The Impact of COVID-19 Infection on a Neurologically Compromised Male With Fahr’s Disease Presenting With Acute Delirium and Aspiration Pneumonia: A Case Report

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Abstract

Fahr’s disease or idiopathic basal ganglia calcification is a rare, sporadic, genetically dominant, and inherited neurological condition that manifests with dysphagia and Parkinson’s disease. The computed tomography (CT) scan is the method of choice to diagnose basal ganglia calcifications seen in Fahr’s disease. This case report elaborates on the emergency management of a 58-year-old male patient with acute respiratory distress, acute delirium, schizophrenia, Fahr’s syndrome, and history of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease 2019 or COVID-19) infection. The patient’s chest X-ray, laboratory workup, and vital signs were suggestive of aspiration pneumonia-induced sepsis and acute hypoxemic respiratory failure. Post-admission antibiotic management reduced sepsis complications without improving the altered mental status. A comprehensive clinical assessment suggested the attribution of Fahr’s disease to the patient’s aspiration pneumonia and other clinical complications. In addition, COVID-19 infection, sepsis-induced inflammatory processes, and pre-existing neurological compromise possibly deteriorated the patient’s neurological outcomes, overall prognosis, and recovery.

Keywords: delirium, covid-19, toxic metabolic encephalopathy, sepsis, fahr’s disease or fahr’s syndrome

Introduction

Fahr’s disease or syndrome is a rarely reported sporadic neurological condition with an autosomal dominant inheritance pattern that develops with the abnormal deposition of calcium phosphate and carbonate in the basal ganglia, cerebellar subcortical white matter, cerebral cortex, dentate nucleus, hippocampus, and thalami [1]. The other predominant locations of idiopathic calcification include the lenticular nucleus, brain stem, cerebellum, subcortical white matter, centrum semiovale, thalamus, dentate nucleus, caudate, and putamen [1]. Fahr’s syndrome was first recognized in 1930, and it has a prevalence of less than 1:1,000,000, with the majority of cases being described in males ranging from 30 to 60 years old [2-3]. Fahr’s syndrome progresses due to a rapid decline in mental health, early mortality in children, psychiatric symptoms in young adults, and dementia in middle-aged patients [4]. The commonly reported manifestations of this disease include extrapyramidal symptoms, orofacial dyskinesia, chorea, athetosis, eye impairment, seizures, headache, movement disorder, and decline in motor function [5]. Oropharyngeal dysphagia in Fahr’s disease progresses due to a rapid decline in the function of the stomatognathic system [6]. Recent studies reveal the role of the XPR1, PDGFB, PDGFRB, and SLC20A2 genes in triggering primary familial brain calcification in patients with Fahr’s disease [4,7]. In addition, Fahr’s syndrome potentially dysregulates the phosphate metabolism, blood-brain barrier (BBB), and cAMP pathway, which adds to the incidence of hypoparathyroidism and cerebral circulatory disturbances [1,3,8-10]. A computed tomography (CT) scan is a method of choice to diagnose calcifications in the dentate nuclei, corona radiata, thalami, and lentiform nuclei, while the non-calcified inflammatory processes are detected by magnetic resonance imaging (MRI) in the setting of Fahr’s disease [11]. In addition, the assessment of other associated conditions, including lipid proteinosis, mitochondrial myopathy, tuberculoc sclerosis, neuroferritinopathy, brucellosis infection, hyperparathyroidism, pseudo-hypothyroidism, secondary hypoparathyroidism, and idiopathic hypoparathyroidism is paramount to ruling out Fahr’s disease [12]. The treatment algorithms for Fahr’s disease aim to manage neuropsychiatric symptoms and their underlying etiologies [13]. This case study pertains to a 58-year-old male patient with a history of Fahr’s disease, acute delirium, aspiration pneumonia, and recent exposure to severe acute respiratory syndrome coronavirus (SARS-COV-2) infection.

