International Journal of Research and Review
Vol. 10; Issue: 7; July 2023
Website: www.ijrrjournal.com
Case Report *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

Cognitive Impairment in Patient with Fahr's Syndrome Related to Hypoparathyroidism: A Case Report and Literature Review

Richard Suherlim, AAA Putri Laksmidewi, AAA Meidiary, Sri Yenni Trisnawati GS

Department of Neurology, Faculty of Medicine, Universitas Udayana, Prof. Dr. IGNG Ngoerah General Hospital, Denpasar, Bali Indonesia

Corresponding author: AAA Putri Laksmidewi

DOI: https://doi.org/10.52403/ijrr.20230756

ABSTRACT

Fahr's syndrome is a very rare neurological disease, in which there is symmetrical and bilateral abnormal calcium deposit in brain areas such as basal ganglia, thalamus, cerebral cortex, subcortical, and hippocampus. Based on epidemiological studies, prevalence of Fahr's syndrome is less than 1 case per 1 million. Fahr's syndrome can be caused by a variety of conditions, the most common of which is hypoparathyroidism. This article reports a 51-year-old female patient with seizures and cognitive impairment in the memory and visuospatial domains with Fahr's syndrome associated with hypoparathyroidism caused by complication of her previous thyroidectomy. This is thought to be caused by the presence of calcifications in areas that interfere with neuronal function and also decreased glucose metabolism in these areas. It is important for the patient and family to know the disease. In addition to pharmacotherapy, education to the patients and their families is also very important. They have to do regular check-ups to evaluate the occurrence of long-term complications of Fahr's syndrome.

Keywords: Fahr's syndrome, cognitive impairment, hypoparathyroidism, seizure

INTRODUCTION

Fahr's syndrome is a very rare neurological disease. This condition was first introduced by a German neurologist named Karl Theodor Fahr in 1930. This condition is characterized with symmetrical and bilateral abnormal calcium deposit in brain areas such as basal ganglia, thalamus, cerebral cortex, subcortical, and hippocampus. Based on epidemiological studies, prevalence of Fahr's syndrome is less than 1 case per 1 million. [1,2]

Fahr's syndrome and Fahr's disease are distinguished by their etiology, whereas Fahr's disease must be proven by a genetic abnormality, while Fahr's syndrome is a condition with features similar to Fahr's disease caused by another condition. One of the conditions that often causes Fahr's syndrome is hypoparathyroidism. [3]

The pathophysiology of calcification in the brain parenchyma starts from the walls of blood vessels and perivascular spaces which eventually spreads to neurons. In hypoparathyroidism, reduced parathyroid hormone causes hyperphosphatemia and hypocalcemia leading to calcification. [1] The most common symptoms of Fahr's syndrome were movement disorders (55%), cognitive impairment (39%), speech disorders (36%), cerebellar disorders (36%), and psychiatric symptoms (31%). [4]

The management of Fahr's syndrome is to treat the underlying disease and monitor the progress of the symptoms. Currently there is no treatment that can reduce calcifications in

the brain. [5] The prognosis of patients with Fahr's syndrome is very difficult to predict because there is no significant correlation between age, extent of calcium deposits, and neurological symptoms that appear. [6]

CASE PRESENTATION

A 51-year-old Balinese woman, was referred from a private hospital to the ER of Sanglah Hospital with the main complaint of seizures that occurred 2 times that day. The first seizure occurred at around 10:00 AM when the patient was sitting suddenly fell on his back with the whole-body stiff. The duration of the seizure is about 15 minutes. The second seizure occurred in the parking lot of a private hospital, the seizure occurred in the same pattern, after which the patient slowly returned to consciousness. While in the ER, the patient had a non-contrast head CT scan which the results showed many hyperdense lesions. (Figure 1)

