Recurrence of Neurological Deficits in an F/A-18D Pilot Following Loss of Cabin Pressure at Altitude

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INTRODUCTION: Supersonic, high altitude aviation places its pilots and aircrew in complex environments, which may lead to injury that is not easily diagnosed or simply treated. Decompression illness (either venous or arterial) and environmental conditions (e.g., abnormal gases and pressure) are the most likely adverse effects aircrew often face. Though symptomatic aircrew personnel may occasionally require hyperbaric oxygen treatment, it is rare to require more than one treatment before returning to baseline function.

CASE REPORT: This challenging aviation case details the clinical course and discusses the salient physiological factors of an F/A-18D pilot who presented with neurological symptoms following loss of cabin pressure at altitude.

DISCUSSION: Most crucial to this discussion was the requirement for multiple hyperbaric oxygen treatments over several days due to recurrence of symptoms. The likelihood of recurrence during and after future flights cannot be estimated with accuracy. This case illustrates a degree of recurrences for neurological symptoms in aviation (hypobaric exposure to hyperbaric baseline environment) that has not previously been described.

KEYWORDS: aviation, symptoms, decompression sickness, arterial gas embolism.

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Decompression illness, abnormal gases, and effects of pressure are the most likely adverse effects shared by those exposed to supersonic, high altitude aviation.[7] The context of effects during aviation is opposite that of diving (**Table I**),[14] in that aircrew journey into the hypobaric environment and begin off-gassing nitrogen immediately. Conversely, divers journey into a hyperbaric world temporarily, off-gassing inert gas as the dive is completed. Cabin pressure in fighter aircraft is equal to outside ambient pressure as the aircraft rises to 8000 ft (2438 m) of altitude, is maintained at 8000 ft mean sea level (MSL) from 8000 to approximately 23,000 ft (7010 m) of aircraft altitude, then rises at a 5-psi (0.34-ATA) differential above ambient pressure for altitudes above 23,000 ft.[23] Pressures experienced during this flight are represented in **Table II**.

Pressurization in military aircraft flying above 13,000 ft (3962 m) of altitude protects against the effects of the hypobaric environment.[5] A loss of cabin pressure may occur slowly or quickly, potentially resulting in physical or neurological symptoms. Physiological effects from hypobaric exposure and other environmental conditions usually respond to the return of ground level barometric pressure, in-flight emergency procedures, or postflight oxygen.[10,12] Despite these maneuvers, Krause[9] found up to 70% of individuals with hypobaric exposure had venous gas emboli (VGE) upon returning to ground level, and 40% of decompression sickness (DCS) symptoms could still occur after return to ground level pressure.[1]

Breathing oxygen at altitude [especially above 10,000 ft (3048 m)] protects against the likelihood of hypoxia and facilitates nitrogen off-gassing[7] should cabin pressure be lost and the forces promoting bubble formation develop. Fortunately for aviators, returning to the surface (1 ATA) upon landing restores the normobaric physiological state and often relieves any symptoms. Should symptoms present on the surface, 2 h of breathing 100% oxygen may be sufficient treatment.[10,18] Persistent

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Table I. Major Differences Between Diving and Altitude Decompression Sickness (from Pilmanis et al.[14]).

ALTITUDE	DIVING
Decompression starts from a ground level tissue N_2 saturated state	Upward excursions from saturation diving are rare
Breathing gas usually high in oxygen to prevent hypoxia and promote denitrogenation	Breathing gas mixtures usually high in inert gas due to oxygen toxicity concerns
Time of decompressed exposure to altitude is limited	Time at surface pressure following decompression is not limited
Pre-mission denitrogenation reduces DCS risk	Pre-oxygenation not applicable
DCS usually occurs during the mission	DCS risk usually greatest after mission completion
Symptoms usually mild and limited to joint pain	Neurological symptoms are common
Recompression to ground level is therapeutic and universal	Therapeutic chamber recompression is time limited and sometimes hazardous
Tissue pN2 decreases to very low levels with altitude exposure	Tissue pN2 increases to very high levels with hyperbaric exposure
Metabolic gases become progressively more important as altitude increases	Inert gases dominate
Few documented chronic sequelae	Chronic bone necrosis and neurological damage have been documented

symptoms are treated with hyperbaric oxygen therapy (HBO_2) and rarely do symptoms persist beyond the application of HBO_2 (USN Treatment Table 6).

