Evaluating Suspected Malignant Pleural Effusions: Is Sending More Fluid Better?

Sallach SM, Sallach JA, Vasquez E, et al. Volume of pleural fluid required for diagnosis of pleural malignancy. Chest 2002;122:1913–7.

Study Overview

Objective. To determine if the diagnosis of pleural malignancy is dependent on the volume of pleural fluid sampled.

Design. Single-center retrospective chart review.

Setting and participants. 282 patients who underwent diagnostic thoracentesis at Henry Ford Hospital in Detroit between 1 October 1998 and 30 June 1999.

Methods. Pleural fluid samples included in the analysis had been submitted fresh and unfixed, with the entire volume centrifuged. Resulting sediment was used for cytologic processing using cytospin slide and cell block techniques. Cytology results were categorized as positive for malignancy, negative, or abnormal (including suspicious). For the purposes of this analysis, all results that were not positive were considered negative. Medical records were abstracted for demographics, pleural fluid sample volume, fluid pathologic diagnosis, and clinical diagnosis. The presence of pleural malignancy diagnosed by cytology or pleural biopsy at 6 months served as the gold standard for clinical diagnosis. Samples were classified into quartiles based on volume of fluid collected (0.2–10 mL, 15–80 mL, 100–775 mL, and 800–2800 mL.)

Main outcome measures. Sensitivity and negative predictive value (NPV) for diagnosis of pleural malignancy were calculated within each quartile. Logistic regression models using generalized estimating equation methods were used to compare sensitivities and NPV among the quartiles. Demographics (sex, race, age) and medical history factors (smoking history, history of malignancy) also were correlated with sensitivity and NPV.

Main results. 374 pleural fluid samples were retrospectively identified among 140 men and 142 women. The average patient age was 65 years; 59% smoked and 36.9% had a history of cancer. Pleural malignancy within 6 months of initial thoracentesis was diagnosed in 99 patients (35%). The final diagnosis included lung cancer (non–small cell, small cell, mesothelioma, and other) in 51.6% and metastatic carcinoma in 48%. The sensitivities for pleural fluid quartiles were 53.9%, 52%, 46.9%, and 63.3%, respectively. No differences were detected for sensitivity and NPV for diagnosis of pleural malignancy between any 2 quartiles. Samples collected from nonsmokers had a slightly higher sensitivity for malignancy than samples from smokers (70% versus 56%; $P = 0.057$). Samples collected from women had a higher sensitivity for predicting pleural malignancy (67% versus 37.7%; $P = 0.0011$). Samples collected from patients with no history of malignancy had a significantly higher NPV than samples collected from patients with a history of malignancy (91.4% versus 59.8%; $P < 0.001$). After adjusting for these demographic and medical history factors, the association of the pleural fluid volume quartiles with sensitivity and NPV did not change.

Conclusion. The sensitivity for diagnosis of pleural malignancy is not dependent on the volume of pleural fluid extracted during thoracentesis.

Commentary

An isolated pleural effusion can be the presenting sign of occult primary or metastatic cancer, usually indicating advanced disease. Pathologic proof is necessary to establish the diagnosis and accurately stage the cancer. The standard evaluation of a suspected malignant pleural effusion includes performing a thoracentesis to obtain fluid for cytology. Historically, initial cytologic evaluation will be positive in 50% to 70% of patients with malignant effusions, particularly when metastatic. A smaller percentage will be picked up on repeat thoracentesis and when the cell blocks and smears are examined [1,2]. However, no formal recommendations exist regarding the volume of fluid needed for optimal cytologic evaluation. It remains unclear whether increasing the volume leads to results that are more accurate.

Sallach and colleagues attempted to address this issue by performing a chart review at a large teaching hospital. After identifying nearly 300 patients who had undergone diagnostic thoracentesis, the authors next determined that a third of these patients were subsequently found to have malignant effusions. The sensitivity of fluid cytology for malignancy

ranged from 46.9% to 63.3% among the quartiles, which is consistent with other reports in the literature. There was a slight trend suggesting that sensitivity increased with greater fluid volumes obtained; however, this was not statistically significant ($P = 0.193$). Perhaps more important, the NPV ranged from 74.7% to 84.6% among the quartiles, with a nonsignificant trend suggesting that the NPV decreased with increasing volume ($P = 0.095$). Of interest, malignant effusions in nonsmokers or in women were more likely to test positive on cytologic review than in smokers or men, respectively.

The study's merits include its use of regression analysis and data from 374 fluid samples. The authors should be congratulated for contributing to an area where there is limited evidence or guidance. While it is easy to recognize the several shortcomings of a single-center chart review (eg, documentation errors, sample bias, institutional/provider bias), the results are provocative. Sending 10 mL of fluid may be as useful as sending 2 L in identifying malignant cells. This has important implications for patients undergoing thoracenteses for diagnostic purposes only, since collecting smaller samples may limit potential procedure-related complications. Obvious questions are whether these results would hold up to prospective analysis or a study that included thousands of samples from hundreds of patients with cancer.

Applications for Clinical Practice

Suspected malignant pleural effusions should be evaluated for cytology using cell block and smear preparations in order to establish a diagnosis as well as appropriately stage the patient. The volume obtained should be based primarily on patient safety, therapeutic intent, and institutional collection requirements for requested testing.

–Review by David R. Spigel, MD

References

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