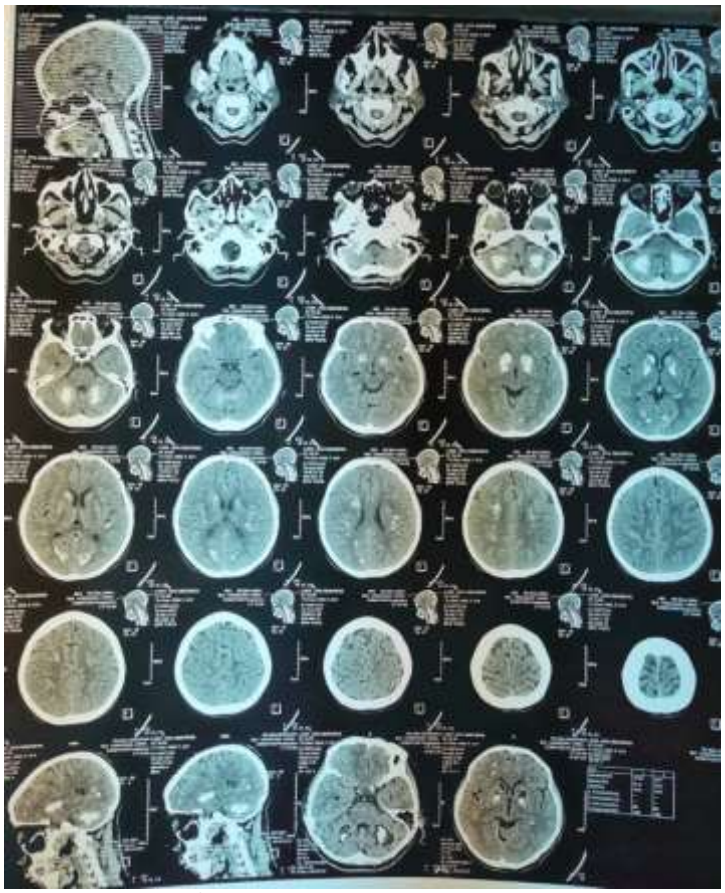

Figure 1. CT scan of the head without contrast in an outside private hospital

In the ER at Sanglah Hospital, the patient was aware although sometimes she was a little restless. According to the family, she often complains of forgetfulness since the last 2 years. Patients often forget to store their belongings and forget the names of friends or relatives. However, the patient is still able to carry out daily activities without assistance so that these complaints are not paid much attention.

The patient has a history of hypertension since 2002 but is not routinely monitored. In 1986 she had undergone thyroid surgery. There are no routine medications that she is currently taking. According to the patient and family, there was no family member who had a history like that experienced by the patient. The patient daily works as a trader in the market. The patient's last education was grade 4 elementary school, but the patient could read and write well.

On physical examination, the patient was aware with stable hemodynamics. On neurological examination, there was no

cranial nerve palsies, motor was within normal limits, no pathological reflexes were found, and neither Chvostek's sign nor Trousseau's sign was found. Laboratory examinations in the ER showed almost all results were within normal limits except for calcium and phosphate. CBC, blood sugar, hemostasis function, liver function, kidney function, blood gas analysis, sodium, potassium, and magnesium were within normal limits. Inflammation markers increased with ESR 111 and CRP 8.38. The patient's calcium was very low (5,6 mg/dL) and accompanied by elevated phosphate levels (6,01 mg/dL).

The patient was treated with phenytoin 3x100 mg IV and folic acid 1x1 mg PO. Hypocalcemia was consulted to an internist and given calcium gluconate drip and periodic evaluation of calcium levels. The condition of hypertension was consulted to a cardiologist and given ramipril 1x2.5 mg PO and planned for a full study echocardiography.

The patient was then subjected to laboratory tests of thyroid function and thyroid ultrasound. TSH and FT4 results were still within normal limits. Thyroid ultrasound revealed a decrease in the right and left parathyroid echo parenchyma with calcifications. She also underwent an EEG examination, which was within normal limits. The patient was also checked for intact PTH levels, the results showed that she has low parathyroid hormone with a PTH of 6.08 pg/mL.

During hospitalization, the patients were examined for MoCa-Ina and MMSE, then continued with ADL/IADL examinations, the Hamilton depression scale, and the Galveston orientation test. The ADL/IADL examination, the Hamilton depression scale, and the Galveston orientation test were within normal limits. For the MoCa-Ina examination, the patient scored 15 out of 30, for the MMSE the score was 22 out of 30. (figure 2)

