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CASE REPORT

Fahr's Syndrome Presenting with Dementia and Severe Hypocalcemia Decades after Total Thyroidectomy in A Woman Affected by Chronic Renal Failure and Psoriatic Arthritis: A Precipitating Role for Risankizumab?

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Abstract

Introduction: Fahr's phenomenon is a rare neurological disorder characterized by calcifications of several structurers of the human brain, including the basal ganglia, the dentate nuclei of the cerebellum, the thalamus, and the hippocampus. It may exist in an idiopathic form or it can be associated to calcium dysmetabolism due to parathormone (PTH) defect or signaling. Symptoms may span from parkinsonism to psychiatric syndromes, ataxia, convulsive seizures and dementia.

Case presentation: A 68-years old woman who had undergone to thyroidectomy for nodular thyreopathy at age 20, was referred to my attentions from her relatives for the recent onset of a rapid progressive dementia syndrome characterized by memory impairment, mutacism, social withdrawal, and digital stereotypies. Comorbidities included juvenile cataract surgery, mild chronic renal failure and a recent diagnosis of psoriatic arthritis which was being challenged with Risankizumab, a humanized immunoglobulin (Ig) G1 monoclonal antibody directed against the p19subunit of interleukin (IL)-23. Magnetic Resonance Imaging (MRI) of the brain revealed bilateral although asymmetric basal ganglia calcifications. Blood exams revealed severe hypocalcemia and hypoparathyroidism.

Conclusion: Treatment in these cases is directed toward hypocalcemia and the underlying primary pathologies, even reviewing ongoing therapies which may interfere with calcium metabolism.

Keywords

Fahr's syndrome, Hypoparathyroidism, Chronic renal failure, Hypocalcemia, Psoriatic arthritis, Risanzikumab

Case Report

Fahr's disease and Fahr's syndrome are two conditions characterized by calcification in the brain resulting in neurological or psychiatric sequelae. Fahr's disease is a congenital (autosomal dominant or recessive) disorder with an age of onset from 40 to 60 years [1]. Fahr's syndrome presents at variable age, and the bilateral intracranial calcification is associated with an underlying disorder such as idiopathic hypoparathyroidism, secondary hypoparathyroidism, pseudohypoparathyroidism, or hyperparathyroidism [2].

Parathormone (PTH) is critical for calcium and phosphate metabolism and defects in its levels as it may occur in complete remotion of all parathyroids during total thyroidectomy lead to chronic hypocalcaemia and to a complex chronic syndrome which includes cataract, moniliasis of the nails, increased neuromuscular excitability, as well as heterotopic calcification of soft tissues [3].

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Clinical Report

A 68-years old female was referred to my attention complaining the rapid onset of memory impairment, mutacism, difficulties in planning her daily activities and tapping her finger in a stereotyped manner. Her past medical history was significant for a total thyroidectomy she had undergone for a nodular thyropathy when she was 20. Some years later she received a bilateral surgery for cataract. Five years before my examination, she was diagnosed with mild renal failure of undetermined origin. Two years before she received diagnosis of psoriatic arthritis and started therapy with Risankizumab, a humanized immunoglobulin (Ig) G1 monoclonal antibody directed against the p19 subunit of interleukin (IL)-23. Ongoing pharmacological therapy included levotiroxine, furosemide, atenolol and ezetimibe.

Neurological examination revealed a dysexecutive syndrome including failure of mental flexibility, phonemic fluency, self-inhibition and of sequential complex tasks. Frontal Assessment Battery (FAB) was 11/18 and MMSE was 25/30. Speed and amplitude in rapid alternating movements of hands and feet were slightly reduced on the left side but rigidity was absent. No other pathologic signs were apparent.

Brain MRI was prescribed and showed bilateral deposition of calcium within basal ganglia although more pronounced on the right side (shown in Figure 1).

Additional blood examinations showed severe hypocalcemia (4.9 mg/dl reference normal values: 8.8-10.5), hyperphosphatemia (6.5 mg/dl; n.v. 2.5-4.5), reduced PTH (5.1 µg/ml; n.v. 6.5-36.0), as well as reduced renal excretion of calcium (34 mg/24h; v.n. 50-250) and phosphate (0.2 g/24 h; v.n. 0.3-10), creatinine (125 πmol/l; v.n. 62-106), urea (8.7 mmol/l; v.n. 2.8-8.1).