An open source search revealed no cases similar to the one described in this paper. This challenging aviation case details the operational and clinical course of an F/A-18D pilot who presented with both immediate and delayed neurological symptoms following loss of cabin pressure, requiring multiple hyperbaric oxygen treatments over several days due to recurrence of symptoms. This case highlights aviation decompression pathology, the challenges in diagnosis, and the current science, medical practice, and disposition of supersonic aircraft pilots who may suffer recurrent neurological symptoms following loss of cabin pressure at high altitude.

CASE REPORT

This 36-yr-old male USMC F/A-18D senior test pilot experienced a loss of cabin pressure at both 27,000 ft (8230 m) and 35,000 ft (10,668 m) (level flight, without gravitational force maneuvers). Internal cabin pressures changed from 10,220 ft MSL to 16,000 MSL (3115 to 4877 m; 10 to 7.9 psi; 0.68 to 0.54 ATA) and 14,390 MSL (4386 m; 8.5 psi, 0.59 ATA) to 18,000 MSL (5486 m; 7.3 psi, 0.50 ATA), respectively. Following the 35,000-ft spike, he was breathing normally, but felt disoriented and missed his usual turnaround marker. He was soon able to turn the aircraft, engage his normal flight path and maneuvers, and then land the plane with normal mental capacity. He felt normal during the taxi to the hangar and the walk across the tarmac. About 35 min after the initial depressurization, he noted confusion, inability to fill out his postflight forms, and trouble speaking, with pauses up to 45 s before answering questions. He recalled that his internal (mental) dialogue involved knowing what was happening and what he needed to do, but being unable to make himself do it. His flight surgeon noted the aphasia and called EMS.

This was his second flight of the day. The first flight occurred in a different aircraft [maximal altitude 29,000 ft (8839 m)], lasted one hour, maintained cabin pressure, and was well within his allowable maximum of three flights per day, or 6.5 h of flight time in 24 h.

Table II. Pressures at Altitude.

	AMBIENT PRESSURE			CABIN PRESSURE			
AIRCRAFT ALTITUDE (ft)	mmHg	psia	ATA	MSL	psia	ATA	PRESSURE DIFFERENTIAL
0	760	14.7	1.0	Same	14.7	1.0	
3000	681	13.2	0.89	Same	13.2	0.89	0.11 ATA* (surface to 3000 MSL)
5000	632	12.2	0.83	Same	12.2	0.83	
8000	565	10.9	0.74	Same	10.9	0.74	
9000	548	10.5	0.71	8000	10.9	0.74	0.03 ATA** (8000 to 9000 MSL)
10,000	553	10.1	0.69	8000	10.9	0.74	
12,000	484	9.3	0.63	8000	10.9	0.74	
14,000	447	8.6	0.59	8000	10.9	0.74	
15,000	429	8.3	0.56	8000	10.9	0.74	
16,000	412	7.9	0.54	8000	10.9	0.74	
18,000	380	7.3	0.50	8000	10.9	0.74	
20,000	350	6.8	0.46	8000	10.9	0.74	
25,000	282	5.5	0.37	9000	10.5	0.71	
27,000	259	5.0	0.34	10,270	10.0	0.68	2.1 psi/0.14 ATA*** (10,270 to 16,000 MSL)
30,000	226	4.4	0.30	11,850	9.4	0.64	
31,000	216	4.2	0.29	12,4000	9.2	0.63	
35,000	179	3.5	0.24	14,390	8.5	0.58	1.2 psi/0.08 ATA*** (14,390 to 18,000 MSL)
40,000	141	2.7	0.18	16,500	7.7	0.52	

* Transalveolar membrane rupture threshold.[7,21]

** Benign pressure fluctuations experienced in this flight ("feet" = outside ambient pressure and "MSL" = cabin pressure).

*** Change in pressure experienced by this pilot.

In the ED, he was awake and verbal, though agitated and unable to follow commands. His confusion (disoriented to person, place, time, and situation) waxed and waned to stuporous, nonverbal, and lethargic. He intermittently slurred his words and had emotional lability. He developed progressive weakness in the bilateral lower extremities, except the hip flexors, and soon was unable to move his left arm and only minimally move his right. He developed hand cramps, appearing like carpal spasm. His blood glucose at this time was 85, serologies were normal other than a CK of 357, and his CXR unremarkable. A stroke code was called (simultaneously with contacting the hyperbaric medicine team) and brain CT angiography and diffusion-weighted MRI were both normal.

