Brain Natriuretic Peptide Levels in Six Basic Underwater Demolitions/SEAL Recruits Presenting with Swimming Induced Pulmonary Edema (SIPE)

LCDR Damon Shearer, DO (DMO/UMO); CDR Richard Mahon, MD (DMO/UMO)

Abstract

Swimming induced pulmonary edema (SIPE) is associated with both SCUBA diving and strenuous surface swimming; however, the majority of reported cases and clinically observed cases tend to occur during or after aggressive surface swimming.[1] Capillary stress failure appears to be central to the pathophysiology of this disorder. Regional pulmonary capillaries are exposed to relatively high pressures secondary to increased vascular volume, elevation of pulmonary vascular resistance, and regional differences in perfusion secondary to forces of gravity and high cardiac output.

Acute pulmonary edema can be classified as either cardiogenic or noncardiogenic or both. Cardiogenic pulmonary edema occurs when the pulmonary capillary hydrostatic pressure exceeds plasma oncotic pressure. Noncardiogenic pulmonary edema occurs when pulmonary capillary permeability is increased. Given the pathophysiology noted above, SIPE can be described as a cardiogenic pulmonary edema, at least in part, since an increased transalveolar pressure gradient has been implicated in the pathogenesis of SIPE.[2]

Brain natriuretic peptide (BNP) is used in the clinical setting to differentiate cardiac from pulmonary sources of dyspnea, specifically to diagnose cardiogenic pulmonary edema.[3,4] During clinical management, BNP levels were drawn on six BUD/S recruits simultaneously presenting with pulmonary complaints consistent with SIPE, after an extended surface bay swim. This paper analyzes that data after de-identification and reviews the pathophysiology and clinical management of SIPE.

Learning Objectives

1. Describe the signs and symptoms of SIPE.
2. Describe the immediate care and treatment of SIPE.
3. Demonstrate understanding of the fundamental pathophysiology of SIPE.

Background

The pathophysiology of SIPE is multifactorial. Numerous physiologic, environmental, and behavioral factors have been implicated. However, capillary stress failure appears to be central to the pathophysiology of this condition. The pulmonary capillary measures approximately two to six microns in diameter. This structure has the difficult task of facilitating gas transfer between the alveoli and pulmonary vasculature whilst maintaining structural integrity. Capillary stress failure occurs when the capillary is exposed to relatively high transmural pressures.

Intense exercise is capable of generating these elevated pressures. Stress fracture of the pulmonary capillaries has been documented with electron microscopy in equine models when exposed to capillary transmural pressures of 75-100mmHg. Additionally, necropsy of equine athletes has demonstrated evidence of pulmonary capillary stress failure.[5] Lower pressures are required to cause fracture in canines and rabbits (40mmHg) and likely in man.[6]

Elite human athletes are capable of generating mean pulmonary artery pressures of 37mmHg. Reeves

et al. demonstrated that both right atrial and wedge pressures rise with heavy exercise in normal men with some wedge pressures measured greater than 30mmHg. They surmised that these high cardiac filling pressures "could contribute both to elevated pulmonary arterial pressure and to increased filtration of water into the lung."[7] Bernheim et al. demonstrated exercise induced increases in systolic right ventricular to atrial pressure gradients (RVPGs) in 39 subjects. Of note, individuals susceptible to high-altitude pulmonary edema (HAPE) demonstrate greater increases in RVPG from baseline than normal controls.[8]

Bronchoalveolar lavage (BAL) findings in such athletes indicate elevated levels of protein and red blood cells. Intense exercise impairs the integrity of the blood-gas barrier in elite athletes. Vigorous exercise not only may result in increased RBCs and total protein on BAL, but also a lack of pro-inflammatory markers. This supports the hypothesis that the insult to the barrier is mechanical.[9] Ludwig et al., demonstrated BAL evidence high molecular weight protein edema fluid and red blood cells consistent with capillary fracture, in five BUD/S trainees diagnosed with SIPE.[10]

The factors that lead to elevated pulmonary artery pressures and capillary fracture are both physical and physiological. Partial immersion, gravity dependent flow in the pulmonary vasculature, and extreme exertion combine to elevate pulmonary artery pressures beyond physiologic norms and lead to failure of the pulmonary capillary.

Head above water immersion has both cardiovascular and pulmonary effects. Increased venous return leads to central pooling of blood, which thereby increases cardiac preload.[11] Additionally, immersion independently leads to elevated pulmonary artery pressures. Arborelius et al., described a 700cc increase in thoracic blood volume and a 32% increase in cardiac output along with elevations of mean pulmonary artery pressure associated with head above water immersion.[12] Exercise with head out immersion leads to significantly greater stroke volume and cardiac output when compared with exercise on land.[13] Additionally, immersion alone increases sympathetic activity, thereby contributing to additional peripheral vasoconstriction and central pooling of blood volume.

