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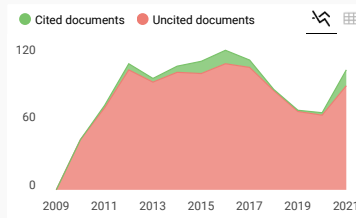
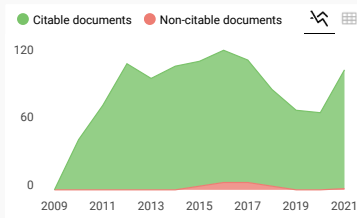
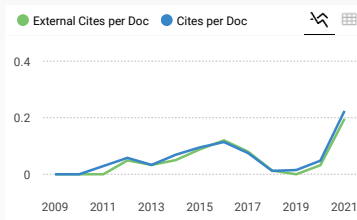
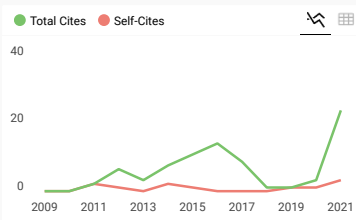
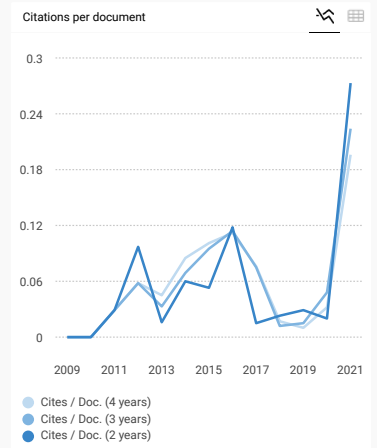
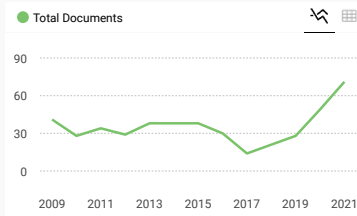
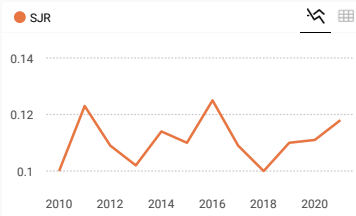
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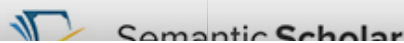
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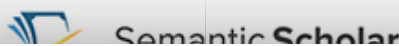
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Secondary Fahr's disease: A differential to be considered in a COVID-19 pneumonia patient with neuropsychiatric presentations

Felicitas Farica Sutantoyo, Paulus Sugianto

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ABSTRACT

Background, aim. Fahr's disease is a rare neurodegenerative disease caused by intracranial calcifications. This case report aims to accentuate the importance of considering rare disease like Fahr's disease as the differential diagnosis of neuropsychiatric deficits, especially in patients with a history of thyroidectomy.

Case presentation. A 50-year-old female who underwent thyroidectomy 5 years previously presented with incoherent speech, behavioural problems, and hand stiffness. On evaluation, several neurobehavioral deficits and carpopedal spasms were observed, along with low Mini-Mental State Examination (MMSE), Hachinski, Activities of Daily Living (ADL), and Instrumental Activities of Daily Living Scale (IADL) score of 22, 4, 13, and 12, respectively. Clinically significant laboratory abnormalities include low serum calcium of 4.7 mg/dl, low thyroid stimulating hormone (TSH) level of 0.113 mIU/l, and low parathyroid hormone (PTH) level of 1.2 pg/ml. In addition, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) reverse transcription-polymerase chain reaction (RT-PCR) test showed a positive result. Meanwhile, brain computerized tomography (CT)-scan results showed multiple bilateral calcifications in the basal ganglia, bilateral cortical-subcortical calcifications in the frontal lobe, and subcortical calcification in the left frontal lobe.

