Pleural Effusion in Congestive Heart Failure

Pleural effusions are commonly seen in patients with congestive heart failure. They are usually bilateral or right sided and are rarely left sided. An important step in the evaluation of any pleural effusion is the classification of the fluid into a transudate or an exudate. Transudative effusions develop when there is a change in systemic factors such as an increase in capillary hydrostatic pressure or a decrease in colloid oncotic pressure. Exudates are the result of pleural inflammation, infection, injury, or lymphatic obstruction. An exudative process always requires a more extensive and often invasive workup and often a search for occult malignancy. It is believed that congestive heart failure causes transudative effusions.

In the past, specific gravity and protein concentration of the fluid were used to separate transudates from exudates. More than 50 years ago, Gilligan et al studied the effect of diuresis on the protein concentration of pleural effusion. A decrease in the volume of the fluid and a small increase in the protein concentration were reported. Pillay studied six patients with pleural effusion due to heart failure at the time of hospital admission and after diuresis with mercurials. The mean fluid protein concentration increased from 1.5 to 2.0 g/dl. In one patient it rose from 1.3 to 3.1 g/dl.

Criteria proposed by Light et al are now used to classify effusions. The fluid is classified as an exudate if the pleural fluid/serum protein ratio is greater than 0.5, or the pleural fluid lactate dehydrogenase (LDH) is greater than 200 IU, or the pleural fluid/serum LDH ratio is greater than 0.6. Even when these criteria are used, effusions due to heart failure may be misclassified. Peterman and Speicher studied 495 pleural effusions to evaluate the criteria of Light et al. Of the 57 patients with heart failure and no other cause for pleural effusion, 19 (33 percent) had exudative effusions. Recently we studied eight patients with pleural effusion due to heart failure. Thoracentesis was performed at the time of hospital admission and after diuretic therapy. Significant increase in the protein level (2.2 to 3.2 g/dl) and the fluid/serum ratio of LDH (0.39 to 0.64) was found. In three patients the fluid was classified as a transudate at the initial study (by the criteria of Light et al) but met the criteria for an exudate after treatment of heart failure. It is clear that treatment of heart failure causes significant changes in the pleural fluid chemistry; in some cases a transudate may be converted into a “pseudoexudate.” It is likely that with diuresis, water from the effusion is reabsorbed more rapidly than other molecules and the concentrations of protein and LDH rise.

Since pleural effusions are common in heart failure, thoracentesis of all such effusions is not practical. The health and public policy committee of the American College of Physicians noted that “the indication for a diagnostic thoracentesis is the presence of any pleural effusion of unknown cause. An exception would be a patient presenting with clear clinical manifestations of recurrent left ventricular failure. In this circumstance, a trial of diuresis may precede consideration of thoracentesis.” However, the physician faces the dilemma that diuresis will alter the pleural fluid chemistry.

In this issue (see page 546), Roth et al used the serum-effusion albumin gradient in the evaluation of pleural effusions. The criteria of Light et al misclassified five effusions due to heart failure as exudates, but the serum-effusion albumin gradient classified them correctly. However, the gradient misclassified two malignant effusions as transudates. The criteria of Light et al are very sensitive for diagnosing exudates and the gradient appears to be more specific. However, only 15 patients with heart failure were studied. In this and other studies, if a patient with heart failure had pleural effusion, it was assumed that the effusion was secondary to failure; an associated silent pulmonary embolism is difficult to exclude. If the serum-effusion albumin gradient is confirmed to be a useful test in larger numbers of patients with heart failure, it may become a useful clinical tool. Clinicians should be aware of the fact that diuresis may convert a transudative effusion of heart failure into a pseudoexudate. Thoracentesis is not indicated in every patient with heart failure and pleural effusion; however, if a comorbid condition is suspected, thoracentesis should be done early and not after a trial of diuretic therapy.