Water temperature may have a role in SIPE as well. Immersion in cold water is known to cause peripheral vasoconstriction. Conceivably, this could contribute to increased vascular resistance (afterload), as well as contribute to the central pooling of blood (preload). Cold-water immersion has been demonstrated to increase central vascular volume and forearm vascular resistance and cold showers have been documented to increase pulmonary vascular resistance and increase cardiac output by as much as 59-100%.[14,15]

The pulmonary effects of immersion are also prominent, such as decreased vital capacity, decreased functional residual capacity, and increased closing volume. These effects induce a non-uniform pulmonary vasoconstriction. Capillaries not protected by arterial constriction experience high pressures and are prone to micro-fracture. Negative pressure breathing of head out immersion results in an alveolar pressure less than mouth pressure. This produces hydrostatic forces that favor a fluid shift from the vasculature to the alveoli.[16]

There is a 65% increase in respiratory work associated with immersion to the xiphoid process compared with immersion to the neck.[17] Extreme effort, induced by both intense swimming and this increased work of breathing, could increase peak airway pressures and result in increased capillary permeability.[18]

Gravity dependent flow in the pulmonary vasculature is an additional contributing factor to SIPE. There is a 200% increase in perfusion in the gravity-dependent lung, while swimming in the lateral decubitus position.

This combination of cardiovascular and pulmonary effects can increase capillary transmural pressure via a decrease in the amount of capillary bed available for thoracic blood to flow through. Additional contributing factors have been proposed. Over-hydration could reasonably be presumed to increase central blood volume and increase preload, thus predisposing to elevated pulmonary pressures and capillary fracture. Weiler-Ravell et al. described six cases of SIPE occurring in Israeli soldiers after the individuals drank five liters of water in the two hours preceding the exercise. His team deduced that over-hydration was a contributing factor in these cases.[19] Finally, constrictive wet suits have also been implicated as a causative agent in at least one case report of SIPE.[2] Presumably, the causality in this case would be similar to the effects of submersion, resulting in increased work of breathing. Of note, there is also evidence that tight-fitting wetsuits likely do not play a significant role in SIPE, as evidenced by the lack of significant influence on pulmonary function studies.[20]

Brain natriuretic peptide (BNP) is secreted by myocardial ventricular cells, mainly cardiomyocytes. BNP is known to have natriuretic, diuretic, and vasorelaxant properties. It plays an important role in fluid homeostasis and blood pressure. Elevations in BNP reflect myocardial wall stress and are often in response to high ventricular filling pressures. Numerous studies have shown elevations in plasma BNP levels in left ventricular systolic and diastolic dysfunction, left ventricular hypertrophy, and right ventricular dysfunction in pulmonary hypertension, cardiomyopathy, acute coronary syndromes, and pulmonary embolism.[21-23] Additionally BNP correlates with pulmonary artery pressures.[24]

BNP levels have been utilized clinically in differentiating cardiac from non-cardiac causes of dyspnea. Berdague et al. demonstrated that NT-proBNP is a sensitive and specific means of distinguishing pulmonary from cardiac causes of dyspnea in elderly patients. They demonstrated 86% sensitivity and 71% specificity with

overall accuracy of 80% for cardiac dyspnea.[4] Additionally, brain natriuretic peptide has a sensitivity of 82% and specificity of 92% for identification of cardiac causes of syncope, when a cut-off value of 40pg/ml is used.[25]

It is of note, that resting BNP concentrations are not elevated in physiologically hypertrophied hearts of endurance athletes.[26]

Clinical Considerations

Typical symptoms of SIPE include dyspnea, cough which may be productive of pink or white frothy sputum, chest pain or tightness, and hemoptysis. Upon initial symptom onset, patients may exhibit confusion secondary to hypoxemia. Typical signs include labored breathing, tachypnea, and hypoxemia.

SIPE can be confidently diagnosed in any patient presenting with the above noted signs and symptoms occurring during or immediately after a swimming event, in association with a demonstrable chest radiograph abnormality. The treatment of SIPE is primarily supportive. It is imperative to deliver supplemental oxygen to the patient, titrated to maintain normal oxygen saturation. In the military setting, Corpsmen or First Responders covering training evolutions with an inherent risk for the development of SIPE, should be equipped with pulse oximetry, supplemental oxygen, and inhaled beta agonists. They should be trained in Basic Life Support (BLS/CPR). Prompt evaluation by a physician with access to radiography, Advanced Cardiac Life Support (ACLS) capability, and laboratory support is important for moderate to severe cases of SIPE. However, there is no evidence in the literature that ACLS has been necessary in the treatment of SIPE.

