Pelvic Organ Prolapse in a Fighter Pilot with Alpha-1 Antitrypsin Deficiency

Kerry Buckley; Jami Gann; Heather Barbier; Joy Greer

BACKGROUND: Few researchers have studied symptomatic younger to middle-aged women with pelvic organ prolapse. The association between highly strenuous activity and prolapse symptoms is largely theoretical. It is also known that a genetic component likely contributes to early-onset pelvic organ prolapse, but prevention and treatment with respect to this has not been explored. Service restrictions differ for active duty women who are diagnosed with symptomatic pelvic organ prolapse.

CASE REPORT: We present a case of a 33-yr-old Gravida 1 Para 1 fighter pilot who developed symptomatic pelvic organ prolapse after a vaginal delivery. Her prolapse symptoms initially prevented her from flying due to exacerbation of pain and pressure. Her exam demonstrated Stage III pelvic organ prolapse. She was treated with a course of physical therapy and ring with support pessary which allowed the patient to return to flight status after 5 mo. After completing the course of physical therapy, her physical exam improved to Stage II pelvic organ prolapse. A few months later, the patient reported that distracting vaginal pain recurred with the highest G forces. Coincidently, the patient was also diagnosed with pulmonary sequela of alpha-1 antitrypsin deficiency and disqualified from flight status.

DISCUSSION: This case illustrates the capability of decreasing pelvic organ prolapse with conservative measures, even in extreme environments, but it also identifies a possible association between an elastase activity defect and susceptibility to pelvic organ prolapse.

KEYWORDS: pelvic organ prolapse, elastase activity, alpha-1 antitrypsin deficiency, anti-G straining maneuver.

Buckley K, Gann J, Barbier H, Greer J. *Pelvic organ prolapse in a fighter pilot with alpha-1 antitrypsin deficiency*. Aerosp Med Hum Perform. 2018; 89(1):66–69.

Pelvic organ prolapse (POP) continues to affect a growing number of women and is a well-documented condition in aging populations. Parity, vaginal delivery, age, and body mass index are generally accepted risk factors for the development of POP.[13] Over the past several decades, women continue to fill and advance in occupations that require routine high stress levels on the body. POP is one condition that continues to be evaluated for its correlation with increases in gravitational forces (Gs) and intra-abdominal pressure. Few studies have explored the connection in younger women between high stress physical activity and urinary incontinence; even less information is available about the relationship to POP.

A 1999 survey of 246 female U.S. Air Force fighter pilots ultimately found that the women, despite repeated exposure to >9 Gs, had no difference in rates of incontinence relative to the general population. It also reaffirmed the association between vaginal delivery and increased rates of incontinence, showing a 52.6% vs. 22.0% prevalence in parous vs. nulliparous aviators, respectively.[4] A 2000 study looking into high G exposure in centrifuge training found that only 1 out of 25 aviators reported any urine leakage during the testing event, even though 5 had previously experienced episodes of incontinence in other settings. The authors postulated that the decreased urinary leakage may have occurred due to the additional voluntary muscle recruitment during performance of a Kegel-like procedure—the anti-G straining maneuver (AGSM).[2]

Both urinary incontinence and pelvic organ prolapse were studied in a group of nulliparous U.S. military cadets; 37 of the 116 cadets went through rigorous paratrooper training. The

From the Women's Health Department, Division of Urogynecology, Naval Medical Center Portsmouth, Portsmouth, VA; and the Aviation Medicine Department, Naval Air Station Oceana, Virginia Beach, VA.

This manuscript was received for review in July 2017. It was accepted for publication in October 2017.

Address correspondence to: Jami L. G. Buckley, M.D., Aviation Medicine Department, Branch Health Clinic Oceana, 1550 Tomcat Blvd., Virginia Beach, VA 23460; jamigann@hotmail.com.

