The diagnostic criteria of International Classification of Diseases, 10th edition (ICD-10) for "Dementia in diseases classified elsewhere" (F02.8) were fulfilled. He was treated with piracetam 3.6 g per day, together with training of cognitive functions. After 6 weeks he was discharged home, with the prospect of further care in a nursing home because 24-hour nursing care was necessary.

DISCUSSION:

Globus pallidum is the most common location of calcium deposits in Fahr's syndrome/disease. Calcifications may also be found in putamen, nucleus caudatus, capsula interna, nucleus dentatus, thalamus, cerebellum, and in the white matter, as it was in our patient. The clinical features corresponded well to the findings of imaging techniques. The observed mnestic disorders and severe alterations in the executive functions were in accord with the thalamic dammage and with the hypoperfusion in the frontoparietal cortex. The extrapyramidal syndrome with hypokinesis and rigidity was clearly connected to the calcification in basal ganglia.

With regard to calcium/phosphorus metabolism, a mild (subclinical) hypoparathyrodism was observed in our patient. Its cause and possible relation to the observed multiple brain calcifications remain uncertain. None of the obvious causes of parathyroid disorder were found (parathyroid development failure or destruction, hypomagnesemia, pseudohypoparathyroidism). It may tentatively be explained by an overactivity of calcium sensing receptor (Pearce *et al*. 1996); this would lead to hypocalcemic hypercalciuria, with urinary calcium to urinary creatinine ratio similar to our observations. Also, his respiratory alkalosis (if prolonged or repeated) may have decreased PTH activity in the kidneys (Krapf *et al*. 1992).

By definition, finding a mild hypoparathyroidism makes "Fahr's syndrome" a more appropriate diagnosis in our patient than "Fahr's disease". It may be argued, however, that in the published cases of Fahr's disease the tests mostly relied on serum calcium, phosphorus and parathormone levels, so that mild abnormalities might have been missed. Also, the abnormal (ectopic) calcifications do suggest a disorder in calcium/phosphorus metabolism (though still unresolved) in both entities.

Apart from hypoparathyroidism or pseudohypoparathyroidism, in a patient with the symptoms described above other disorders should be excluded (Sobrido *et al*. 2002). Most of them are rather rare metabolic abnormalities, e.g. Kenny-Caffey or Kearns-Sayre syndrome, chronic progressive ophthalmoplegia, Hallervorden Spatz disease (Zumrova *et al*, 2005). Also infections, both congenital (toxoplasmosis, rubella, cytomegalovirus or herpes simplex infections) and recent (AIDS) may be related to brain calcifications. None of them were present in our patient.

Finally, calcifications in basal ganglia may incidentally be found in elderly people with no important clinical symptoms. Thus, their relation to the mental and neurological symptoms may be less clear. In our patient, however, the calcifications in basal ganglia were already found 25 years ago – at the age of 37 – during his hospital stay for a depressive disorder. It is tempting to speculate that his depressive symptoms might have already been connected to this finding but no clear-cut relation could be postulated. We presume that further calcium deposits developing thereafter in other brain regions have gradually impaired his mental capacity, leading to dementia.

The severe decline of his cognitive abilities, and namely of executive functions, has caused his financial problems. He got several ill-judged loans, could not manage his financial affairs properly, and his enterprise plans were never fulfilled. Finally he got into this life crisis.

As he contemplated suicide he was admitted to the department of psychiatry. Here, the diagnosis of dementia in Fahr's syndrome was made.

This case clearly demonstrates the importance of thorough neurosomatic examination, laboratory tests and brain imaging in patients with predominating psychiatric symptoms.

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