Results. The patient was diagnosed with Fahr's disease secondary to post-thyroidectomy hypoparathyroidism and coronavirus disease 2019 (COVID-19). The patient was treated with calcium lactate, levothyroxine, donepezil, favipiravir for COVID's infection, vitamin B1, B6, and B12.

Conclusions. Fahr's disease should be considered in patients with neuropsychiatric deficits and spasm disorders, especially in patients with a history of thyroidectomy. Routine follow-up CT-scans after thyroidectomy are recommended.

Keywords: basal ganglia calcification, Fahr's disease, hypoparathyroidism

INTRODUCTION

Fahr's disease is one of the rarest neurodegenerative diseases with a very low prevalence (approximately less than one per million population) and is considered underreported. It was first discovered in 1930 by a German pathologist, Karl Theodor Fahr, who described a case of a male patient presented with symmetrical calcifications of the basal ganglia and cerebral cortex [1,2]. Fahr's disease can be classified as primary and secondary. Primary Fahr's disease is an inherited disease characterized by the presence of an abnormal autosomal dominant or

recessive genetic trait. Meanwhile, secondary Fahr's disease (also known as Fahr's syndrome) is caused by known etiologies and commonly characterized by the presence of endocrinopathies [3]. Patients with a history of thyroidectomy are at risk of developing hypoparathyroidism which is considered a rare metabolic disorder. Hypoparathyroidism causes a decrease in parathyroid hormone secretion which eventually causes hypocalcaemia and calcifications.[4] In this case report, we reported a case of a COVID-19 female patient with a history of thyroidectomy and was diagnosed with Fahr's disease. We

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aim to accentuate the importance of considering rare disease like Fahr's disease as the differential diagnosis of neuropsychiatric deficits, especially in patients with hypoparathyroidism who underwent thyroidectomy.

The patient has given permission and informed consent for the publication of this case report.

CASE PRESENTATION

A 50-year-old female patient was admitted to the hospital upon a previous hospital referral with suspected encephalitis. The patient's family noticed changes in the patient's overall behaviour, including incoherent speech, forgetfulness, and blank stare since the last 9 days before admission. Incoherent speech was fluctuating, however, since the last 3 days before admission, it has gotten worse and the patient was unable to carry out daily activities as a housewife. According to the patient's family, the patient has never experienced similar complaints before. Moreover, the patient's hands often looked stiff and have gotten worse since the last 2 days before admission, the patient's family was worried that these symptoms are part of seizures. In addition, the patient also had complaints of cough and cold with white nasopharyngeal discharge since the last 7 days before admission. Weakness or tingling of the body, headache, fever, shortness of breath, sore throat, and micturition or

defecation disorders were denied. The patient had undergone a thyroidectomy in November 2016, with anatomical pathology examination results, namely an adenomatous goitre with bleeding without signs of neoplasm. The patient consumed levothyroxine after the thyroidectomy for an unknown period of time until her thyroid value was considered normal. History of stroke, tumour, trauma, central nervous system infection, autoimmune disorder, similar symptoms in the family, contact with COVID-19 patients was denied. History of narcotic and psychotropic drugs consumption, smoking, alcohol consumption, tattoo, and unhealthy sex was also denied.

On admission, the patient's vital signs were within normal limits, the patient had a blood pressure of 120/70 mmHg, heart rate of 110/minute, respiratory rate of 20/minute, and oxygen saturation of 98% on room air. The patient's neurological examination results were also within normal limits. The patient later underwent neurobehavioral assessments. Based on neurobehavioral assessments, cognitive impairments in memory, attention, language/verbal and visual-spatial domains were observed, with a Mini-Mental State Examination (MMSE) total score of 22/30. Next, laboratory test results showed low serum calcium of 4.7 mg/dl, low thyroid stimulating hormone (TSH) level of 0.113 mIU/l, and low parathyroid hormone (PTH) level of 1.2 pg/ml, which indicated hypocalcaemia and hypoparathyroidism.