DOI: https://doi.org/10.3357/AMHP.4964.2018

female cadets received pelvic organ prolapse quantification (POP-Q) examinations prior to and after summer training. Of the 37 women undergoing paratrooper training, 14 (38%) participants developed Stage II POP with exposure to just 5 jumps. The study concluded that exposure to the stresses associated with opening shock and impact at landing were directly correlated to the development of pelvic organ prolapse. An association with urinary incontinence did not achieve statistical significance. The results of this study, however, seem slightly extreme. Even in the population of 79 women that did not do paratrooper training, 17 originally Stage 0 participants developed at least Stage I POP after summer training. From the study data you can conclude that 53.3% of the originally Stage 0 17–21 yr old women (32 out of 60), with exposure to a summer of military training, develop some level of POP.[7]

While vaginal delivery is a well-known risk factor for the development of POP, another less well-known contributor to POP may be a genetic deficiency. Many studies have discussed that POP appears to have a genetic component given its propensity for afflicting sisters and other close female relatives.[6] In a 2004 paper completed at Stanford University, it was discovered that women with stress urinary incontinence and/or pelvic organ prolapse had a statistically significant decrease in alpha-1 antitrypsin mRNA and protein levels within the vaginal tissue.[3] Although the relationship between alpha-1 antitrypsin deficiency (A1AD) and liver/lung disease has been established, A1AD has the potential to affect all tissues in which the gene may be expressed. Alpha-1 antitrypsin is an enzyme that is responsible for breaking down neutrophil elastase, a pro-inflammatory enzyme that is released in inflammatory states and implicated in damaging host tissue and causing tissue remodeling. The process of childbirth is increasingly thought to be controlled by inflammation.[11] It is highly likely that the pro-inflammatory sequence continues in the immediate postpartum period as the mother's tissues respond to injury and attempt to prevent infection. Tissue remodeling may be affected in A1AD individuals, possibly impairing the mother's ability to adequately heal the pelvic floor.

CASE REPORT

A 33-yr-old Gravida 1 Para 1 military aviator presented to her flight surgeon with complaints of vaginal discomfort 3 mo after undergoing a spontaneous vaginal delivery. She was symptomatic while running and with prolonged standing, and also observed a bulge in her vaginal area. Additionally, she noted occasional frequent and more urgent urination, but denied any episodes of incontinence. Her obstetric history was notable for a spontaneous vaginal delivery of a viable 6-lb, 12-oz female infant at 38 wk gestational age.

Upon referral to urogynecology, she was evaluated and POP-Q examination revealed an anterior Stage III POP (Aa +2, Ba +2). Pelvic floor physical therapy was initiated and the patient was fitted with a #3 ring with support pessary. Surgical intervention was discussed but deferred as the patient desired future child-bearing within the year and wanted to delay surgical correction until her child-bearing was completed.

After approximately 2 mo of pessary use and physical therapy, the patient no longer noticed any vaginal bulge or pain at rest. However, on flights where she was exposed to a stress of 4 Gs or greater, she noticed some non-incapacitating pain and discomfort. It was noted, though, that throughout the flight, as the patient was anticipating the high G maneuvers more by performing the AGSM, her pain decreased.

Following 3 mo of pessary use, additional physical therapy sessions, a home exercise program, and flying on missions only requiring less than 4 Gs of stress, the patient noted substantial improvement. After 4 mo of continued physical therapy, home exercises, and pessary use, the patient felt comfortable executing maneuvers that would routinely sustain 6 Gs. Reevaluation with a POP-Q examination was completed after 5 mo, noting an improvement to Stage II POP (Aa +1 and Ba +1). At this time the patient was cleared for full flight status with reports that the realm of forces sustained during all aspects of flight caused nothing more than a nondistracting discomfort. She also felt that the discomfort she sometimes felt was not necessarily due to the G forces at the instant, but more likely the position of the pessary at that moment in time as the pain did not consistently correlate to the Gs pulled.

After a few months, however, the patient returned, stating that at the highest G maneuvers she did experience vaginal pain at a level that she found distracting and possibly unsafe. Around this same time, the patient developed an upper respiratory infection with an aggravating episode of constant chest pain exacerbated by deep inspiration and cough. An X-ray showed pneumomediastinum and her subsequent workup identified pulmonary blebs and an underlying diagnosis of A1AD. Due to the finding of pulmonary blebs (a known sequela of A1AD) and theoretical risk of in-flight pneumothorax, the aviator was permanently grounded. Further investigation into her healing and final state of recovery/G tolerance with respect to her POP was unable to be obtained.

