



Case Report

New-Onset Transient Global Amnesia: A Clinical Challenge in an Air Medical Transportation Pilot With a History of Coronavirus Disease 2019

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A B S T R A C T

A 43-year-old male Bell 214C helicopter pilot presented to the emergency ward with flu-like syndrome. His nasopharyngeal severe acute respiratory syndrome coronavirus 2 real-time polymerase chain reaction test was positive, and a chest computed tomographic scan confirmed coronavirus disease 2019 pneumonia. He was admitted, received treatment, was discharged, and returned to flying. During the mission debrief, copilots who had flown with him reported that he experienced episodes of in-flight dizziness and blacked out. They occurred briefly during the cruise and hovering flight, perhaps for a few seconds of disorientation and unconsciousness. Rapid identification of the copilot and control of the helicopter prevented any incident or accident. Afterward, he explained the sudden onset and unexpected brief periods of loss of consciousness after a headache. The flight safety office referred him to the aviation medical center for further investigations. The cardiovascular, neurologic, laboratory, and toxicologic assessments were inconclusive with the approach to sudden-onset transient loss of consciousness. The only abnormal finding was hippocampus lesions on brain magnetic resonance imaging (MRI). Because of the possible diagnosis of transient global amnesia, the aviation medical examiner suspended him from flight duties until complete recovery and the absence of any probable complications.

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Extremely contagious severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants produce coronavirus disease 2019 (COVID-19) pneumonia and affect the world's health care systems for an unknown time. Extrarespiratory multisystemic involvement has also been reported, especially neurologic complications, during the acute phase, after recovery, and even after vaccination. In particular, SARS-CoV-2 variants are neurotrophic and neuroinvasive viruses. So far, different neurologic complications (eg, stroke, encephalopathy, encephalitis, headache, dizziness, loss of smell and taste, seizures, refractory status epilepticus, acute disseminated encephalomyelitis, myelitis, myopathy, leukoencephalopathy, neuroleptic malignant syndrome, Kawasaki syndrome, and Guillain-Barré syndrome) have been reported in these patients.¹⁻³

Selection, training, and continuing health surveillance of air medical crew (pilots and nonpilots) require a large budget and resources.

Continuous health surveillance can prevent personnel loss due to disability or death. These days, emergency medical service staffs are at high risk of mental or physical damage, and taking care of their health is very important.⁴ We report a case of new-onset transient global amnesia (TGA) in an air transportation pilot with a history of COVID-19.

Case Report

A 43-year-old male air medical transportation Bell 214C helicopter pilot presented to the emergency ward with flu-like syndrome that started and progressed 9 days earlier (37 days before the in-flight neurocognitive episodes). His vital signs included the following: an oral temperature of 38.6°C, blood pressure of 105/65 mm Hg, heart rate of 92 beats/min, respiratory rate of 21 breaths/min, and pulse oximetry of 91% on room air. The nasopharyngeal sampling for the SARS-CoV-2 real-time polymerase chain reaction test and the chest computed tomographic scan confirmed COVID-19 pneumonia. He was admitted to the COVID-19 ward, received sufficient treatment, and spent 28 days recovering at home. Afterward, he was

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Table 1
Significant Laboratory Results Related to Transient Global Amnesia

Laboratory Tests	Results	Reference Range
Biochemistry	FBS = 85 mg/dL	70–99
	TG = 124 mg/dL	Up to 150
	HbA1C = 5.1%	Up to 5.7
	Total cholesterol = 150 mg/dL	Up to 200
	LDL = 67 mg/dL	Up to 100
	HDL = 52 mg/dL	—
	Potassium = 4 mmol/L	3.6–5.2
	Sodium = 139 mEq/L	135–145
	Magnesium = 0.95 mmol/L	0.85–1.10
	Calcium = 9.4 mg/dL	8.6–10.3
	TSH = 3.1 mU/L	0.4–5
	T4 = 8.3 µg/dL	5–12
	T3 = 142 ng/dL	80–220
	Anti-TPO = 1.2 IU/mL	Up to 9