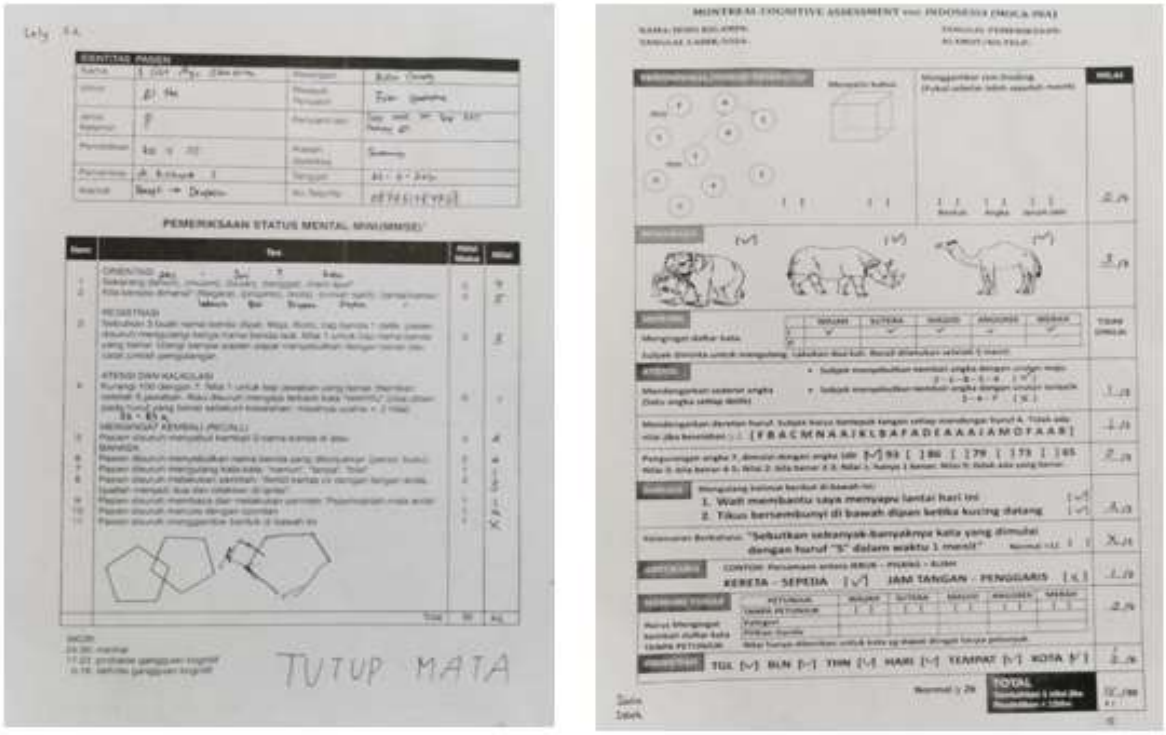

Figure 2. MMSE and MoCa-Ina

Based on the examination, the most disturbed domains were memory and visuospatial so that the examination was continued with a memory test, trail making test, cancelation test, and constructional praxis test. (Figure 3) The results of the memory test confirmed that

the patient had difficulty in recalling recent memory, she also could not perform the TMT test and the score on the constructional praxis test was only 7 out of 11, although the cancelation test could still be performed well. The patient never had a seizure during his hospitalization and was discharged in good condition. One month later, the patient was re-evaluated for MMSE, MoCa-Ina and mini-Cog tests. The test results have not changed much, the patient obtained an MMSE score of 23/30, a MoCa-Ina score of 15/30, and a mini-Cog 3 score of 0.