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A Role for Intermediate, Heterozygous Alpha1-Antitrypsin Deficiency in Obstructive Lung Disease

Alpha1-antitrypsin (AAT) is one of the body's defense mechanisms that protects against tissue damage from the proteolytic enzymes of inflammatory cells. The antitrypsin protein is synthesized by the liver and has a molecular weight of 52,000 daltons, which is small enough to allow diffusion from the blood into the tissue spaces of the various organs. The most recognized function of this protein is to bind and inactivate lysosomal proteases that are released during inflammatory reactions. The lungs are dependent upon AAT for this type of protection, so that chronic obstructive lung disease can develop when the protein is deficient, either through inheritance of a deficient variant of AAT, or through development of a relative deficiency from excessive cigarette smoking. Panacinar emphysema is the type of lung disease usually observed with AAT deficiency, although cases may present with bronchiectasis, chronic bronchitis or even asthma.

Alpha1-antitrypsin is a polymorphic protein for which approximately 75 molecular variants have been described to date. Simple mutation of a single amino acid alters the mobility of the protein upon electrophoresis in an acid gradient. The molecular variants are named with letters of the alphabet depending upon whether they move slower or faster than normal. Fortunately, only a few of the variants are found with any frequency in different populations. The normal type is labeled as Pi**. The most common variant causing AAT deficiency is Pi*, which is present mostly in those of Northern Europe descent and in the Maoris of New Zealand. The Pi* variant causes lesser degrees of deficiency, and is most commonly found among those of Spanish or Portuguese heritage.

Whether heterozygous or intermediate AAT deficiency is actually a predisposing factor for development of lung disease has been debated ever since one of the current authors (JL) first called attention in 1969 to the increased number of patients with intermediate AAT deficiency among a group with pulmonary emphysema.1 COPD patients with an intermediate AAT deficiency (usually from heterozygous inheritance of a deficient AAT variant) are more prevalent than are patients with a severe, homozygous deficiency of AAT (18 vs 8 percent of emphysema patients, and 5 vs 0.04 percent of healthy subjects). However, those with a severe deficiency usually develop emphysema at an earlier age than do heterozygotes, most frequently between 25 and 40 years of age, and after much less exposure to cigarette smoke. In this issue of Chest (see page 594) Townley and co-authors call attention to an association between the MS, heterozygous, AAT phenotype and bronchial hyperresponsiveness to methacholine in members of both asthmatic and non-asthmatic families. Townley et al suggest that the MS phenotype may be an additional risk factor for the development of asthma.

It is of interest that we have found increased numbers with variant Pi types among Puerto Ricans in New York City attending clinics at the Beth Israel Medical Center.2 The MS phenotype occurred in 16 percent as compared to 8 percent in American Caucasians, the MZ in 5 percent as compared to 2.5 percent in Caucasians, and the MV in 2 percent as compared to none in Caucasians. We had also noted that Puerto Ricans had a much greater prevalence of bronchospastic disease than other ethnic groups in New York City; emphysema was present in only one of 55 such Puerto Rican patients, whereas the remainder had asthma. These asthma did not differ significantly from a Puerto Rican control group in their prevalence of variant AAT phenotypes. However, it is of interest that none of 14 asthmatics with AAT variants and only 2 of 13 non-asthmatics with AAT variants smoked, compared to 38 percent of 89 subjects with normal AAT, both with and without asthma. We suspect that Puerto Ricans with AAT variants may be especially sensitive to lung irritants, leading them to avoid cigarettes and other noxious irritants. This intuitive but appropriate behavior may actually reduce the number of such subjects who develop lung disease.

The observations by Townley et al of increased bronchial hyperreactivity in subjects with the MS phenotype, and to a lesser degree in those with the MZ phenotype, supports our speculation regarding Puerto Rican subjects in New York City. A previous study by Kabiraj et al did not find increased bronchial reactivity in subjects with an MZ phenotype, but MS subjects were not studied.