FBS = fasting blood sugar; HbA1C = hemoglobin A1C; HDL = high-density lipoprotein; LDL = low-density lipoprotein; TG = triglyceride; TPO = thyroid peroxidase; TSH = thyroid-stimulating hormone.

qualified for flying by the aviation medical center (AMC) based on the policy memo regarding aviation medical examiner (AME) evaluations of airmen and air traffic control specialists (ATCSs) with a history of COVID-19. In the first month of returning to flight during the mission debrief, copilots who had flown with him reported that he experienced episodes of in-flight dizziness and blackouts. These episodes occurred briefly when he was the on-the-job pilot during the cruise and Hoover flight phases, perhaps for a few seconds of disorientation and unconsciousness. Rapid identification of the copilots and control of the helicopter prevented any incident or accident. At the end of operations, he explained the sudden onset and unexpected brief periods of loss of consciousness after a headache that lasted for several hours and was not associated with head movement or position. The flight safety office suspended him from flying duties and referred to the AMC for further investigations. He had no other problems or past medical history, and he denied any use of medications or dietary

supplements. The AME assessed him with the approach to sudden-onset transient loss of consciousness. The cardiovascular examinations (lying and standing blood pressure, resting and exercise electrocardiography, echocardiography, 48-hour electrocardiographic Holter monitoring, tilt table test, and color Doppler of carotid and vertebral arteries), neurologic assessments (awake and asleep electroencephalography and brain imaging), and laboratory and toxicologic assessments (glucose, electrolytes, alcohol, drugs, and herbal supplements) were inconclusive (Table 1).

The only abnormal finding was hippocampus lesions on brain MRI without gadolinium (Fig. 1). The patient's clinical features and hippocampal lesions presented TGA as the primary diagnosis, which may be a possible complication of COVID-19. Based on the Federal Aviation Administration (FAA) regulations (title-14/chapter-1/subchapter-D/part-67/subpart-C/section-67.209), the AMC suspended him from flight duties until complete recovery and the absence of any possible complications confirmed by the AME.

Discussion

Transient global amnesia is a rare clinical syndrome that is more common in middle-aged and elderly women. TGA presents as a sudden onset of temporary short-term anterograde memory loss that generally resolves within 24 hours, and the patients cannot form new memories.^{3,5–8} TGA incidence in the general population is about 3.4 to 10.4/100,000 per year. Since the COVID-19 outbreak in Germany at the end of January 2020, an increasing number of patients have been reported. Numerous theories have been proposed for TGA; however, none of them has been confirmed, and the exact underlying mechanism remains unclear. These hypotheses include focal hippocampal ischemia (associated with hypotension or vasospasm), venous congestion, hypoxic-ischemic events, metabolic stress, epilepsy, migrainelike episodes with cortical spreading depression, and psychogenic background as related to underlying conditions.^{3,5–7}

The hippocampus is a curved structure in the temporal lobe in each hemisphere of the brain just above each ear. This region is