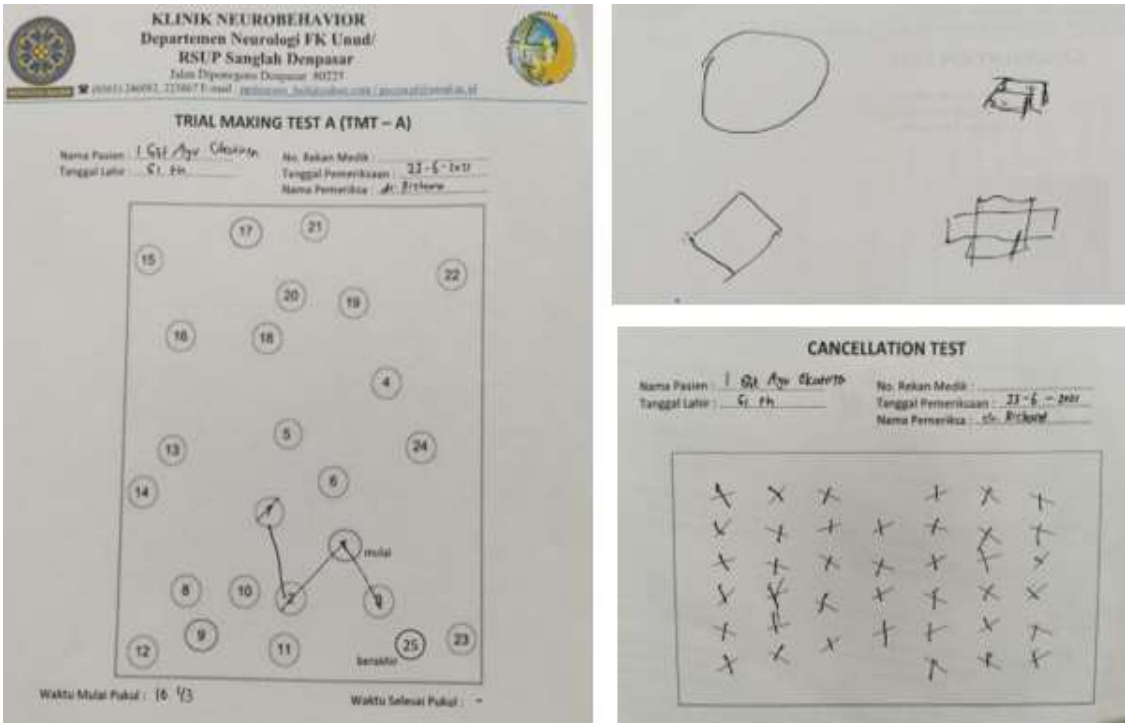

Figure 3. A) TMT-A. B) Constructional praxis. C) Cancelation test

DISCUSSION

Hypoparathyroidism is the most common etiology of Fahr's syndrome in adult patients. Hypoparathyroidism is a clinical syndrome caused by insufficient secretion of PTH. This condition is characterized by hypocalcemia, hyperphosphatemia, increased neuromuscular excitability, and calcification of soft tissues. Neck surgery is the most common cause which accounts for 75% of all cases of hypoparathyroidism. [7] In this case, the most likely cause of hypoparathyroidism is a history of thyroid surgery. [3]

The most common clinical manifestation of Fahr's syndrome is movement disorders, while cognitive impairment is the second most common symptom. [8] This patient had multiple seizures and cognitive impairment. Seizures in Fahr's syndrome are related to hypoparathyroidism as in this case can be caused by 2 mechanisms, namely due to hypocalcemia that increases neuronal excitability and due to dysfunction of cortico-basal and interhemispheric connections.[9] The pathogenesis of cognitive impairment is related to the breakdown of the connection between the basal ganglia and the cerebral cortex, frontotemporal atrophy, the formation of cortical neurofibrillary aggregates, and the loss of neurons in the cortex and basal ganglia. [4]

Cognitive impairment in this patient is mainly in the memory and visuospatial domain. The immediate recall examined using the digit span test and the long-term memory examination was still normal. [10,11]

The most disturbed part was when the patient was asked to recall 5 names of unrelated objects and asked to repeat 5 minutes later, she does not remember at all despite being given clues. The patient also could not

remember the examiner's name and the food she ate that morning.

Memory is divided into explicit and implicit. Explicit or declarative memory is consciously regulated. Explicit memory can be divided into 3, namely short memory (working memory), episodic memory, and semantic memory. Short term memory can only last 2-18 seconds. If it is more than that, the memory will be transferred to episodic memory that lasts minutes to days, which is used to remember certain events in life. Semantic memory is a long-term memory that is used to store general knowledge. This patient has episodic memory impairment. Declarative memory is all influenced by the hippocampus and the frontal lobe of the brain. Disturbance or damage to these structures will cause disturbances in declarative memory. [(12)] In this patient, the frontal lobes show calcium deposits which can cause memory impairment.

Visuospatial disturbances in the patient were spotted when the patient could not draw imitate shapes, the patient also refused to draw a clock because. The patient initially tried trail making test-A, but gave up because she felt confused. She also refused to do a trail making test-B. On the cancellation test, the patient was still able to do well, as well as the initial constructional praxis. The patient begins to have difficulty when asked to draw a cube (a 3-dimensional object).

Visuospatial is a cognitive process needed to identify, integrate, and analyze space, form, detail, structure, and spatial relationships of objects. Vision begins initially in the striate cortex in the occipital lobe and moves to other parts of the brain via the dorsal and ventral pathways. The dorsal pathway or occipitoparietal circuit is then continued by the parieto-frontal, parieto-premotor, and medial parieto-temporal pathways. The parieto-frontal pathway is for spatial working memory, the medial parieto-temporal pathway is for spatial navigation, and the parieto-premotor pathway is for visually guided actions. [(13)] Damage or disruption of these pathways can impair visuospatial function. In this patient there is calcification in the occipital lobe which may interfere with the pathways described previously so that the patient's visuospatial function is disturbed.