Based on these findings, hyperbaric oxygen therapy (HBO_2) was initiated using a U.S. Navy treatment table 6 (USN TT6). Symptoms resolved early in the first oxygen period. No extensions were conducted. Following treatment, his neurological exam was normal, but 1 h later, his deficits in cognition, motor, and cerebellar function recurred, though in slightly lesser degree than initial presentation. A repeat USN TT6 was begun (less than 4 h from previous treatment). He responded well to the second USN TT6, which was extended by two oxygen periods at 60 and 30 fsw. He surfaced asymptomatic, but within minutes he began to manifest recurrent neurological deficits. A surface interval was allowed and the patient received subsequent TT9s, with the plan to treat until symptoms either resolved or plateaued for two consecutive treatments.

Following the first TT9 (6 h after the previous TT6), speech fluency improved. Cerebellar function improved as well (right better than left). The remainder of the neurological exam was normal. The second TT9 was conducted 8 h after the first, following which the patient had resolution of all symptoms except a mild deficit in Sharpened Romberg. Because symptoms continued to improve, twice daily TT9s were planned.

An echocardiogram with bubble study was performed. During the baseline portion of the echocardiogram, the patient was mildly disoriented for a few moments but soon responded appropriately. When bubbles were injected, no bubbles returned to the left heart immediately or within 15 cardiac cycles, revealing no evidence of cardiopulmonary shunt or other cardiac abnormality. The patient stated at this point that he did not feel right, then no longer responded verbally. He was breathing, but showed aphasia and weakness in the bilateral legs. Following hospital Rapid Response and Code Blue team assessments, he was taken to the hyperbaric chamber for a presumed arterial gas embolism (AGE).

The patient responded to HBO_2, which was extended to the institution's full length (USN TT6 with three extensions each at 60 and 30 fsw). Given his response to treatment, both the neurology and hyperbaric teams decided to proceed with HBO_2 without the need for immediate neuroimaging. With the ongoing pattern of recurrent symptoms during the surface intervals and the marked symptoms that appeared to be exacerbated by the bubble study, two further TT9s were planned for the following day.

Significant study results to this point included: follow-up CK of 233 $U \cdot L^{-1}$, S-100 beta protein 26 $ng \cdot L^{-1}$ (0–96 $ng \cdot L^{-1}$), and neuron specific enolase 2.9 $mcg \cdot L^{-1}$ (3.7–8.9 $mcg \cdot L^{-1}$), indicating some muscle injury (potentially AGE), but no ischemic brain insult. Other markers for inflammation and damage were likewise unremarkable (CRP < 0.1 $mg \cdot dl^{-1}$; ESR 3). Basic chemistries and CBC were unremarkable and transaminases normal. The patient returned to the chamber the following morning feeling "completely myself," with a normal neurological exam. In accordance with the previous plan, the patient completed a TT9. However, upon surfacing, the patient had a recurrence of mild neurological symptoms. A comprehensive brain MRI (diffusion weighted, FLAIR, T1, T2, MRA) while symptomatic was normal. Later EEG and psychological screening were normal. The patient had no history or complaint of musculoskeletal pain and no cervical spine studies were conducted. Because symptoms recurred during HBO_2, no further HBO_2 sessions were planned. The patient was observed for an additional 24 h and, following a normal examination, he was discharged to the care of his flight surgeon.

DISCUSSION

The differential diagnoses in those who lose pressure at altitude and develop neurological symptoms include: DCS, secondary effects of VGE that arterialize across a right-to-left shunt, AGE, gravitational effects, hypoxia, and normobaric disease not related to the flight. This patient represents a tightly monitored population engaged in high-risk hypo/hyperbaric occupations (pilots, astronauts, divers, and special operators) who perform at a peak of physical and mental wellness, yet must endure extreme physical and psychological stresses. The patient had no record of acute or chronic illnesses or musculoskeletal injuries, and none were discovered during or following his hospital stay. His most recent flight physical was unremarkable, as was post-discharge psychological testing.