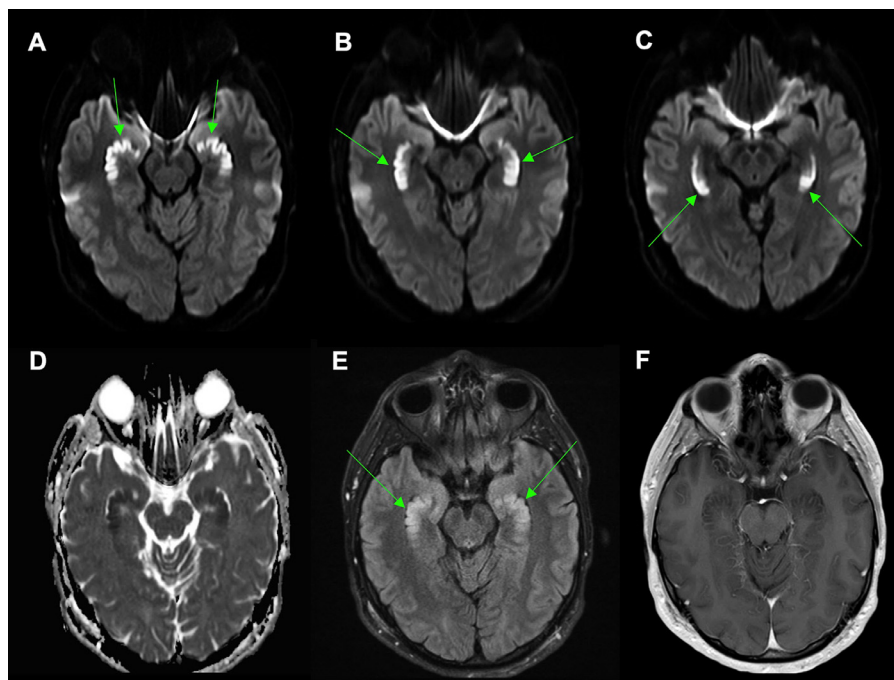


Figure 1. MRI of the brain without gadolinium. Diffusion-weighted imaging demonstrates bilateral, symmetric hyperintensity in the (A) heads, (B) bodies, and (C) tails of the hippocampus. (D) The apparent diffusion coefficient correlate map shows a corresponding low signal consistent with diffusion restriction. (E) Abnormal T2 fluid-attenuated inversion recovery hyperintensity is present in the Hippocampi. (F) Axial T1-weighted imaging shows no abnormal contrast enhancement.

important in the organization and storage of new memories (especially those that are declarative memories), spatial memory and navigation, and the transfer of long-term memories. Hippocampal dysfunctions may present with 1 or more of the following symptoms: memory loss, disorientation, inability to form new memories, inability to remember directions, inability to remember locations that should be familiar, inability to recall words, and inability to memorize new information.⁹

The clinical symptoms of TGA are thought to arise from the hippocampus, particularly the CA-1 and Sommer sector, and the medio-basal temporal lobe. The hippocampal region is a watershed area of the brain that is especially subject to cytotoxic glutaminergic uptake or release. This region can be affected bilaterally or unilaterally, but the left side is most commonly affected. One third of the patients perform complex activities before an episode, which is often precipitated by particularly vigorous exertion, coitus, severe stress, or migraines. The symptoms are not present when the patient awakens in the morning but occur later in the day. Patients typically have sudden and unpredictable anterograde amnesia, most often lasting from 4 to 8 hours, and ask repetitive questions. They may be disoriented concerning time and place but still have the ability to recognize themselves and other people. Patients present impairment in learning new verbal material; however, the ability to speak, visual-motor coordination, working memory, executive functions, and the ability to perform complex tasks remain intact. The symptoms, once resolved, rarely recur; the clinical picture is distinctive, but its recognition requires good interviewing and observation skills.^{3,5-8,10}

The neurologic examination is generally intact, and no symptoms or signs are detected.³ The bilateral cases exhibit both visuospatial and speech-related memory deficits. The dominated brain lesions demonstrate speech-related memory deficits.¹⁰ Substance intoxication, Wernicke encephalopathy, transient ischemic attack, cardioembolic stroke, basilar artery thrombosis, lacunar syndrome, posterior cerebral artery stroke, toxic encephalopathy, hypoxia, head injury, temporal lobe epilepsy, absence seizure, complex partial seizures, migraine variants, syncope, and Wolff-Parkinson-White syndrome must be ruled out in these patients. TGA comorbidities include hypertension, dyslipidemia, smoking, autoimmune thyroiditis, ischemic heart diseases, diabetes, and atrial fibrillation.^{7,8,10}

The suspicious cases should be admitted and monitored until the amnesia resolves. Detailed cardiovascular, neurologic, laboratory, toxicologic, and imaging assessments must be considered. Table 2 presents the necessary assessments.