Clinical experience has shown long acting inhaled beta agonists, such as salmeterol, to be of utility. This agent accelerates resolution via improved alveolar fluid clearance and also provides symptomatic relief to the patient.[16] Diuretics generally are not necessary in the treatment of SIPE.[27]

Occasionally patients with SIPE will require inpatient admission, though frequently patients can be discharged directly from the emergency department after a period of treatment and observation, once oxygen saturation has returned to baseline on room air.

A hallmark of SIPE is rapid resolution. Frequently, symptoms resolve within 12 to 24 hours with chest radiographs demonstrating resolution within 24 to 48 hours. Frequently, patients can be returned to full duty within 72 hours.

Historically, there is no evidence that individuals who suffer from an episode of SIPE are predisposed to have additional occurrences. Typically, BUDS candidates who suffer from SIPE have graduation rates commensurate with their fellow students who have not had a SIPE event. In fact, testing in dry conditions of individuals previously diagnosed with SIPE revealed that they do not have abnormal pulmonary function tests, abnormal exercise capacity, or abnormal pulmonary arterial pressure response to hypoxemia.[10]

There are no definite predisposing factors for SIPE. However, Shupak et al. did demonstrate that baseline FVC, FEV1, and FEF were 25 to 75% lower in twenty-one individuals diagnosed with SIPE. Thus lower initial lung volumes and flows may be predictive of vulnerability to SIPE.[28]

Methods

Six BUD/S recruits presented to the ED with pulmonary complaints after a surface bay swim. The diagnosis of SIPE was made on all six individuals based on presenting complaint, chest radiograph findings, and physical examination. BNP levels were drawn on these individuals as part of the clinical evaluation of dyspnea, cough, and pulmonary edema in the emergency department setting. Transport time to the ED was approximately thirty to forty-five minutes from symptom onset. Labs were drawn within two hours of swim termination.

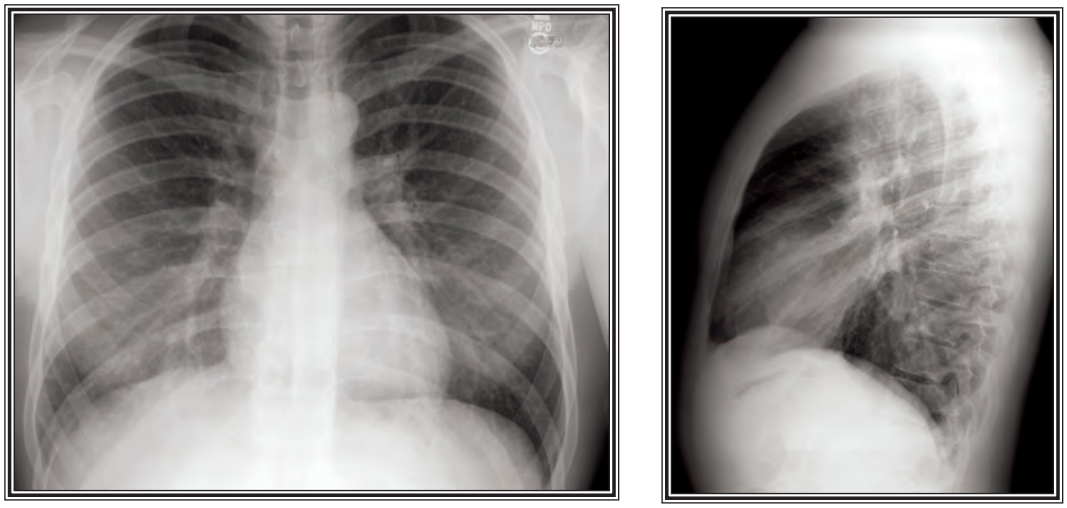
The case definition of SIPE for the purposes of this report is hypoxemia occurring during or immediately after a swimming event, a demonstrable chest radiograph abnormality, improvement or resolution of said abnormality in less than 48 hours, absence of evidence of pulmonary infection, and absence of a history of breathing against a closed glottis or aspiration of water.

Results and Patient Data

See Table 1 on page 47

Results

BNP levels ranged from 6.3pg/ml to 39.7pg/ml. The average was 26.55pg/ml. All values fell within the NMCSD laboratory range of normal, 1-100pg/ml. All six individuals demonstrated abnormal chest radiographs with both interstitial and airspace processes. The cardiac and mediastinal silhouettes were normal in all cases. Three patients were admitted to the internal medicine service. One patient was admitted to the ICU. Two patients were discharged to their command. The patients admitted to the hospital stayed an average of twenty-four hours. Their treatment consisted of supplemental oxygen and beta-agonists (alveolar fluid clearance). All were returned to full duty within seventy-two hours. Two of the six individuals went on to complete BUD/S training and became SEALs. This graduation rate of 33% is consistent with normal rates in individuals attending BUD/S. This likely indicates that a single episode of SIPE does not cause long-term decrements in physical performance from a cardiovascular standpoint.