DISCUSSION

This complex case of POP brings to light many questions about a common diagnosis. Our patient was subjected to multiple exposures of extremely high Gs both before and after pregnancy in the setting of an A1AD. It is not yet known whether either of these may have contributed to her development of or susceptibility to POP. For the aviation community it is relevant to know if repeated exposure to high Gs causes or predisposes a woman to POP. The prior study on paratroopers is concerning that repeated exposure may be a risk. Currently, however, we have many female fighter pilots who have repeatedly sustained high Gs and only one known case of symptomatic POP which developed postpartum, not as a direct result of a high G maneuver.

Additionally, given the fact that female aviators are in their childbearing years most commonly during the peak of their

career, it would be beneficial to review all additional cases of pelvic organ prolapse to further understand treatment options. Some military service branches automatically ground aviators with POP regardless of symptoms or treatment. The U.S. Air Force Medical Standards Directory states that "malposition of the uterus or vaginal walls (uterovaginal prolapse, cystocele, rectocele), if symptomatic" is disqualifying for Flying Class I/IA, II, III, and ground-based missile operation duty.[12] The U.S. Air Force Flying Class standards are briefly described below: I/IA) undergraduate navigator training and initial medical qualification for Special Operations Combat Systems Officer; II) officers for duty in restricted aircraft categories (low-G aircraft or nonejection set aircraft); III) individuals qualified for unrestricted aviation.[5] In contrast, the U.S. Army and Navy only ground pilots when they are no longer able to perform their duties as determined by the active duty service member and her medical team. The U.S. Army refers a soldier to a Physical Evaluation Board when, because of a medical impairment, she may be unable to perform her duties worldwide under field conditions and optimal hospital benefits have been obtained.[1] Similarly, U.S. Navy guidance allows the patient and medical treatment team to tailor the work restrictions based on the patient's symptoms and examination findings. A Physical Evaluation Board to determine fitness for duty is only required if the condition constitutes an impairment in the ability to perform the duties as a member of the Department of the Navy or requires an untoward number of visits for medical care or hospitalizations.[10] Our aviator, due to her desire for another child within a year, was not a surgical candidate. For other female pilots the desire for future children may also be a factor, so the patient's initial positive response to conservative management shows promise. And ultimately, given her underlying genetic deficiency, it is possible that a different patient may have continued to heal and eventually recovered to sustaining high G forces pain free. It is impossible to draw any conclusions on the ideal management at this time as our patient declined surgery, but surgical correction may provide for a faster return to full flight duties.

G stresses and gravity on the pelvic floor warrant additional study. While in flight, aviators perform the AGSM to prevent blood draining from the brain down into the legs and mitigate the risk of gravity-induced loss of consciousness. We know that the maneuver increases intra-abdominal pressure and, therefore, the stress on the pelvic floor; however, we do not fully understand the muscle activation that may ultimately lead to a strengthening/conditioning of the pelvic floor. Aviators may be at higher risk of developing POP, similar to an obese patient with elevated intra-abdominal pressure, or their repeated exposure and resultant muscle recruitment may in fact be protective. During flight, the AGSM is repeatedly performed and could be compared to a patient completing Kegel exercises.

In a recent article, dynamic MRI was used to evaluate lengthening and angular movements of the cardinal and deep uterosacral ligaments when exposed to increased intra-abdominal pressure. The data was able to show that the cardinal ligament lengthened and the deep uterosacral ligament angle changed during the Valsalva maneuver. Consistently, patients with POP had more exaggerated changes in length and angle.[9] Perhaps future investigation could reveal changes in the pelvic floor with active countermeasures in place, such as a Kegel or AGSM. This may aid in further understanding the multitude of forces involved at the pelvic floor. However, a more revealing analysis would be a long-term study of ligamentous changes in patients routinely exposed to short duration increases in intra-abdominal pressure (pilots, gymnasts, weightlifters, etc.) compared to controls.

The confounding diagnosis of A1AD in our patient brings to light a number of unknowns. Inflammation within the pelvis is a commonly seen condition in postpartum women, often falling under the diagnosis of endometritis. After such a large insult to the body, an inflammatory reaction is not only expected, but needed to facilitate recovery. However, with A1AD, it is possible that this inflammatory response may be responsible for excessive damage to the host tissue due to unrestrained neutrophil elastase activity. Given that alpha-1 antitrypsin levels were lower in the vaginal tissues of individuals with incontinence and prolapse, it seems possible that there may be a correlation.

