Our patient was hospitalized for 7 d and discharged from the hospital in Okinawa after a 5-d course of IVIG. On discharge the patient had a normal ophthalmologic exam and his ataxia had completely resolved. His only remaining neurological deficit was persistent areflexia. He was sent home to his home base in Jacksonville, FL. This patient's areflexia completely resolved 1 mo after the onset of his symptoms and, after passing autonomic testing and a treadmill exercise test, he was recommended for a waiver to return to full flight status as a pilot. His waiver was granted 2 mo after the onset of his symptoms.

Cagniart P-EC. ***You're the flight surgeon: Miller-Fischer syndrome.*** **Aerosp Med Hum Perform. 2015; 86(10):918–920.**

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REFERENCES

1. Anthony SA, Thurtell MJ, Leigh RJ. Miller Fisher syndrome mimicking ocular myasthenia gravis. Optom Vis Sci. 2012; 89(12):e118–e123.
2. Arakawa Y, Yoshimura M, Kobayashi S, Ichihashi K, Miyao M, et al. The use of intravenous immunoglobulin in Miller Fisher syndrome. Brain Dev. 1993; 15(3):231–233.
3. Connolly J, Van Syoc D. Guillain-Barré syndrome (acute inflammatory demyelinating polyradiculoneuropathy) (Jul 14). In: Air Force waiver guide. Wright-Patterson AFB (OH): U.S. Air Force School of Aerospace Medicine; 2014:369–373.
4. Diamond S, Schear HE, Leeds MF. Pseudo-internuclear oculomotor ophthalmoplegia secondary to Guillain-Barré polyneuronitis simulating myasthenia gravis in an air transport pilot. Aviat Space Environ Med. 1975; 46(2):204–207.
5. Fisher M. An unusual variant of acute idiopathic polyneuritis (syndrome of ophthalmoplegia, ataxia and areflexia). N Engl J Med. 1956; 255(2):57–65.
6. Hughes RA, Rees JH. Clinical and epidemiologic features of Guillain-Barré syndrome. J Infect Dis. 1997; 176(Suppl. 2):S92–S98.
7. Ito M, Kuwabara S, Odaka M, Misawa S, Koga M, et al. Bickerstaff's brainstem encephalitis and Fisher syndrome form a continuous spectrum: clinical analysis of 581 cases. J Neurol. 2008; 255(5):674–682.
8. Lo YL. Clinical and immunological spectrum of the Miller Fischer syndrome. Muscle Nerve. 2007; 36(5):615–627.
9. McFarlin DE. Immunological parameters in Guillain-Barré syndrome. Ann Neurol. 1990; 27(Suppl.):S25–S29.
10. Mori M, Kuwabara S, Fukutake T, Hattori T. Plasmapheresis and Miller Fisher syndrome: analysis of 50 consecutive cases. J Neurol Neurosurg Psychiatry. 2002; 72(5):680.
11. Mori M, Kuwabara S, Fukutake T, Yuki N, Hattori T. Clinical features and prognosis of Miller Fisher syndrome. Neurology. 2001; 56(8):1104–1106.
12. Naval Aerospace Medical Institute. 10.4. Guillain-Barre syndrome (acute inflammatory demyelinating polyneuropathy – AIDP). In: U.S. Navy aeromedical reference and waiver guide. Pensacola (FL): Naval Aerospace Medical Institute; 2015.
13. Toone KP. Persistant esophoria following a diagnosis of Guillain-Barré syndrome with Miller Fisher variant. Federal Air Surgeon's Med Bull (NY). 2012; 50(1):12–13.
14. U.S. Army Aeromedical Activity. Guillain-Barre syndrome (acute inflammatory demyelinating polyneuropathy): ICD9 357.0. In: Flight surgeon's aeromedical checklists. Ft. Rucker (AL): U.S. Army Aeromedical Activity; 2014.
15. Willison HJ, O'Hanlon GM. The immunopathogenesis of Miller Fisher syndrome. J Neuroimmunol. 1999; 100(1-2):3–12.
16. Yuan CL, Wang YJ, Tsai CP. Miller Fisher syndrome: a hospital-based retrospective study. Eur Neurol. 2000; 44(2):79–85.
17. Zifko U, Drlicek M, Senautka G, Grisold W. High dose immunoglobulin therapy is effective in the Miller Fisher syndrome. J Neurol. 1994; 241(3): 178–179.