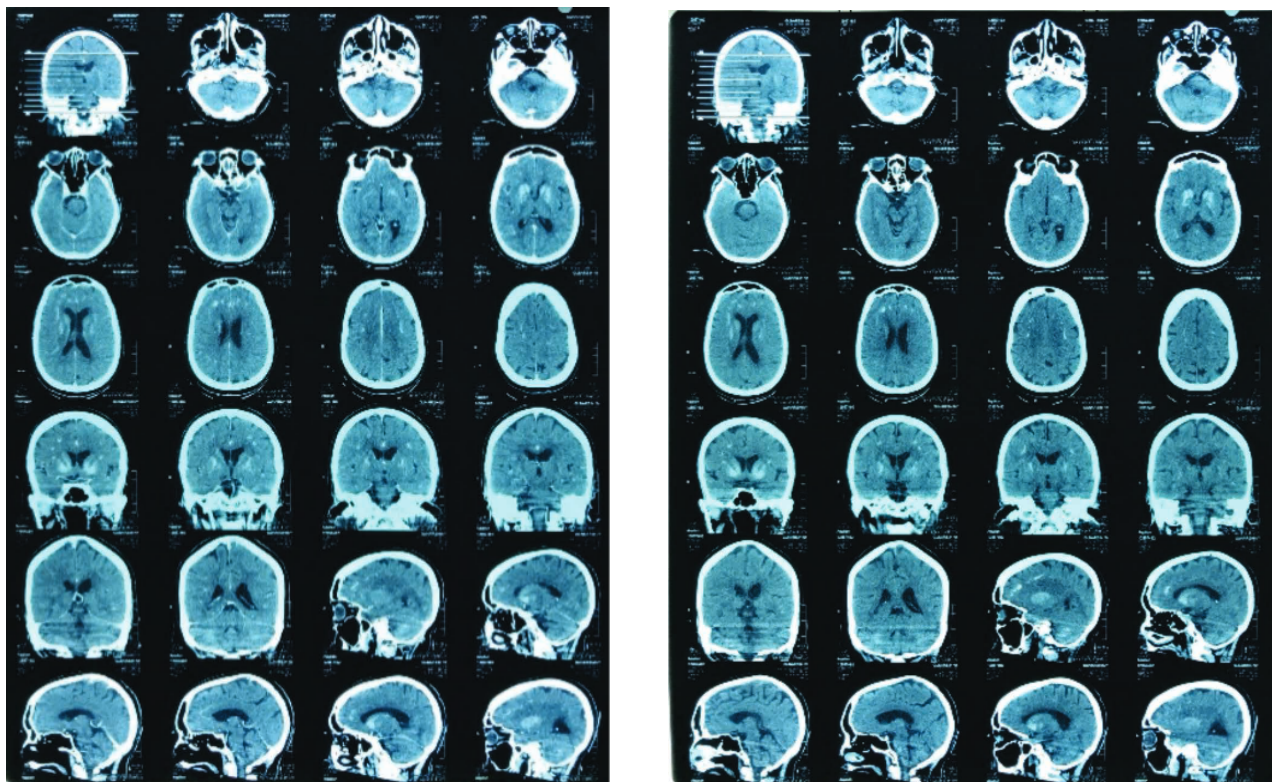


FIGURE 1. CT-scan of the brain shows multiple intracranial calcifications

Electroencephalogram (EEG) showed normal results which excluded the suspicion of seizures. In addition, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) reverse transcription-polymerase chain reaction (RT-PCR) test showed a positive result. Furthermore, brain computerized tomography (CT)-scan results showed multiple bilateral calcifications in the basal ganglia, bilateral cortical-subcortical calcifications in the frontal lobe, and subcortical calcification in the left frontal lobe (as shown in Figure 1).