Therapy included 10 ml vial of 10% calcium gluconate diluted to 5% glucose solution once a day for five days. At the end of intravenous cycle, she started calcium carbonate 1000 mg tablet t.i.d. a day and calcitriol 0.25 µg b.i.d. up to normalization of calcemia which was achieved four weeks later.

Discussion

The causes of hypoparathyroidism are varied and include surgery on the neck as the most frequent cause, accounting for about 75% [3]. In this case, juvenile thyroidectomy had been critical for development of hypoparathyroidism. The patient, indeed, had developed bilateral cataract early in her life which is often a consequence of chronic hypoparathyroidism. Onset of chronic renal failure later in her life may had augmented loss of serum calcium which was not counteracted by a balancing increase of PTH due to already existing hypoparathyroidism. Fahr's syndrome may arise from hypoparathyroidism [4-6] and may present with either dementia, extrapyramidal or psychiatric symptoms although at different age of onset [6-8]. Of note, the patient had never reported, nor she had at neurological examination, signs of increased neuromuscular excitability such as tetany or spasms, which are extremely frequent with an underlying severe hypocalcemia [3]. This may suggest that, even though hypoparathyroidism was persistent from almost five decades, some other precipitating factors, in addition to chronic renal failure, may have disrupted her labile steady-state more recently. Hypocalcemia

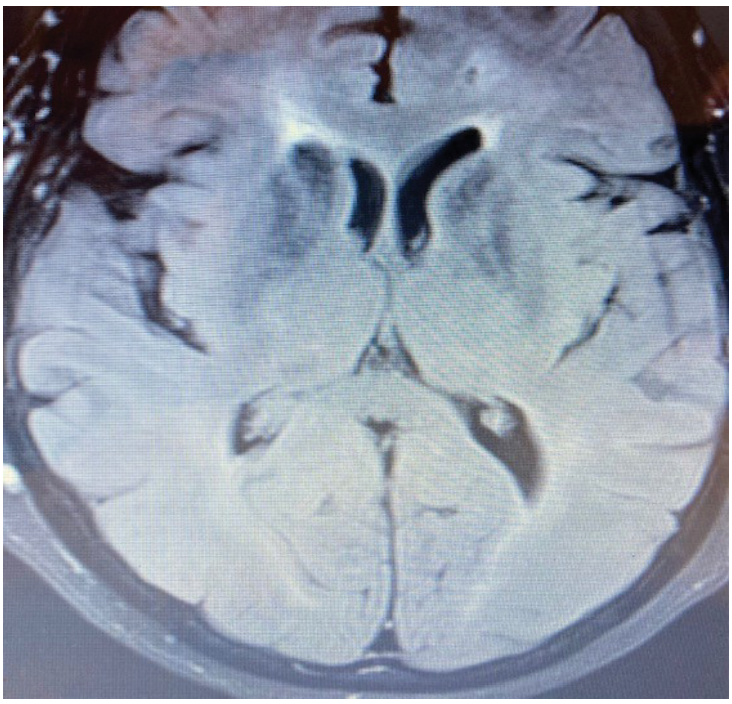

Figure 1: Magnetic resonance imaging of subject's brain showing bilateral basal ganglia calcification.

associated with disorders of the parathyroid gland may precipitate psoriasis vulgaris and pustular psoriasis [9]. The etiological role of calcium in psoriasis pathogenesis remains unclear. Of relevance, the patient was diagnosed with psoriatic arthritis two years earlier. It is noteworthy that IL-23, a cytokine considered critical in development and pathogenesis of psoriatic arthritis, induces bone erosion through stimulation of osteoclasts [10]. Administration of Risankizumab in this patient may have counteracted subsidiary mechanisms of bone adsorption associated to inflammatory cascade thus worsening metabolism associated to calcium.

The proposed pathogenic cascade leading to severe hypocalcemia and Fahr's syndrome in this patient should have started with thyroidectomy-associated hypoparathyroidism fifty years later, augmented by chronic renal failure and finally acutely precipitated by Risankizumab administration.

Rapid progressive dementia, especially when associated to "red flags" such as hypo or hyperkinetic movement disorders or their coexistence, should strongly suggest an etiology other than Alzheimer's disease and indicate MRI as well as a complete metabolic screening.

Acknowledgement

None.

Data Availability

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

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None.

Author Contributions

Maurizio Giorelli conceived the work, Tommaso Scarabino performed and discussed MRI, Donato Jacobone discussed the case, and Pasquale Difazio provided supervision indispensable suggestions.

Figures

The figure is the original one made by the authors for this article and have not been published previously.

Conflict of Interest

There is no conflict of interest to disclose.

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