This article was prepared by Maximilian Lee, M.D., M.P.H.

A 29-yr-old female flight test engineer reports to the flight medicine clinic with a history of fatigue, headache, nausea, and skin sensitivity. Her symptoms were present for many weeks but have recently worsened. Patient denies fevers, chills, recent travels, contact with ill persons, or history of trauma. Past medical history is significant for history of pancreatitis as a child. Past surgical history included wisdom tooth extraction. She takes over-the-counter multivitamins, but no prescription medications. The patient is not pregnant.

1. What is an appropriate next step in the work-up?

A. Detailed history and physical.
B. Complete metabolic and hematologic work-up including a thyroid panel.
C. Computed tomography and magnetic resonance imaging studies of the brain.
D. Behavioral health referral.

ANSWER/DISCUSSION

1. A. Detailed history and physical. The patient appears to have symptoms associated with multiple diseases without a unifying diagnosis. She has been a flight test engineer for 4 yr and denies significant changes in her crew duties. The aviator states that she has been training for an ultra-marathon and has lost approximately 5 lb over the course of 2 wk. She also reports a past medical history of chronic subclinical

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pancreatitis since high school with a current Air Force Flying Class III waiver for her condition. Although she averages 7 h of sleep, she feels fatigued most days and denies changes to her symptoms despite her increased exercise regimen. The aviator does not feel depressed and states that although she is tired, it does not prevent her from accomplishing her work-related duties or activities of daily living. She characterizes her headaches as being diffuse without localization. Patient denies throbbing, auras, focality, or band-like qualities to her headache. She states that the headache is present at all times without temporal association. She denies experiencing focal neurological deficits. She denies rashes on her face or shins or purple streaks on her abdomen, but states that the skin on her arms and neck feels rough and sensitive. The patient has never been pregnant and reports having regular menstrual cycles. She does not report history of cold or heat intolerance.

Physical exam reveals a well-developed, well-nourished woman in no acute distress with normal head, eyes, ears, nose, and throat exam. The skin shows mild xerosis and erythema on the sun-exposed surfaces of her face, neck, and arms. There is no dermatological evidence of jaundice. Head hair distribution and density are normal, with normal eyebrow follicle density and distribution. Abdominal exam is normal without hepatosplenomegally. Neurological exam is normal with normal cranial nerves. Gross motor strength, sensation, proprioception, cerebellar function, deep tendon reflexes, and gait are normal. The patient then asks if her symptoms might be related to increased training and increased use of her sport supplements.

2. Which of the following vitamins are metabolized and stored primarily in the liver?

A. Vitamin A.
B. Vitamin B1.
C. Vitamin B12.
D. Vitamin C.

ANSWER/DISCUSSION

2. A. Vitamins A, D, E, and K are fat-soluble vitamins. Vitamin A is primarily bio-transformed and stored in the liver.[7] Other vitamins, including B1, B6, B12, and C, are water-soluble and are primarily excreted by the kidneys. Natural sources of vitamin A and its precursors occur in yellow- and orange-colored fruits and vegetables such as squashes and carrots.[9] Beta-carotene is a provitamin that is hydrolyzed into two molecules of vitamin A. A single 7.5-in carrot has approximately 8666 IU of vitamin A.[9] Vitamin A is also found in high concentration in animal liver and can undergo bio-amplification in the food chain in animals such as polar bears, wolves, and Hapuka fish.[5] The polar bear liver contains 6285 $\pm$ 2228 IU $\cdot$ g^{-1} of vitamin A, which can result in a lethal dose in as little as 160 g ingested orally. Acute lethal dose to adults has occurred at 1,000,000 IU, with chronic toxicity occurring with ingestion of 20,000 IU.[7,14]

