You're the Flight Surgeon

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You're the flight surgeon at a small military base, where you are responsible for providing medical care to more than 300 operators of remotely piloted aircraft. Your last patient of the day is a 19-yr-old female sensor operator with complaints of 3 d of a fever up to 100.7°F orally as well as chills that are worse in the evening. She reports that her two young children, her husband, and several close coworkers are experiencing similar illnesses. She also endorses a slight cough that worsens with physical activity, but she denies any other symptoms, including nausea, vomiting, or diarrhea. She presented to you today because she is unable to focus on her work secondary to her distracting symptoms, and she is becoming increasingly fatigued and "achy."

On physical examination, she appears well and is afebrile. The remainder of her vital signs are also within the normal range. You note that she has several enlarged lymph nodes in the anterior cervical chain that are "rubbery" in consistency but not tender to palpation. Otherwise, her exam is unremarkable, including normal-appearing tonsils without erythema or exudate, despite her complaints of a mild cough.

1. What is your next course of action for workup of this patient's complaints?

A. Symptomatic treatment and test for influenza with clear instructions to return to the clinic if condition worsens or does not improve within 2 wk, as this is likely a virus and will resolve on its own.
B. Urgent referral to general surgery for biopsy of her anterior cervical lymphadenopathy.
C. Empiric antibiotics to treat what is most likely streptococcal pharyngitis.
D. Immediate admission to the local hospital for expedited workup of this patient's complaints.

ANSWER/DISCUSSION

1. A. Expectant management of what is likely a viral illness is an appropriate treatment option in this case. The patient's recent exposure to sick contacts with similar symptoms, her nontoxic appearance, and her characteristic symptoms support this presumptive diagnosis and plan of care. Alternatively, Infectious Disease Society of America guidelines recommend testing certain individuals for influenza if confirmation of this diagnosis is likely to influence treatment or infection-control decisions. As the patient is presenting within the 72-h window when the use of neurominadase inhibitors could be considered, performing an influenza diagnostic assay could be considered.[3] It is reasonable to give this patient acetaminophen and/or ibuprofen to take as needed for her fever, chills, and muscle aches and to place her on quarters (i.e., excuse her from duties) for 24–48 h due to her reported inability to focus on her work because of her symptoms. This patient should be given clear instructions to return to the clinic if her symptoms persist past 2 wk or if they start to worsen. Urgent referral to general surgery for her anterior cervical lymphadenopathy is not indicated at this time, as acute infection is the most likely diagnosis for this patient's complaints at the present time, and bilateral, anterior cervical lymphadenopathy is an expected finding in viral upper respiratory tract infections. Treatment for streptococcal pharyngitis is not appropriate in the absence of sore throat. The presence of lymphadenopathy and fever fulfills two of the four Centor criteria, the criteria used to assist clinicians in the identification of patients who warrant further evaluation or treatment for streptococcal pharyngitis. Even if the patient did complain of sore throat, fulfilling only two criteria is insufficient to justify the prescription of empiric antibiotics. In the setting of a sore throat but questionable pretest probability of a positive streptococcal pharyngitis diagnosis, it is best to perform a diagnostic test prior to administering antibiotics.[1] Although this patient undoubtedly desires immediate resolution of her symptoms given that she is highly symptomatic with worsening fatigue and achiness that is affecting her quality of life and duty performance, it is unlikely that admission to the local hospital would affect the course of her recovery. Her symptoms are likely caused by a virus and are therefore unlikely to respond to any treatments or diagnoses that could be expedited by a hospital admission. Additionally, inappropriate hospitalization would place the patient at increased risk of nosocomial complications with likely little benefit in terms of shortening her recovery from her current illness.

DOI: https://doi.org/10.3357/AMHP.5067.2018

You decide to treat this patient symptomatically with acetaminophen and ibuprofen as needed, placing her on quarters for 48 h. Her flu test is negative. You ensure that she understands to return to the clinic if her symptoms worsen or if her symptoms persist beyond 2 wk.