Case Presentation

We report the case of a 58-year-old African American male with a past medical history of hypertension,
diabetes mellitus, atrial fibrillation, coronary artery disease, cerebrovascular accident, schizophrenia, and benign prostatic hypertension who presented to the emergency department (ED) from a nursing home with altered mental status and respiratory distress. While being transported in the ambulance, the patient was hypoxic with an oxygen saturation of 80%. His oxygen saturation improved to 95% when provided with 4 liters of oxygen supplementation via nasal cannula. He then had a cardiac arrest and cardiopulmonary resuscitation was initiated, however, return of spontaneous circulation was achieved without any medications. In the ED, he was tachycardic, tachypneic, hypotensive, and had a fever of 101.5 F. He was very lethargic and nonverbal but moving all four extremities. Lung examination was significant for bilateral diffuse rhonchi. Point-of-care ultrasound examination revealed left lower lobe consolidation. Initial labs revealed a leukocytosis of 22.81 x 10³/mcL (normal range: 4.80-10.80 x 10³/mcL), hyperkalemia of 5.8 mmol/L (normal range: 3.5-5.1 mmol/L), and mild acute kidney injury (AKI) with a creatinine of 1.28 mg/dL (0.7-1.2 mg/dL). Lactate was mildly elevated at 1.7 mmol/L (normal range: 0.6-1.4 mmol/L). See Table 1. SARS-CoV-2 (coronavirus disease 2019 (COVID-19)) PCR test was negative. CT of the head revealed mild, vague patchy areas of low attenuation in the periventricular white matter, likely ischemic/hypertensive in nature. In addition, CT of the head showed dense bilateral near-symmetric areas of increased density/mineralization in the left and right basal ganglia and to a lesser degree, the left and right posterior thalamus dentate nuclei as well, likely representing Fahr’s disease (Figure 1). CT chest pulmonary angiogram showed atelectasis in the right middle lobe and bilateral lower lobes, significantly worse in the left lower lobe (Figure 2). Blood, urine, and sputum cultures revealed no bacterial growth. Based on these findings, the patient met the criteria for sepsis, and antibiotics treatment was initiated.

| Lab            | Normal Reference Range with units | Value |
|----------------|----------------------------------|-------|
| White blood cells | 4.80-10.80 x 10³/mcL             | 22.81 |
| Hemoglobin     | 14.0-18.0 g/dL                   | 9.8   |
| Platelet       | 150-450 x 10³/mcL                | 522   |
| Lactate        | 0.6-1.4 mmol/L                   | 1.7   |
| Sodium         | 136-145 mmol/L                   | 137   |
| Potassium      | 3.5-5.1 mmol/L                   | 5.8   |
| BUN            | 6-23 mg/dL                       | 30    |
| Creatinine     | 0.7-1.2 mg/dL                    | 1.7   |
| Albumin        | 3.5-5.2 g/dL                     | 2.9   |

**TABLE 1: Initial laboratory findings**
BUN: blood urea nitrogen
FIGURE 1: CT of the head shows mild, vague patchy areas of low attenuation in the periventricular white matter, likely ischemic/hypertensive in nature.

Dense bilateral near-symmetric areas of increased density/mineralization in the left and right basal ganglia and to a lesser degree, the left and right posterior thalamus dentate nuclei are seen as well, likely representing Fahr’s disease.
The patient was admitted for acute hypoxic respiratory failure and sepsis secondary to aspiration pneumonia. Initially, he required oxygen supplementation with a high-flow nasal cannula, however, his supplemental oxygen was de-escalated to the nasal cannula and eventually room air within two days. He received 10 days of piperacillin-tazobactam and vancomycin as well as three days of azithromycin. His leukocytosis and acute kidney injury (AKI) improved, and he remained afebrile for the remainder of his hospital stay. As aspiration pneumonia improved, the patient’s mental status remained unchanged. Electroencephalogram showed the posterior dominant rhythm consisting of 6-hertz theta waves with an amplitude of 25 uV. Diffuse slowing, but no focal slowing or epileptiform waves are seen. As per the patient’s nursing home, he had contracted the SARS-CoV-2 (COVID-19) infection one month prior to presentation, and since then he had not been behaving like himself and was more non-verbal than usual. Neurology was consulted and assessed that the patient’s altered mental status was likely due to acute delirium in the setting of sepsis and pre-existing Fahr’s disease. Psychiatry was also consulted and recommended minor dosage adjustments to his home psychiatric medication, quetiapine. By hospital day nine, the patient’s mental status improved, and he was discharged safely back to his nursing home.