The patient revealed that she was taking four tablets of a specially ordered vitamin with a total calculated vitamin A dose of 20,000 IU per day. She reported that she had been taking her vitamins more diligently and increased her caloric intake of protein during her training sessions. She stated that she restarted taking the high-dose vitamin for the past 6 mo due to concerns for nutrient malabsorption from chronic pancreatitis.[6,8]

3. Which lab values can help confirm the diagnosis of chronic vitamin A toxicity?

A. Retinol levels.
B. Retinoic acid levels.
C. Isoretinoin levels.
D. Ascorbic acid levels.

ANSWER/DISCUSSION

3. B. Since the patient was not on any other medications, the best test for chronic vitamin A toxicity is a retinoic acid level. Isoretinoin is a form of retinol used in oral acne preparation. Retinol or vitamin A levels are unreliable for chronic vitamin A toxicity because they are rapidly metabolized and will likely be normal at the time of presentation.[5] Ascorbic acid is vitamin C.

Laboratory work-up showed normal complete blood cell count, normal basic chemistries, and mild elevation of liver transaminases [aspartate transaminase = 54 IU $\cdot$ L^{-1} (4–40 IU $\cdot$ L^{-1}) and alanine transaminase = 52 IU $\cdot$ L^{-1} (5–56 IU $\cdot$ L^{-1})]. Serum lipase and alkaline phosphatase were normal. The patient's serum retinol was normal at 70 mcg $\cdot$ dl^{-1} (30–72 mcg $\cdot$ dl^{-1}), but retinoic acid level was elevated at 9.5 ngm $\cdot$ ml^{-1} (2.7–4.2 ngm $\cdot$ ml^{-1}).

4. In the United States, what is the most common cause of vitamin A toxicity?

A. Oral acne medications.
B. Ingestion of carnivorous animal livers.
C. Excess ingestion of beta carotene containing vegetables.
D. Vitamin A supplementation.

ANSWER/DISCUSSION

4. D. Vitamin A supplementation. A common source of exogenous vitamin A ingestion results from dietary supplements according to a Gallup poll where 50% of Americans admitted using supplements.[11] The recommended daily unit ingestion of vitamin A is 5000 IU; however, some multivitamins and specific nutritional supplements that advertise promotion of eye health contain carotenoids and can have more than the recommended daily allowance. Nutritional supplements for body building have doses up to 20,000 IU per day. Literature review found sporadic reports of mild and reversible hepatotoxicity from dietary intake of vegetables, usually in patients with eating disorders or diets promoting carrots as a sole source of snacks.[3,5] Oral acne medication is associated with increased risk or potential teratogenic effects rather than long-term chronic vitamin toxicity. Teratogenic effects of isoretinoin found in oral antiacne medication include structural malformation of the brain, head and face, heart and great vessels, and thymus.[7] Vitamin A itself has teratogenic effects shown in a large prospective cohort study. Outcomes of women talking

supplements of more than 10,000 IU per day compared to 5000 IU per day found a 4.8-fold (95% confidence interval 2.2 to 10.5) increased relative risk for cranial-neural crest defects.[2,7] Toxic ingestion of carnivorous animal livers is reported in the literature; however, toxicities involved with liver ingestion tend to be acute in presentation and more common in children.[3,5] People on diets rich in beta carotene tend to develop yellow-orange skin discoloration in the stratum corneal level of the skin, sweat, and sebum rather than systemic toxicity.

Hypervitaminosis involving vitamin A has been associated with nausea, headache, dry skin and mucous membranes, and bone pain. Rarely, it can lead to hypercalcemia, cerebellar edema, intracranial hypertension, cardiac arrhythmias, and syncope. For chronic hypervitaminosis, the aeromedical concern mainly involves loss of performance secondary to the associated symptoms and the potential for incapacitation from rare and sudden events such as arrhythmias and syncope.