Aviation DCS and AGE originate from the same fundamental mechanisms as seen in diving injury.[7] Two potential pathological pressure thresholds were crossed in this case: alveolar rupture pressure leading to AGE, and VGE formation threshold leading to DCS. The degree and rate of internal cabin pressure loss governs these risks. The Doppler detectible threshold for VGE is 14,763 ft (4500 m) in the absence of preoxygenation with an F_IO_2 of 1.0,[7,23] though these VGE are not necessarily clinically significant.[5,7] DCS risk increases from 5% at 19,028 ft MSL (5800 m) to 90% at 25,000 ft MSL (7620 m), with an ascent rate of 5000 ft (1525 m) MSL/min (1000 ft MSL every 12 s).[7] Symptoms are more likely to develop when rapidly exposed to ambient pressure aircraft altitudes higher in elevation than 8.5 psi (0.58 ATA).[5,15,17] Thus, the possibility for DCS (though small) existed, since the internal cabin pressure ultimately changed from 1.0 to 0.50 ATA [at 18,000 ft (5486 m) MSL].[7]

The USAF defines a fast rate as >5000 ft/min (1524 m/min), and the cabin pressure in this case dropped 15,000–20,000 ft

(4572–6096 m) MSL/min (Table II). Faster rates of cabin pressure loss have been compared [5000 ft/min (1524 m/min) to 80,000 ft/min (24,384 m/min) following a 90-min oxygen prebreathe] where incidence and onset rates for DCS or VGE were not significantly different.[17] These DCS cases occurred in the context of oxygen prebreathing, but this pilot's aviation unit does not routinely conduct oxygen prebreathe procedures. Though the rate of rise in this pilot could be considered "slow," the risk of DCS was still present.

The type of aviation DCS symptoms is also a factor. Symptoms are most often musculoskeletal[10,19] and rarely pulmonary,[19] but neurological DCS may be anticipated in approximately 19.7% of aircrew exposed to high altitude.[2] Infrequently, symptomatic aircrew personnel may require hyperbaric oxygen treatment, yet it is rare to require more than one treatment before returning to baseline function,[10] especially if recompression is initiated within 7-18 h of symptoms onset.[18,22] Confounding this picture is the finding that repeat high altitude flights (as occurred in this case) tend to decrease, rather than increase, the incidence of DCS and VGE.[16]

Pulmonary alveolar membrane injury was also possible (Table I), since a 0.14 ATA pressure change developed and a gradient of 0.11 ATA has been shown to cause alveolar membrane rupture, predisposing to AGE.[7,21] No radiographic evidence of barotrauma was found, though imaging has been unreliable and cannot rule out such events in the etiology of AGE.[4] Smith and Neuman[20] found that AGE from diving were likely to disseminate to multiple organ systems, causing abnormal elevations in transaminases. In this case, aspartate amino transferase was 17 IU $\cdot$ L^{-1} and alanine amino transferase was 16, and neither rose to the level expected in the presence of AGE. The serum CPK, however, did rise modestly to 357 U $\cdot$ L^{-1}, suggesting the possibility that bubbles arterialized to cause diffuse end organ injury.[19] AGE could account for the immediate neurological symptoms at altitude; however, by Weenink's criteria[22] (evidence of brain involvement by CT/MRI/EEG, thoracic evidence, other air emboli findings), the likelihood of a cerebral arterial gas embolism was "possible" rather than "probable" or "proven." Additionally, aviation DCS rarely presents as severely as found in this case[19] and the initial stroke code noncontrast head CT and MRI (diffusion weighted images) showed no evidence of hemorrhage, inflammation (cerebritis or neuritis), edema, ischemia, infarct, or mass.