**Discussion**

Fahr’s disease progresses with worsening neurological dysfunction, bilateral basal ganglia calcification, and systemic or mitochondrial conditions (including endocrinopathies) [14]. The affected patients usually present with a family history of autosomal dominant inheritance. The patient described in this case study presented with Fahr’s disease and comorbidities, including schizophrenia and toxic metabolic encephalopathy [4]. He appeared with altered mental status despite showing improvements in clinical symptoms and biochemical outcomes. The patient’s schizophrenia did not require urgent medical management in the absence of active hallucinations and a history of medication adherence. The medical management subsequently aimed to mitigate sepsis progression and Fahr’s disease.

The diagnostic management of encephalopathy from a systemic illness warrants the assessment of its contributing factors (including toxic-metabolic and drug-induced encephalopathies) and their neurological manifestations [15-17]. The brain MRI findings in acute sepsis often indicate ischemic lesions (in the cortex and hippocampus regions), cytotoxic edema, vasogenic edema, posterior reversible encephalopathy
This case study could not determine the hospitalization history of the patient; however, the diagnostic assessment did not rule out the possible impact of SARS-CoV-2 infection on overall functional/cognitive decline and other neurological manifestations. A similar case study by Demir et al. elaborated on Fahr’s syndrome of an elderly patient with SARS-CoV-2 pneumonia who experienced tonic-clonic convulsions in the intensive care unit [22]. The study, however, did not rule out the possible impact of COVID-19-related inflammation and hydroxychloroquine therapy on the reported seizure. These findings warrant the regular monitoring of neurological symptoms in similar patient scenarios for determining their etiology and improving the treatment outcomes. The outcomes of this case study revealed the deleterious impact of oxidative stress, severe inflammation, and immune insult from sepsis in patients with SARS-CoV-2 infection, Fahr’s syndrome, and neurological complications [23-26]. This study proved to be another potential opportunity to explore complex pathological pathways contributing to the clinical presentation of a patient with COVID-19 infection, Fahr’s disease, acute delirium, and aspiration pneumonia.

Conclusions

The patient in this case study presented with aspiration pneumonia, sepsis, toxic metabolic encephalopathy, acute delirium, and neurocognitive decline potentiated by SARS-CoV-2 infection and Fahr’s disease. The aspiration pneumonia and its clinical complications correlated with the patient’s history of Fahr’s disease and its metabolic manifestations. This case study elaborated on possible mechanisms of sepsis-induced inflammatory changes and their role in triggering neurological complications. The complex pathophysiology of Fahr’s syndrome and toxic metabolic encephalopathy restricted the assessment of infection severity and treatment response. The case outcomes also emphasized the long-term neurological complications of COVID-19 infection in the context of Fahr’s disease. The clinical studies emphasize the adverse impact of SARS-CoV-2 infection on the central nervous system of patients with preexisting neurological complications; however, the underlying pathophysiology is not completely explored. This case report emphasizes the need for monitoring the neurological status of COVID-19-infected patients with preexisting neurological impairments and severe sepsis. Future research should aim to unravel mechanisms and pathways leading to progressive neurocognitive deterioration in patients with systemic inflammation and a known history of neurological disorders.

