Circulating Immune Complexes in Lung Disease

Hypersensitivity lung diseases, of which allergic aspergillosis is a prototype, are an immunologic curiosity. Organisms usually of little virulence grow in plugs of airway mucus. These organisms are protected by the mucous matrix which seems to serve as an adjuvant. The ensuing brisk immunologic response is ineffective in clearing the bronchial tree. The presence in the airway of high titers of antibody and complement plus soluble antigen from the microbes causes intense complement-mediated damage of surrounding airway tissues. High dosage corticosteroid therapy inhibits inflammation and shuts down the disease process, possibly by diminishing neutrophil response to complement fragment chemo-attractants. The acute phase of the disease is marked by the presence in the sera of circulating immune complexes (CIC). These presumably represent a complex of microbial antigens, complement, and excess antibody which occupies all of the antigenic sites and forms a soluble unit rather than a precipitating lattice. These CIC do not appear to cause disease elsewhere in the body and are regarded as immunologic flotsam from a reaction originating in the airways.

There is increasing evidence that the airway disease in cystic fibrosis (CF) may in part be due to a hypersensitivity pneumonitis. Sera of CF patients contain factors which influence ciliary and mucus activity of cells and inhibit the phagocytosis of Pseudomonas aeruginosa by alveolar macrophages. Certainly the colonization of CF mucus by a variety of organisms, and the magnitude of the IgE and IgG response to these organisms, set the stage for immune complex formation. Nelson et al reported a high incidence of allergic aspergillosis in CF using rigorous adherence to diagnostic criteria. Poor prognosis in CF is associated with high antibody titers to specific pathogens, and good prognosis in younger children is associated with hypogammaglobulinemia. The presence of CIC in high concentrations in the sera of CF patients may be a clue to the pathophysiology of the lung disease.

In this issue of Chest (see page 405), Church and colleagues have confirmed the presence of CIC in CF sera, particularly during acute illness. They also have begun the important task of evaluating the various means of measuring CIC. What do the CIC mean? Do they represent merely the normal opsonization of large numbers of airway pathogens? Are they a sensitive, quantitative indicator of airway pathogen burden? Do they represent a significant hypersensitivity airway reaction to Pseudomonas sp or other organisms?

The therapeutic implications of such questions are important. The hypersensitivity pneumonias do not respond well to specific antimicrobial therapy alone; in fact, treatment of allergic aspergillosis with parenteral amphotericin B was a failure. The 20,000-40,000 CF patients in the United States seem doomed to progressive pulmonary disease despite antimicrobial therapy. Should they be treated with anti-inflammatory agents as soon as the sputum is colonized and before widespread lung damage takes place? Are there alternatives to high-dose corticosteroids in the treatment of hypersensitivity pneumonias?

Further developments in this field may alter the therapeutic approach and prognosis in CF.

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Management of Recurrent Sustained Ventricular Tachycardia Complicating Chronic Ischemic Heart Disease

Recurrent sustained ventricular tachycardia is one of the late complications following recovery from myocardial infarction. Our definition of “sustained” ventricular tachycardia relates to episodes which necessitate either cardioversion or parenteral medication for termination. In our experience, once a patient experiences a single episode, future recurrence is the rule.

Sustained ventricular tachycardia in the patient with chronic ischemic heart disease is rarely asymptomatic and usually produces symptoms of congestive heart failure, presyncope, syncope and sometimes sudden death. It has become more evident that in patients dying suddenly after recovering from acute myocardial infarction, the initiating arrhythmia may have been ventricular tachycardia.

In a post-infarction patient who is hospitalized for an episode of symptomatic sustained ventricular tachycardia, it is important to define an effective therapeutic regimen, which will prevent the recurrence of the ventricular tachycardia. Traditionally, prophylactic treatment for sustained ventricular tachycardia has been empiric, based on trial and error.

This empiric approach depends upon giving an antiarrhythmic medication with expectation that the medication will prevent the recurrence of the ventricular tachycardia, but without direct knowledge if the medication has the ability to act favorably on the arrhythmia, namely, totally prevent its appearance, reduce the incidence of attacks, or significantly decrease the rate of the tachycardia so it will be better tolerated by the patient.

Suppression of premature ventricular contractions is a poor guide to effectiveness of prophylaxis for recurrent sustained ventricular tachycardia in the patient with chronic ischemic heart disease. In a great majority of patients, the pattern of occurrence of ventricular tachycardia is sporadic, necessitating weeks or months to define the efficacy or inefficacy of drugs. During this period, the patient is exposed to the short- and long-term toxicity which accompanies all antiarrhythmic agents. In addition, if the patient is on an ineffective agent, he or she is exposed to the risk of recurrent ventricular tachycardia and possibly sudden death. Once a drug is found ineffective (or toxic), the patient is given another drug and the cycle is repeated. Frequent, the patient does not respond to multiple antiarrhythmic medications alone or in combination and is considered to have drug resistant ventricular tachycardia. In these cases, experimental antiarrhythmic drugs, surgery, or some pacing modality may be utilized.

Electrophysiologic studies in patients with recurrent sustained ventricular tachycardia utilizing ventricular stimulation have reliably replicated the patients’ clinical arrhythmia, suggesting that these arrhythmias are reentrant. The ability reliably to induce and terminate sustained ventricular tachycardia in the catheterization laboratory has offered the opportunity to test acutely antiarrhythmic drugs and their ability to prevent the induction of ventricular tachycardia. Following initial electrophysiologic study (demonstrating ability to replicate ventricular tachycardia), a pacing catheter is left at the right ventricular apex (introduced from an arm or subclavian vein). On subsequent days, different antiarrhythmic agents are given and tested, and an appropriate medical regimen may be defined. If a drug is found that prevents induction of ventricular tachycardia, this strongly implies that this agent will prevent subsequent ventricular tachycardia. If an effective drug is not found (induction of ventricular tachycardia with all tested drugs), the use of one of these ineffective drugs will usually not prevent recurrent ventricular tachycardia.

In cases where conventional antiarrhythmic agents such as procainamide, quinidine, and disopyramide do not prevent induction of sustained ventricular tachycardia, experimental agents such as aprindine, mexiletine, tocainide, amiodarone can be tested on the same basis.

In cases where all antiarrhythmic agents have failed and surgery is not feasible, an antiarrhythmic agent (or combination of drugs) which is felt to offer more security regarding the characteristics of the patient's ventricular tachycardia can be chosen. Electrophysiologic study may demonstrate that a specific drug is particularly effective in slowing the rate of induced ventricular tachycardia in an individual patient. This would be a favorable attribute of a chosen “ineffective agent.” There is also recent evidence demonstrating that the degree of difficulty in inducing ventricular tachycardia relates to the frequency of spontaneous attacks. If a drug makes the induction of ventricular tachycardia more difficult, it is likely to be effective in preventing these attacks.

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