The patient had diffused intracerebral and intracerebellar calcifications. However, the symptoms that appear are still relatively mild. It is also reported that there is no significant relationship between the extent of calcified lesions and the severity of symptoms that appear in patients with Fahr's syndrome. [(14)] In addition to calcification, other factors that can cause clinical symptoms in patients with Fahr's syndrome are reduced focal cerebral blood flow and glucose metabolism. Benke et al demonstrated that patients with Fahr's disease had decreased glucose metabolism in the basal ganglia and frontal lobes as seen on 18-fluorodeoxyglucose positron emission tomography (PDG-PET) imaging of the brain. [(15)]

Fahr's syndrome is be treated according to the underlying etiology. In cases of hypoparathyroidism, calcium and vitamin D can be given. The recommended dose is a calcium supplement of 500-1000 mg given 2-3 times per day and for active preparations of vitamin D, calcitriol (0.25-2 g/day) and 1 alpha-hydroxy vitamin D (0.5-3 g/day). If calcium and vitamin D supplementation therapy is insufficient, PTH replacement therapy with rhPTH1-34 or rhPTH1-84 may be considered. In addition to pharmacotherapy, education to patients and families is also very important. They should have a basic knowledge of the disease and the importance of regular follow-up to evaluate the occurrence of long-term complications. [(7)]

CONCLUSION

Fahr's syndrome is a very rare case. Hypoparathyroidism is one of the most common causes of Fahr's syndrome. This article reports a 51-year-old woman who presented initially with seizures and frequent forgetfulness diagnosed with Fahr's syndrome associated with hypoparathyroidism. Her treatments are not intended to eliminate the brain calcifications

that have formed but rather to treat the underlying etiology to prevent worsening of the condition, and the patient must undergo long-term follow-up to evaluate her symptoms.

Declaration by Authors

Acknowledgement: None
Source of Funding: None
Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Saleem S, Aslam HM, Anwar M, Anwar S, Saleem M, Saleem A, et al. Fahr's syndrome: Literature review of current evidence. Orphanet J Rare Dis. 2013;8(1):1.
2. Prasetya D and Sumadiono. Fahr's syndrome in teenage girls' systemic lupus erythematosus: A case report. Indonesian Journal of Medicine and Health. 2020: 290-4.
3. Perugula ML and Lippman S. Differential Diagnosis: Fahr's Disease or Fahr's Syndrome? Innovations in Clinical Neuroscience. 2016; 13(7): 45-46.
4. Savino E, Soavi C, Capatti E, Borrelli M, Vigna GB, Passaro A, et al. Bilateral strio-pallido-dentate calcinosis (Fahr's disease): Report of seven cases and revision of literature. BMC Neurol [Internet]. 2016;16(1). Available from: http://dx.doi.org/10.1186/s12883-016-0693-1
5. Tai XY and Batla A. Fahr's disease: current perspectives. Orphan Drugs: Research and Reviews. 2015;5;43–9.
6. Sunday MA, Kamal S, Salma U. FAHR'S Syndrome: A rare Neurodegenerative Disorder. Med Today. 2017;29(1):39–41.
7. Zhou YY, Yang Y, and Qiu HM. Hypoparathyroidism with Fahr's syndrome: A case report and review of the literature. World J Clin Cases. 2019; 7(21): 2662-70.
8. Calabro RS, Spadaro L, Marra A, Bramanti P. Fahr's disease presenting with dementia at onset: A case report and literature review. Behavior Neurol. 2014; 2014:10–2.
9. Manea MM, Sirbu A, Dragos D, Dobri AM, Sirbu AG, Tuta S. Epileptic seizures as the first manifestation of fahr's syndrome. Acta Endocrinol (Copenh). 2020;16(3):370–4.
10. Cascella M, Al Khalili Y. Short Term Memory Impairment. StatPearls [Internet]. 2019;(August). Available from: http://www.ncbi.nlm.nih.gov/pubmed/31424720
11. Perdossi. Neurobehavior module. Indonesian College of Neurology. 2008.
12. May CP, Einstein GO, Diehl N, Kong H, Tam ST, Freedman S. Memory: A Five-Day Unit Lesson Plan for High School Psychology Teachers. Teach Psychol Second Sch Am Psychol Assoc. 2013.
13. Tres ES, Brucki SMD. Visuospatial Processing: A review from basic to current concepts. Dement e Neuropsychol. 2014;8(2):175–81.
14. Amin O. Fahr's disease and frontal lobe-like cognitive dysfunction. J Mood Disord. 2012;2(3):119.
15. Benke T, Karner E, Seppi K, Delazer M, Marksteiner J, Donnemiller E. Subacute dementia and imaging correlates in a case of Fahr's disease. J Neurol Neurosurg Psychiatry. 2004;75(8):1163–5.

How to cite this article: Richard Suherlim, AAA Putri Laksmidewi, AAA Meidiary et.al. Cognitive impairment in patient with Fahr's syndrome related to hypoparathyroidism: a case report and literature review. *International Journal of Research and Review*. 2023; 10(7): 460-465.
DOI: *https://doi.org/10.52403/ijrr.20230756*

******