Additional Information

Disclosures

**Human subjects:** Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Amisha FN, Munakomi S: Fahr Syndrome. StatPearls [Internet], Treasure Island (FL); 2022. https://www.ncbi.nlm.nih.gov/books/NBK560857/.
2. Saleem S, Aslam HM, Anwar M, Anwar S, Saleem M, Saleem A, Rehmani MA: Fahr’s syndrome: literature review of current evidence. Orphanet J Rare Dis. 2015, 8:156. 10.1186/1750-1172-8:156
3. Otu AA, Anikwe JC, Cocker D: Fahr’s disease: a rare neurological presentation in a tropical setting. Clin Case Rep. 2015, 3:806-8. 10.1002/ccr3.349
4. Jaworski K, Styczyńska M, Mandecka M, Walecki J, Kosior DA: Fahr syndrome – an important piece of a puzzle in the differential diagnosis of many diseases. Pol J Radiol. 2017, 82:490-5. 10.16659/PJR.90204
5. Shahidi GA, Safdarian M: Fahr disease: Idiopathic basal ganglia calcification. Iran J Neurol. 2017, 16:53-4.
6. Santos KW, Fraga BF, Cardoso MC: Dysfunctions of the stomatognathic system and vocal aspects in Fahr’s disease: case report. Codas. 2014, 26:164-7. 10.1590/1757-1782/2014486in
7. Guo XX, Zou XH, Wang C, et al.: Spectrum of SLC20A2, PDGFRB, PDGFB, and XPR1 mutations in a large cohort of patients with primary familial brain calcification. Hum Mutat. 2019, 40:392-403.
10.1002/humu.23703
8. Haider A, Liang X, Khan M: Fahr’s syndrome in the setting of abnormal calcium-phosphate metabolism and lupus nephritis. Cureus. 2022, 14:e22298.
9. Zhou YY, Yang Y, Qiu HM: Hypoparathyroidism with Fahr’s syndrome: a case report and review of the literature. World J Clin Cases. 2019, 7:3662-70. 10.12998/wjcc.v7.i12.3662
10. Carpenter TO: Primary Disorders of Phosphate Metabolism. Feingold KR et al. (ed): Endotext, South Dartmouth (MA); 2000.
11. Govindarajan A: Imaging in Fahr’s disease: how CT and MRI differ?. BMJ Case Rep. 2015, 2013:bcr2013201523. 10.1136/bcr-2013-201523
12. Ooi HW, Er C, Hussain I, Kuthiala N, Meyyur Aravamudan V: Bilateral basal ganglia calcification: Fahr’s disease. Cureus. 2019, 11:e4797. 10.7759/cureus.4797
13. Mufaddel AA, Al-Hassani GA: Familial idiopathic basal ganglia calcification (Fahr’s disease). Neurosciences (Riyadh). 2014, 19:171-7.
14. Thillaigovindan R, Arumugam E, Rai R, Kesavan PRR: Idiopathic basal ganglia calcification: Fahr’s syndrome, a rare disorder. Cureus. 2019, 11:e5895. 10.7759/cureus.5895
15. Frontera JA, Melned K, Fang T, et al.: Toxic metabolic encephalopathy in hospitalized patients with COVID-19. Neurocrit Care. 2021, 35:695-706. 10.1007/s12028-021-01220-5
16. Hansen N, Finzel M, Block F: Antiepileptic drug-induced encephalopathy [Article in German]. Fortschr Neurol Psychiatr. 2010, 78:590-8. 10.1055/s-0029-1245632
17. Jeon SJ, Choi SS, Kim HY, Yu IK: Acute acquired metabolic encephalopathy based on diffusion MRI. Korean J Radiol. 2021, 22:2034-51. 10.3348/kjr.2019.0503
18. Sonnevile R, Verdonk F, Rauturier C, et al.: Understanding brain dysfunction in sepsis. Ann Intensive Care. 2013, 3:15. 10.1186/2110-5820-3-15
19. Chung HY, Wickel J, Brunkhorst FM, Geis C: Sepsis-associated encephalopathy: from delirium to dementia?. J Clin Med. 2020, 9:705. 10.3390/jcm9030703
20. Chaudhry N, Duggal AK: Sepsis associated encephalopathy. Adv Med. 2014, 2014:762320. 10.1155/2014/762320
21. Ficke B, Rajaswuya V, Cascella M: Chronic Aspiration. StatPearls [Internet], Treasure Island (FL); 2022.
22. Denir G, Balaban O, Tekeci MH, Jiss Z, Erdem AF: Fahr’s syndrome presenting with seizures in SARS-CoV-2 (COVID-19) pneumonia—a case report. Neurol Sci. 2020, 41:5065-5. 10.1007/s10072-020-04733-7
23. Cecchini R, Cecchini AL: SARS-CoV-2 infection pathogenesis is related to oxidative stress as a response to aggression. Med Hypotheses. 2020, 145:110102. 10.1016/j.mehy.2020.110102
24. Galea I: The blood-brain barrier in systemic infection and inflammation . Cell Mol Immunol. 2021, 18:2489-501. 10.1038/s41423-020-00757-x
25. Sharifian-Dorche M, Huot P, Otherov M, et al.: Neurological complications of coronavirus infection; a comparative review and lessons learned during the COVID-19 pandemic. J Neurol Sci. 2020, 417:117085. 10.1016/j.jns.2020.117085
26. Kwassnicki A, McGuire LS, Lichtenbaum R: Neurologic clinical manifestations of Fahr syndrome and hypoparathyroidism. World Neurosurg. 2020, 144:115-6. 10.1016/j.wneu.2020.07.160