U.S. Air Force regulations stipulate that performing aviation duties while using over-the-counter medications is prohibited. Furthermore, dietary, herbal, and nutritional supplements can only be used with the approval of a flight surgeon.[12] The U.S. Navy Aeromedical Reference and Waiver Guide recommends that the flight surgeon ask about dietary supplements and that the intake should not exceed tolerable upper intake levels as determined by the Institute of Medicine.[10] Similarly, U.S. Army aviation regulations prohibit the use of over-the-counter medications, including dietary supplements, unless cleared by the flight surgeon or aeromedical physician assistant in consultation with the applicable aeromedical policy letter.[13] According to the Federal Food, Drug, and Cosmetic Act, dietary supplements including vitamins are classified as foods[4]; therefore, the Federal Aviation Administration application for medical certificate history does not require disclosure from civilian airmen.[1] However, the Federal Air Surgeon's Bulletin recommends that the aviation medical examiner ask about dietary supplements and seek to clarify the underlying medical condition for which the applicant is taking the medication (e.g., St. John's Wort for depression).[1]

After discussing the potential dangers of supra-therapeutic doses of vitamins while awaiting laboratory results, the patient discontinued the use of the high-dose vitamins while performing duties not including flying for 3 wk. The aviator reported gradual improvement of her headache symptoms over the course of 4 wk while also reporting decreased erythema and pain on her arms and neck. She was able to resume her marathon training regimen 7 d after stopping supplements. At 4 wk she was completely symptom free.

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REFERENCES

1. Borrillo DJ. Herbal medication and flying: when having an alternate is not a good thing. Federal Air Surgeon's Medical Bulletin (NY). 1999; 37(1):10.
2. Davies JS, Poole CD. Vitamin D: too much of a good thing? Br J Gen Pract. 2014; 64(618):8–9.
3. Ertekin V, Selimoğlu MA, Tan H. Pseudotumor cerebri due to hypervitaminosis A or hypervitaminosis D or both in Alagille syndrome. Headache. 2010; 50(1):152–153.
4. Federal Food, Drug, and Cosmetic Act C. 21 U.S.C. 321(ff). 2010:35. [Accessed 8 Sep. 2014]. Available from http://www.gpo.gov/fdsys/pkg/USCODE-2010-title21/html/USCODE-2010-title21-chap9-subchapII-sec321.htm.
5. Hayman RM, Dalziel SR. Acute vitamin A toxicity: a report of three paediatric cases. J Paediatr Child Health. 2012; 48(3):E98–E100.
6. Lankisch PG. Conservative treatment of chronic pancreatitis. Digestion. 1987; 37(Suppl. 1):47–55.
7. Muller AA, Henretig FM. The vitamins. In: Shannon MW, Borron SW, Burns MJ, editors. Haddah and Winchester's clinical management of poisoning and drug overdose, 4th ed. Philadelphia (PA): Saunders Elsevier; 2007:1089–1094.
8. Niederau C, Schultz HU, Letko G. Involvement of free radicals in the pathophysiology of chronic pancreatitis: potential of treatment with antioxidant and scavenger substances. Klin Wochenschr. 1991; 69(21-23): 1018–1024.
9. Sansone RA, Sansone LA. Carrot man: a case of excessive beta-carotene ingestion. Int J Eat Disord. 2012; 45(6):816–818.
10. Sather TE, Woolsey CL. Nutritional and ergogenic supplements: aircrew guidance and policy. In: U.S. Navy aeromedical reference and waiver guide. Pensacola (FL): Naval Aerospace Medical Institute; 2014. [Accessed 8 Sep. 2014]. Available from http://www.med.navy.mil/sites/nmotc/nami/arwg/Documents/WaiverGuide/19_Waiver_Guide_Dietary_Supplements_130604.pdf.
11. Swift A. Half of Americans take vitamins regularly. 2013. [Accessed 8 Sep. 2014]. Available from http://www.gallup.com/poll/166541/half-americans-vitamins-regularly.aspx.
12. U.S. Air Force. Medical examinations and standards. Washington (DC): Department of the Air Force; 2013:45. Air Force Instruction 48-123.
13. U.S. Army. Temporary flying restrictions due to exogenous factors affecting aircrew efficiency. Washington (DC): Department of the Army; 2007:1–2. Army Regulation 40–8.
14. Vyas AK, White NH. Case of hypercalcemia secondary to hypervitaminosis A in a 6-year-old boy with autism. Case Rep Endocrinol. 2011; 2011:424712.