TYPICAL CHEST RADIOGRAPH FINDINGS IN SIPE: Mixed interstitial & airspace process, prominent pulmonary vasculature, Kerley B-lines, normal cardiac, and mediastinal silhouettes.

Table 1

PT	Age (yrs)	Onset of Symptoms	Initial O2 Sat	Chest Radiograph Findings	BNP (pg/ml)	HgB (g/dl)	Disposition
1	28	0.25 miles into swim	89%	Bibasilar interstitial and airspace process	**38.5**	13.5	Admit to ICU, supportive treatment
2	31	Completed swim	97%	Interstitial prominence in the lung bases	**36.9**	13.2	DC to command w/ salmeterol
3	23	20 minutes into swim	99%	Mixed interstitial and airspace process	**11.1**	13.9	DC to command w/ salmeterol
4	25	5 minutes into swim	87%	Mixed interstitial and airspace process	**6.3**	14.9	Admit to GEN MED, supportive treatment
5	29	45 minutes into swim	87%	Bibasilar diffuse interstitial and air space process	**39.7**	14.7	Admit to GEN MED, supportive treatment
6	27	Not documented	Not documented	Linear opacities in right lung base	**26.8**	13.8	DC to command w/ salmeterol

Discussion of Results

It is well known that BUD/S training is extremely arduous. The extreme physical and psychological demands of the training, in concert with the environment in which the training is conducted, frequently results in illness and injury. Pulmonary infections are relatively common in this population. Therefore, utilization of BNP as a method for differentiating the source of dyspnea in these BUD/S trainees was prudent. Our experience indicates that plasma BNP is not elevated in SIPE. However, these findings may be limited by a delay of up to two hours from symptom onset to blood draw. There is currently little data in the literature describing the amount of BNP reserve in the ventricular cells. The time course for BNP elevations to occur is not incredibly well defined. BNP is significantly elevated above baseline within one hour after ventricular septal defect repair in children and BNP rapidly rises (within hours) in the setting of acute myocardial infarction. [29,30] Serial BNP levels were not drawn in these patients, thus it is theoretically possible that BNP levels may have elevated after initial diagnostic work-up was performed in the emergency room. This seems unlikely however, in that BNP levels are thought to increase within a very short time period of the development of clinically significant pulmonary edema.

Discussion of Patients

These six patients all experienced symptoms consistent with SIPE at various points or timeframes during the same surface bay swim. These swims were performed in the lateral decubitus position. Water conditions were reported as "cold and rough."

These patients share several similarities in presentation and symptoms, physical examination findings, and laboratory abnormalities. All six patients presented with various symptoms of shortness of breath, cough, chest pain/tightness, and hemoptysis. Several of the patients were noted to be hypoxemic by pulse oximetry in the field. This hypoxia is common in SIPE, as noted in two of three patients reported on by Lund et al. and as noted by Adir et al. [16,31] Additionally, mild hypothermia was commonly noted.

Several of the individuals' laboratory studies exhibit a mild anemia. This slight anemia is common in BUD/S trainees. One of the three SIPE patients reported on by Lund et al., exhibited this phenomenon.[16] BUD/S trainees admitted to NMCSD for other diagnoses such as cellulitis and pneumonia, frequently demonstrate a mild anemia. Though not specifically addressed in the literature, this common finding in BUD/S trainees is likely due to the extreme daily physical stress of this course of instruction. The anemia is not likely related to the development of SIPE.

Conclusion

Swimming induced pulmonary edema is of clinical significance, particularly in the military, and most notably in Special Operations trainees and recruits. It is a clinical entity noteworthy for its rapid onset, rapid recovery, and return to full duty. The rapid diagnosis of this condition by medical personnel covering strenuous surface swims in the Naval Special Warfare community is critical to avoid serious morbidity and mortality. BNP levels are not elevated in swimming induced pulmonary edema, rendering this laboratory test of little value in the clinical evaluation of pulmonary edema associated with swimming. Further study of the pathophysiology, etiology, and treatment of swimming induced pulmonary edema is required.

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LCDR Shearer, MD served as the Medical Department Head for Mobile Diving and Salvage Unit TWO and the Senior Medical Officer of Naval Special Warfare Group FOUR while on active duty as a Diving Medical Officer. He is currently a PGY3 resident in radiology at Loyola University Medical Center in Chicago and serving in the Navy Reserves. LCDR Shearer has spoken at the Royal Navy Institute of Naval Medicine, the Armed Forces Operational Medicine Symposium, and Eastern Virginia Medical School on the subjects of undersea and hyperbaric medicine.

CDR Richard T. Mahon, MD is a Navy Undersea Medical Officer and a board certified specialist in pulmonology and critical care medicine. He graduated from the Navy Undersea Medical Institute in 2004 and was subsequently stationed as the Head of the Undersea Medical Department at the Naval Medical Research Center in Bethesda, MD.