A month later, you are returning from a temporary duty assignment at a remote base, and you note that you are scheduled to see this patient again for complaints of persistent fever and worsening fatigue. The patient comes to your office and you immediately notice that she looks much more ill and appears much thinner compared to when you saw her a few weeks ago. She reports to you that her fever has persisted, but until about a week ago, it had not changed in intensity. Her cough is gone and she delayed coming back because she had gotten quite busy preparing for the upcoming wing inspection. She now notes that her temperatures are up to 101.8°F in the evenings and she has started to have drenching night sweats nearly every night (forcing her to change her sheets and clothes), often a couple times per night. She has lost 30 lb since you last saw her, despite not having the energy to work out as much or as often as she was used to doing. This is far more than 20% of her bodyweight and was lost quite unintentionally. She notes additionally that she has had significant shortness of breath with running and, because of this, is now unable to run more than 2 mi at once, which is much less than her usual daily 6-mi runs.

On examination, you note that the patient is febrile to 101.3°F and she appears flushed. On further review of her vital signs, you also note that her heart rate is 123 bpm and her respiratory rate is 21 breaths per minute, with an oxygen saturation of 89% at rest. You again observe the anterior cervical lymphadenopathy, but today you appreciate an increase in the size of the nodes. You also palpate an enlarged supraclavicular lymph node on the left and pronounced splenomegaly, which were not present 1 mo ago. Interestingly, when you mention the splenomegaly, the patient perks up and reports that she "had that before" when she was diagnosed with mononucleosis about 3 yr ago. When you question the patient about her worsening lymphadenopathy, she states that she noticed a developing "lump" on her neck, but she was too busy with work to worry about it, and it did not concern her because it was not painful. Her lung sounds are diffusely muffled, with crackles heard throughout.

Prior to the onset of the present illness, the patient was quite healthy, without any chronic medical conditions. Her only medication is a daily prenatal vitamin. She denies any personal history of cancer, although her grandmother was diagnosed with breast cancer in her 70s and died of this disease several years after diagnosis.

2. What is your next course of action in the evaluation of this patient's presenting signs and symptoms?

A. Continue to treat symptomatically, as the most likely causative etiology remains viral.
B. Urgent referral to general surgery for biopsy of her lymphadenopathy.
C. Immediate admission to the local hospital for expedited diagnostic workup and acute care management.
D. Immediate computed tomography chest scan to further evaluate the nature of your patient's lymphadenopathy.

ANSWER/DISCUSSION

2. C. The patient appears very ill and is presenting with a month of persistent and worsening symptoms, with several alarming findings on clinical evaluation. Therefore, hospitalization for urgent management and an expedited diagnostic evaluation is warranted. Her loss of more than 20% of her bodyweight in such a short period, her progressive lymphadenopathy, and the new physical examination findings (high fevers, muffled lung sounds, and splenomegaly) are highly concerning for a more serious infectious process and/or underlying malignancy. At this point, you are quite concerned about this patient. It would be beneficial for you to call the local hospital admissions department to set up this transfer so that she may be directly admitted from your clinic to the hospital. Continued symptomatic treatment is no longer an appropriate option in light of the multiple high-risk features and toxic appearance of the patient today. If the underlying etiology of the patient's symptoms was viral, improvement would be expected over the course of 1 mo, presuming normal immune function. Because the patient is clearly not improving and is instead worsening, suspicion for malignancy is elevated, and a simple viral infection is less likely. A bacterial or fungal secondary infection in the setting of immune dysfunction due to an underlying malignancy remains on the differential. However, even if a secondary infection is suspected, the patient's current condition still merits hospitalization. Although her evaluation will likely involve a consultation with general surgery for biopsy of her enlarged lymph nodes, pursuing this course as an outpatient is not the most expedient route for stabilizing the patient and establishing a diagnosis. Likewise, although further imaging will be required to further assess the extent of her lymphadenopathy and to attempt to determine the pathology behind her dyspnea and chest findings, the most prudent action is to directly admit the patient to the hospital for prompt medical management of her acutely ill state and immediate initiation of diagnostic testing.