Although treatment for A1AD with enzyme replacement is currently focused toward maintaining pulmonary function, there are likely to be additional applications discovered. For instance, if the majority of damage to the host is done during an acute inflammatory reaction (childbirth, COPD exacerbation, SIRS), while there is active neutrophil penetration in the tissues, a more proactive and timely treatment might prevent damage to the underlying tissue.

Management of pregnant women, both those exposed to repeated episodes of high intra-abdominal pressure and those with a possible genetic mutation, may change with additional research. Numbers have shown that seven Cesarean deliveries would need to be performed to prevent a single case of a pelvic floor disorder in the general population.[8] No data exists for the number of Cesareans needed to prevent POP in targeted populations. Women with repeated high G exposure or genetic deficiencies may decrease their risk of symptomatic POP simply by avoiding vaginal delivery. However, a more aggressive antepartum evaluation of occupational exposures and requirements, and possible genetic components, would be needed to assess risk in these targeted populations. This case illuminates multiple fronts on which both prevention and treatment of POP may be explored, specifically in a younger population who could greatly benefit from improved risk assessment.

ACKNOWLEDGMENTS

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of the Air Force, Department of Defense, or the United States Government.

Authors and affiliations: Kerry Buckley, M.D., Heather Barbier, M.D., and Joy Greer, M.D., Women's Health Department, Division of Urogynecology, Naval Medical Center Portsmouth, Portsmouth, VA; and Jami Gann, M.D., Aviation Medicine Department, Naval Air Station Oceana, Virginia Beach, VA.

REFERENCES

1. Army Regulation 635-40. Personel Separations: Physical Evaluation for Retention, Retirement and Separation, 1SEP1990. Washington (DC): Department of the Army; 1990.
2. Benjamin CR, Hearon CM. Urinary continence in women during centrifuge exposure to high +Gz. Aviat Space Environ Med. 2000; 71(2):131–136.
3. Chen B, Wen Y, Polan ML. Elastolytic activity in women with stress urinary incontinence and pelvic organ prolapse. Neurourol Urodyn. 2004; 23(2):119–126.
4. Fischer JR, Berg PH. Urinary incontinence in United States Air Force female aircrew. Obstet Gynecol. 1999; 94(4):532–536.
5. Guidance Memorandum (GM) – Air Force Instruction 48-123. Medical Examinations and Standards. Washington (DC): U.S. Air Force; 2016.
6. Jack GS, Nikolova G, Vilain E, Raz S, Rodriguez LV. Familial transmission of genitovaginal prolapse. Int Urogynecol J Pelvic Floor Dysfunct. 2006; 17(5):498–501.
7. Larsen WI, Yavorek T. Pelvic prolapse and urinary incontinence in nulliparous college women in relation to paratrooper training. Int Urogynecol J Pelvic Floor Dysfunct. 2007; 18(7):769–771.
8. Lukacz ES, Lawrence JM, Contreras R, Nager CW, Luber KM. Parity, mode of delivery, and pelvic floor disorders. Obstet Gynecol. 2006; 107(6):1253–1260.
9. Luo J, Betschart C, Chen L, Ashton-Miller JA, DeLancey JOL. Using stress MRI to analyze the 3D changes in apical ligament geometry from rest to maximal Valsalva: a pilot study. Int Urogynecol J. 2014; 25(2):197–203.
10. Secretary of the Navy Instruction (SECNAVINST) 1850.4E. Navy Disability Evaluation Manual. Washington (DC): U.S. Navy; 2005.
11. Thomson AJ, Telfer JF, Young A, Campbell S, Stewart CJ, et al. Leukocytes infiltrate the myometrium during human parturtion: further evidence that labour is an inflammatory process. Hum Reprod. 1999; 14(1):229–236.
12. U.S. Air Force Medical Standards Directory, approved by AF SG3/5P on 29 May 2017, Section J65. Washington (DC): U.S. Air Force; 2017.
13. Vergeldt TF, Weemhoff M, IntHout J, Kluivers KB. Risk factors for pelvic organ prolapse and its recurrence: a systematic review. Int Urogynecol J. 2015; 26(11):1559–1573.