Reversible defects or lesions are diagnostic in functional brain MRI. Diffusion-weighted imaging MRI is needed to rule out ischemic stroke, which can have a similar presentation in some cases. However, there is no diagnostic test for TGA other than a diagnosis of exclusion.^{3,10} There is no specific therapy for this condition, and most patients need support and reassurance. Weight loss, smoking cessation, alcohol abstinence, the use of prescribed medications, and regular follow-up with their primary care provider should be advised to these patients. TGA episodes usually subside completely, whereas

there is a possibility of recurrence without mortality in 2.9% to 26.3% of patients.^{7,10}

The Bell 214C is a medium-lift helicopter that uses a powerful engine and twin-blade and upgraded rotor system, giving it a high lifting capacity and good performance at high temperatures and high altitudes. These helicopters are well suited for regional military or commercial (VIP transport, law enforcement, firefighting, search and rescue, and medical transportation) transport needs. The following advantages make them suitable for air medical transportation: 1) a maximum speed of up to 140 knots; 2) the capability of day or night flying; 3) the ability of each pilot to independently control the helicopter; 4) the capability to transport 14 passengers, 6 stretchers, or equivalent cargo; and 5) the use of various types of medical equipment on board to meet extensive patient care needs. Based on the aviation safety protocol, safe Bell 214C flying needs the following minimum requirements: 1) the ideal overhaul, 2) the exact preflight check, and 3) 2 qualified pilots to collaborate side by side.

Each aviation operator has a flight safety office that supervises the safety procedures and prevents flight hazards. The flight safety office should suspend any aviators with possible medical hazards and refer them to the AMC for further assessment and decision making. The AMC is responsible for the pre-employment medical examinations of aviation volunteers, periodic medical assessments, health surveillance, aviation medical councils, and other related medical responsibilities of the aviation population. The AME is a trained and approved physician for medical responsibilities in the AMC. The aviation organization structure in many countries is similar due to the act under the supervision of international authorities and their regulations (such as the International Civil Aviation Organization, the European Aviation Safety Agency, the FAA, and so on). However, some differences may be seen, especially in the field of military aviation.

Based on the FAA regulations (title-14/chapter-1/subchapter-D/part-67/subpart-C/section-67.209), pilots must have intact neurocognitive function, and pilots with TGA may be a potential safety hazard. The complete recovery and absence of any possible complications of aviators with a history of COVID-19 must be considered by the AMC (after outpatient treatment or discharge from the hospital) according to the policy memo regarding AME evaluations of airmen and ATCSs with a history of COVID-19.¹¹ The approach to medical examination of civilian rotary wing aircrew after COVID-19 infection is presented in Table 3.¹²

Conclusions

Since the onset of the COVID-19 pandemic, various extrapulmonary multisystemic involvements (especially neurologic) have been reported during the acute phase of infection, the recovery period, and even after vaccination. In particular, SARS-CoV-2 variants are neurotrophic and neuroinvasive viruses.¹⁻³ The complete recovery and absence of any possible complications of airmen and ATCSs with a history of COVID-19 must be considered by the AMC (after outpatient treatment or discharge from the hospital) based on the policy memo regarding AME evaluations of airmen and ATCSs with a history

Table 2
Necessary Assessments in the Suspicious Patients for Transient Global Amnesia

General	Review of systems, consciousness level, orientation, and vital signs screening
Cardiovascular	Cardiac and vascular examinations, lying and standing blood pressure measurement, resting electrocardiogram, exercise electrocardiogram, echocardiography, 48-h electrocardiographic Holter monitoring, tilt table test, and color Doppler of carotid and vertebral arteries
Neurologic	Central nervous system and peripheral nervous system examinations and electroencephalogram in awake and then asleep condition
Laboratory and toxicologic	The glucose, lipids, electrolytes, thyroid-stimulating hormone, T3, T4, anti-TPO, alcohol, drugs (illicit, over-the-counter, and prescribed only), and herbal supplements levels in the blood
Imaging	Diffusion-weighted imaging MRI

MRI = magnetic resonance imaging; TPO = thyroid peroxidase.