You determine that the patient needs more advanced acute medical care and an urgent diagnostic evaluation due to the severity of her symptoms and rapidly progressive decline. You contact the admissions department at the local hospital and arrange for a direct transfer. While hospitalized, the patient undergoes thorough testing, including extensive bloodwork and computed tomography imaging of the neck and chest, which shows widespread involvement of the anterior cervical lymph nodes, bilateral supraclavicular lymph nodes, bilateral inguinal lymph nodes, the mediastinum, the liver, and the spleen. A biopsy of the anterior cervical lymph nodes identifies Hodgkin lymphoma as the malignancy. The Ann Arbor Staging System with Cotswolds Modifications is used to stage this patient's disease, which is determined to be stage IV.[6] Her blood work (white blood cell count $\geq$15,000/mm^3 and lymphocyte count <600/mm^3), along with her stage IV classification, leads to an International Prognostic Score of 3.[4] The oncologist at the local hospital arranges for treatment with curative intent with doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine (ABVD).[7]

3. If this patient were filling a position on a manned aircraft, which of the ABVD chemotherapeutic agents would be most concerning aeromedically and why?

A. Doxorubicin: pulmonary toxicity.
B. Bleomycin: pulmonary toxicity.

C. Vinblastine: cardiotoxicity.
D. Dacarbazine: cardiotoxicity.

ANSWER/DISCUSSION

3. B. Bleomycin is known to cause interstitial pulmonary fibrosis in up to 10% of all those exposed to this medication at therapeutic doses. The pulmonary fibrosis is fatal in 1–2% of these cases, but its severity can be somewhat mitigated with corticosteroid treatment if it is caught reasonably early in its course. To monitor the patient's personal risk for developing this complication, pre- and post-treatment pulmonary function tests with full lung volumes and diffusing capacity of the lungs for carbon monoxide tests are recommended to ensure there are no changes in these values after treatment with the ABVD.[5] Clearly, in the aerospace environment, healthy lungs are vital for peak performance, so this particular side effect must be closely monitored and ruled out prior to being cleared for duties in manned aircraft.

Because this patient is geographically separated from her extended family, you decide to help facilitate the transfer to a larger hospital in her hometown for treatment of her Hodgkin lymphoma. This will allow her to develop the strong support network that will benefit her in her treatment and recovery. Both the hospital commander and her commander are on board with this transfer, and appropriate approval is obtained. After her treatment with ABVD chemotherapy, repeat scans show remission of her disease in the short term.

After the patient returned from her hometown following completion of her chemotherapy treatment, she was returned to flight status and was returned to full duty following a Medical Evaluation Board. She has an appropriate follow-up schedule in place, but is concerned with her risk of recurrence.

4. What do you tell her is the typical recurrence rate of stage IV Hodgkin lymphoma?

A. 40%.
B. 50%.
C. 30%.
D. 10%.

ANSWER/DISCUSSION

4. A. For patients with advanced disease at diagnosis, such as this patient, the relapse rate is 40%. The relapse rate for Hodgkin lymphoma in a patient diagnosed in the early stages is 10–15%.[4]