Arterialization of venous gas emboli across a right-to-left shunt (patent foramen ovale or intrapulmonary vascular shunt) was also considered. VGE, if present in extreme numbers, can be clinically significant, especially if gas emboli cross over the pulmonary filter into the arterial circulation. Here, the pilot's pressure gradient exposure for VGE was not severe, making vascular crossover less likely. The patient clearly responded favorably to the treatment periods of hyperoxia, but the diagnostic workup (other than a small rise in CK) was unremarkable. During the echocardiogram bubble study, the patient had recurrence of symptoms in the moments prior to the injection of bubbles and had acute exacerbation just following. With no immediate or delayed bubbles detected on the echo bubble study, no pulmonary shunt or patent foramen ovale defect (cardiac shunt) was evident.[6]

Shunting of nonbubble, nonecho detectible secondary products of VGE traversing the pulmonary filter to exert their effects on end organs was suggested by a slightly elevated CK. Markers for AGE, DCS, and cerebral ischemic injury were unremarkable, however. Transaminases,[3] S100 protein, and NSE concentrations have been found to correlate with the degree of ischemic insult to the brain.[8] High serum NSE and S100 are associated with poor outcome in ischemic stroke, and neither value was elevated in this case, indicating a lack of ischemia.[3] It is likely that bubble pathology is actually the result of microparticle formation, platelet aggregation, endothelial activation, and oxidative stress,[11] and the success of HBO_2 may be the result of reversing these effects rather than the simple crushing of a bubble. It may, therefore, be possible that these secondary factors arterialize or persist in the end organ, even in cases where no bubbles are seen traversing a patent foramen ovale.

Considered in the differential diagnosis here are other adverse factors in supersonic, high altitude aviation. The onboard oxygen generating system (OBOGS) was investigated and found to be in normal working order, making simple hypoxia unlikely. G forces can cause hemodynamic effects, but the flight pattern conducted did not trigger sufficient force to do so. G maneuvers in aviators can theoretically displace the vertebral arteries as they pass over the arch of the atlas and through the posterior atlanto-occipital membrane, torsing and narrowing the arteries, causing similar neurological symptoms. The pilot also had no acute or chronic illnesses or injuries which predisposed to these conditions or present with neurological sequelae independent of flight conditions. One should consider these entities, however, as potential etiologies in pilots on OBOGS who are exhibiting neurological symptoms in flight.

Recurrence of symptoms following each HBO_2 (during the surface interval or immediately after treatment) was a distinguishing feature of this case and has bearing on the pathology of the disease and timing of treatment. Recurrence of AGE symptoms have been described in diving and submarine escape training,[13] but is rare in aviation beyond the first hyperbaric recompression treatment. Muehlberger[11] found that 3.9% of symptoms resolved on oxygen at altitude, 6.9% on ground level oxygen, and 84.3% resolved during descent. Additionally, descending from the altitude of symptom onset and increasing the internal cabin pressure by a threshold of 50 mmHg (0.97 psi, 0.07 ATA) began improvement in symptoms (as was noted in this case), with approximately 50% of symptoms resolved with a pressure increase of 138 mmHg (2.67 psi, 0.18 ATA), which did not occur in this case.

This case, however, required five treatments, two with extensions, due to recurrence of symptoms. Consultation with civilian, U.S. Navy, and U.S. Air Force aviation and diving medicine and physiology researchers yielded equally equivocal and sometimes contradictory analyses regarding the etiology and final diagnosis for this event. Nonetheless, a bubble disease (favoring AGE over DCS, or a combination of both) with secondary bubble biochemical effects appears to be most probable.

Because descent and postflight ground level oxygen may be sufficient to relieve the majority of altitude DCS symptoms, it is likely that this case represents AGE and shunting of secondary bubble biochemical factors to the cerebral end organ. Following the second HBO_2, bubbles likely to have been caused by either AGE or DCS had been crushed, off gassed, and resolved. It is possible that the period of hyperoxia and secondary biochemical factor inactivation diminished symptoms temporarily, but ongoing inflammation and vasospasm may have contributed to recurrence of symptoms. Recurrence of symptoms in aviation has been attributed to delays in recompression treatment,[18] where an average of 10.6 to 18.2 h delay have correlated with treatment failure after a single HBO_2. The patient in this case was at 60 fsw on his first TT6, however, within 4 h after landing his aircraft, making delay an unlikely factor.

With no further evidence of ongoing pathology, deficits or disease, the prognosis for recovery appears good, but the likelihood of recurrence during and after future flights cannot be estimated with accuracy. This case illustrates a degree of recurrences for neurological symptoms in aviation (hypobaric exposure to hyperbaric baseline environment) that has not previously been described. Further targeted study is required to elucidate whether the factors in this case represent a new manifestation of AGE, recalcitrant secondary inflammatory effects, or an occurrence of DCS caused by a previously unknown constellation of factors.

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