Table 3

The Approach to Medical Examination of Civilian Rotary Wing Aircrew After Coronavirus Disease 2019

Standard air medical evaluation	Complete blood count, basic metabolic panel, urinalysis Chest radiography electrocardiography Chest radiography electrocardiography Basic pulmonary function tests Audiology and ear, nose, and throat specialist Ophthalmology specialist Flight surgeon evaluation
Ancillary testing	Referral to air medical psychiatrist if suspected psychosocial impact Only if pathology is found in standard air medical evaluation

of COVID-19.¹¹ However, many of these complications have late-onset occurrences and may be detected many days or months later when the AMC has approved the recovered pilots as qualified. We recommend that 1) all pilots must be aware that they will not be allowed to fly if they have any COVID-19 presentations, positive tests (RT-PCR or biochemistry), or other abnormal medical findings (vital signs, pulse oximetry, or computed tomographic scan); 2) the AMC must suspend these aviators from flight duties until complete recovery and the absence of any possible complications confirmed by the AME; 3) these aviators must be medically assessed for possible complications regularly in short intervals; 4) if pilots with a history of COVID-19 or vaccination have any signs or symptoms after recovery and return to flight, they should avoid flying and reassess by the AME; 5) the hippocampus lesions and clinical presentations of TGA may be possible COVID-19 complications with the exact relation and

mechanism still unclear; and 6) this case is an aviation safety concern that needs more accurate investigations and revision of the current regulations in the future.

References

1. Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol.* 2020;77:683–690.
2. Shahali H, Ghasemi A, Farahani RH, Nezami Asl A, Hazrati E. Acute transverse myelitis after SARS-CoV-2 infection: a rare complicated case of rapid onset paraplegia. *J Neurovirol.* 2021;27:354–358.
3. Ramanathan RS, Wachsman A. Coronavirus disease-19 (covid-19) related acute stroke causing transient global amnesia. *J Stroke Cerebrovasc Dis.* 2021;30:105738.
4. Momenzadeh M, Shahali H, Farahani AA. Coronavirus disease 2019 suspicion: a case report regarding a male emergency medical service pilot with newly diagnosed sarcoidosis. *Air Med J.* 2020;39:296–297.
5. Nishizawa T, Kawakami A, Taguchi T, Osugi Y. Transient global amnesia with bilateral hippocampal lesions during the COVID-19 global outbreak. *J Gen Fam Med.* 2020;22:154–155.
6. Werner R, Keller M, Woehrl JC. Increased incidence of transient global amnesia during the Covid-19 crisis? *Neurol Res Pract.* 2020;2:26.
7. Waliszewska-Prosol M, Nowakowska-Kotas M, Bładowska J, Papier P, Budrewicz S, Pokryszko-Dragan A. Transient global amnesia – risk factors and putative background. *Neurol India.* 2020;68:624–629.
8. Heidt SH, Lee AJ, Carnes BG, Pavelites JJ. You're the flight surgeon: altered consciousness while driving. *Aerosp Med Hum Perform.* 2018;89:1092–1094.
9. Bliss T, Collingridge G, Morris R, Reymann K. Long-term potentiation in the hippocampus: discovery, mechanisms and function. *Neuroforum.* 2018;24:A103–A120.
10. Nehring SM, Spurling BC, Kumar A. *Transient Global Amnesia.* Treasure Island, FL: StatPearls Publishing; 2021.
11. Giovanetti PM. *Policy memo regarding aviation medical examiner (AME) evaluations of airmen and air traffic control specialists (ATCS) with a history of COVID-19.* Washington, DC: Federal Aviation Administration; March 26, 2021. Available at https://www.faa.gov/licenses_certificates/medical_certification/media/COVID-19AMEE-valuationPolicy.pdf. Accessed March 26, 2021.
12. Gilad D, Gabbai D, Tehori O, et al. Return to aviation duty after recovery from COVID-19. *J Mil Veteran Fam Health.* 2021;7:116–120.