Based on the clinically significant findings, the patient was diagnosed with Fahr's disease secondary to post-thyroidectomy hypoparathyroidism and coronavirus disease 2019 (COVID-19). The patient was treated with 5 g of 20% MgSO₄ in 0.9% NaCl by drip for 24 hours, 3x2 ampules of calcium gluconate in 0.9% NaCl by drip, 2x1 g of intravenous ceftriaxone, 1x5 mg of oral donepezil, 1 x 100 mcg of oral levothyroxine, 2x1 tablet of oral vitamin B1, B6, and B12, 3 x 1000 mg of oral calcium lactate, and 2 x 1600 mg for loading dose and continued 2 x 600 mg for 5 days of favipiravir. After being discharged from the hospital, the antibiotic therapy was replaced by 2 x 100 mg of oral cefixime and the previous oral therapies were continued.

DISCUSSION

Fahr's disease (or Fahr's syndrome), also known as basal ganglia calcification, is a rare neurodegenerative disease. Fahr's disease is characterized by a wide range of progressive neuropsychiatric symptoms [2,5]. Neuropsychiatric and cognitive impairment are common and progressive. Neuropsychiatric symptoms might be the first or the most common features of Fahr's disease, ranging from mild concentration and memory deficits to personality and/or behaviour changes. In some extreme cases, it might also lead to psychosis and dementia. The patient in this case had a low MMSE score with marked cognitive impairment in memory, attention, language/verbal and visual-spatial domains which might be caused by Fahr's disease-related mild cognitive impairment, however, further evaluation is needed to observe the changes in the patient's behaviour [6,7]. In addition, the patient was also confirmed with COVID-19 pneumonia which could exacerbate the neuropsychiatric symptoms. According to Ticinesi et al., neuropsychiatric symptoms (i.e. delirium) are common in COVID-19 patients, especially in geriatric patients with neuropsychiatric comorbidities [8,9].

Furthermore, it was known that the patient has a history of thyroidectomy with a marked decrease

in serum calcium, TSH, and PTH level, which indicated hypocalcaemia and hypoparathyroidism. According to similar case reports by Arruda et al. and Zhou et al., patients with a history of thyroidectomy are at risk of developing hypoparathyroidism, a rare metabolic disorder that can cause a decrease in parathyroid hormone secretion which later disturb calcium mobilization from bone and calcium reabsorption from kidneys and gut. This condition eventually causes hypocalcaemia and calcifications. Although rare, this condition can also cause intracerebral calcifications which later manifested as Fahr's disease [4,10].

CT-scan and magnetic resonance imaging (MRI) are widely used to identify mineral depositions. Calcified areas are identified as hyperdense lesions on CT-scan which is considered crucial for diagnosis. On brain CT-scans, Fahr's disease is characterized by bilateral basal ganglia calcification and usually associated with phosphorus and/or calcium metabolism disorders. Calcium deposits consist up of calcium carbonate and calcium phosphate which are most commonly located in the basal ganglia, followed by thalamus, hippocampus, cerebral cortex, cerebellar subcortical white matter, and dentate nucleus [2,5,11,12]. In this patient, the brain CT-scan results showed multiple bilateral calcifications in the basal ganglia, bilateral cortical-subcortical calcifications in the frontal lobe, and subcortical calcification in the left frontal lobe, which are considered decisive for the diagnosis of Fahr's disease.

To date, there is no definitive cure for Fahr's disease yet. The treatment for Fahr's disease targets the symptoms and quality of life improvement. Treatment of underlying conditions like hypoparathyroidism has been shown to improve the symptoms, however, there are no specific treatments that can limit the progression of intracerebral calcifications. The prognosis is variable, unpredictable, and is known to be unrelated to the calcification extent. If not treated properly, progressive neurological deterioration may result in disability and death [13,14].

CONCLUSIONS

Fahr's disease should be considered as one of differential diagnoses in patients with neuropsychiatric deficits and spasm disorders, especially in patients who underwent thyroidectomy who are in risk of hypoparathyroidism. Therefore, we recommend routine follow-up CT-scans after thyroidectomy which enables health care providers to detect and treat Fahr's disease as early as possible.

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