

MORNING REPORT

A SICK Veteran

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The patient, a 66-year-old African-American Vietnam War veteran, presented to the outpatient clinic with loss of appetite and an unintentional weight loss of three pounds. He has a history of hypertension, hyperlipidemia, alcoholism, tobacco use, and old, treated pulmonary tuberculosis. While in the army he was treated for pulmonary tuberculosis with Isoniazid. To our knowledge, this was his only prescribed medication while in the army. His daily medications include atorvastatin (10 mg), Lisinopril (40 mg), and fluticasone nasal spray. The patient's family history is notable only for diabetes. He is single and has no children.

On review of systems, he reported post-nasal drainage, but denied fevers, chills, cough, or abdominal pain. He felt his appetite was improving since he had cut back on alcohol.

The patient was a thin appealing man in no acute distress. He was afebrile, BP 125/84, pulse 106 and regular, respiratory rate 16, BMI 22. There was exudate and cobblestoning in his posterior pharynx. Lungs were clear without wheezing. Heart exam was regular without a murmur. Abdomen was soft and nontender without hepatosplenomegaly. There was no peripheral edema or lymphadenopathy.

Basic labs were ordered, including a complete blood count, comprehensive metabolic panel, urinalysis, and sedimentation rate. The white blood cell count (WBC) was 6,800 cells/mL with a normal differential and the hemoglobin was slightly low at 11.9 g/dL. The basic metabolic panel and liver function tests were within normal limits. The sedimentation rate (ESR) was markedly elevated at 110 mm/hr (normal 0–10 mm/hr).

An elevated ESR should prompt a search for a serious underlying cause. In one large retrospective review, an ESR of more than 100 mm/hr was not sensitive but was highly specific for systemic illnesses: 96% for malignancies, 97% for infection, and more than 99% as a “sickness” index. The term sickness index suggests a simple mnemonic. When the sedimentation rate (S) is more than 100 mm/hr, consider infection and inflammatory conditions (I), cancer (C), kidney disease (K).¹ With an elevated ESR, weight loss, and a history of smoking and of tuberculosis, I would order a chest X-ray.

A chest X-ray that was completed a few weeks after the clinic visit revealed a large, left pleural effusion, obscuring the left lower- and mid-lung zones. The right lung was clear. There was a curvilinear opacity with central lucency in the left lung apex.

A unilateral pleural effusion along with parenchymal opacities raise the possibility of empyema/complicated parapneumonic effusion, lung cancer, tuberculosis, or even congestive heart failure. The next step is to perform thoracentesis and pleural fluid analysis.

Thoracentesis was performed yielding pleural fluid that was slightly turbid; cell count 84 cells/uL with 60% neutrophils and 39% lymphocytes and no red blood cells. The pleural fluid glucose was 38mg/dL, cholesterol 46 mg/dL, total protein 4.9 g/dL, and LDH 410 IU/L. Serum total protein was 7.6 g/dL and LDH was 176 IU/L (range: serum LDH<190 IU/L).

Light's Criteria is used to categorize pleural fluid as exudative or transudative, an important distinction for diagnosis and management. An exudative pleural effusion requires one

or more of the following: pleural fluid total protein/serum total protein>0.5, in this case 0.6, pleural fluid LDH/serum LDH>2/3, the upper limit of normal for serum LDH. The pleural fluid LDH of 410 IU/L is well above 2/3 of the upper of normal of the serum LDH. An alternative way to determine exudate includes pleural fluid total protein, LDH, and cholesterol (the three-test rule). A pleural fluid cholesterol>45 mg/dl suggests an exudate.

Despite the relatively low cell count, the neutrophilic predominance suggests an acute response, such as acute pneumonia or complicated effusion. A predominance of mononuclear cells, especially small lymphocytes, would favor cancer or tuberculosis. The presence of the low pleural fluid glucose concentration of less than 60 mg/dL suggests a complicated parapneumonic effusion, tuberculosis, or malignancy.²

This patient's pleural fluid is consistent with an exudate, and has features that are suggestive of malignancy, tuberculosis, or parapneumonic infection. Additional work-ups indicated. Fewer than 40% of patients with pleural tuberculosis have positive cultures, and therefore other clues, such as adenosine deaminase levels, could be sent. A pleural fluid adenosine deaminase level above 40 U/L is highly suggestive of tuberculosis pleural effusion.²

Our patient's pleural fluid adenosine deaminase level was only 4.8 U/L, well below the level suggestive of tuberculosis pleuritis. Pleural fluid cultures, microscopic stains for the tuberculosis bacteria, and cytology were all performed and all tested negative. A second thoracentesis yielded simi-

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lar results; however, the second cell count was 90% lymphocyte predominant. Because of ongoing concern for underlying malignancy, the patient underwent a PET/CT scan that identified a PET avid left upper lobe nodule. A CT-guided transthoracic fine needle aspiration revealed granulomas. Given the concern for underlying tuberculosis, the county health department became involved, and the patient was directly admitted to the hospital for bronchoscopy with bronchoalveolar lavage (BAL). Acid fast stain and MTB complex probe of the BAL sample were positive for tuberculosis. He was started on a four (4) drug regimen with Isoniazid 300mg, Rifampin 600mg, Pyrazinamide 1500mg, Ethambutol 1200mg, and pyridoxine.

Tuberculous pleural effusions can occur in the setting of primary or re-activation tuberculosis. These are

usually unilateral, lymphocytic predominant exudative effusions, seen in concert with lung opacities. Common presenting symptoms are fever and malaise. Diagnosis begins with a thoracentesis and may require a pleural biopsy or a bronchoscopy, as AFB cultures are rarely positive. Treatment is the same as for active pulmonary tuberculosis.

Important points to remember include the following:

- think of ordering a sedimentation rate if concerned about a serious infection or malignancy. If the ESR is more than 100 mm/hr, you will very likely find a serious etiology;
- a unilateral pleural effusion should always prompt further evaluation, usually with thoracentesis;

- determine whether the fluid is an exudate or transudate. If exudative, check cell count, glucose levels, cytology, and cultures; consider markers for tuberculosis; and
- realize that tuberculosis can be difficult to diagnose and that more advanced techniques including bronchoscopy, bronchoalveolar lavage, or pleural biopsy may be required.

References

1. Fincher RM, Page MI. Clinical significance of extreme elevation of the erythrocyte sedimentation rate. *Arch Intern Med* 1986; 146(8):1581-3.
2. Light RW. Clinical practice. Pleural effusion. *N Engl J Med* 2002; 346(25):1971-77.

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