AEROMEDICAL DISPOSITION

Army Regulation 40-501 does not specifically address Hodgkin lymphoma, but it does state that members with malignant neoplasms are disqualified from flying duties. Waivers are possible through the Army medical system and, although malignant neoplasms are not specifically addressed, a member may be potentially eligible for an aeromedical waiver for flying duties if the condition is not progressive, is not subject to aggravation by military service, does not preclude satisfactory completion of training and/or military service, and does not constitute an undue hazard to the individual or to others.[9] The U.S. Navy Aeromedical Reference and Waiver Guide specifically addresses Hodgkin lymphoma and states that for this patient with more advanced disease (stage IIB–IVB), a waiver will be considered 5 yr after completion of therapy. The patient will be grounded while undergoing treatment for the disease.[8] The Federal Aviation Administration (FAA) addresses Hodgkin lymphoma and states that the entire course of treatment and current status of disease must be submitted to the FAA for consideration of a special issuance. After this is granted, repeat special issuances may be given by the Aviation Medical Examiner if allowed by the initial FAA decision and all specifications are met.[2] The Air Force Waiver Guide addresses Hodgkin lymphoma quite extensively. Generally, flyers may return to flying status following completion of therapy and when adverse side effects from therapy have resolved and hematologic abnormalities have normalized. Waivers may be considered for Flying Class III 6 mo after completion of treatment, if the patient is asymptomatic and in full remission. No indefinite waivers are considered for this condition because of its propensity to relapse.[10]

This patient was returned to full duty following the result of a Medical Evaluation Board. She was then granted a waiver following the successful treatment of her disease.

Franz A. *You're the flight surgeon: Hodgkin lymphoma.* Aerosp Med Hum Perform. 2018; 89(5):487–490.

ACKNOWLEDGMENTS

The author would like to thank Dr. Laura Bridge, Aeromedical Consult Service, U.S. Air Force School of Aerospace Medicine, for her professional review of this article. The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Air Force, the Department of Defense or the U.S. Government.

REFERENCES

1. ESCMID Sore Throat Guideline Group, Pelucchi C, Grigoryan L, Galeone C, Esposito S, et al. Guideline for the management of acute sore throat. Clin Microbiol Infect. 2012; 18(Suppl. 1):1–28.
2. Federal Aviation Administration. Guide for aviation medical examiners. Washington (DC): Federal Aviation Administration; 2016:134, 353. [Accessed 23 Aug. 2016]. Available from https://www.faa.gov/about/office_org/headquarters_offices/avs/offices/aam/ame/guide/.
3. Harper SA, Bradley JS, Englund JA, File TM, Gravenstein S, et al. Seasonal influenza in adults and children–diagnosis, treatment, chemoprophylaxis, and institutional outbreak management: clinical practice guidelines of the Infectious Diseases Society of America. Clin Infect Dis. 2009; 48(8):1003–1032.
4. Hasenclever D, Diehl V, Armitage JO, Assouline D, Björkholm M, et al. A prognostic score for advance Hodgkin's disease. N Engl J Med. 1998; 339(21):1506–1514.
5. Jules-Elysee K, White DA. Bleomycin-induced pulmonary toxicity. Clin Chest Med. 1990; 11(1):1–20.
6. Lister TA, Crowther D, Sutcliffe SB, Glatstein E, Canellos GP, et al. Report of a committee convened to discuss the evaluation and staging of patients with Hodgkin's disease: Cotswolds meeting. J Clin Oncol. 1989; 7(11):1630–1636.

7. Moccia AA, Donaldson J, Chhanabhai M, Hoskins PJ, Klasa RJ, et al. International Prognostic Score in advanced-stage Hodgkin's lymphoma: altered utility in the modern era. J Clin Oncol. 2012; 30(27):3383–3388.
8. Naval Aerospace Medical Institute. 9.7 Hodgkin's disease. In: U.S. Navy aeromedical reference and waiver guide. Pensacola (FL): Naval Aerospace Medical Institute; 2016. [Accessed 23 Aug. 2016]. Available from http://www.med.navy.mil/sites/nmotc/nami/arwg/Pages/default.aspx.
9. U.S. Army. Standards of medical fitness. Washington (DC): Department of the Army; 2016:20-21, 36. [Accessed 23 Aug. 2016]. Available from https://armypubs.army.mil/ProductMaps/PubForm/AR.aspx.
10. Wolf J, Van Syoc D. Hodgkin lymphoma (May 15). In: Air Force waiver guide. Wright-Patterson AFB (OH): U.S. Air Force School of Aerospace Medicine; 2016:426–432. [Accessed 23 Aug. 2016]. Available from http://www.wpafb.af.mil/afrl/711hpw/USAFSAM/.