COPD could be a problem with autoimmunity

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Moderate to severe chronic obstructive pulmonary disease (COPD) may be an auto-immunity problem, according to researchers in Spain, who studied the presence of auto-antibodies in patients with COPD and compared them to levels of control subjects. They found that a significant number of patients with COPD had significant levels of auto-antibodies circulating in their blood, about 5 to 10 times the level in controls.

The findings were published online ahead of the print edition of the American Thoracic Society's American Journal of Respiratory and Critical Care Medicine.

"We showed that between one third and one quarter of patients with clinically stable COPD present abnormal levels of circulating auto-antibodies in the blood," said Jaume Sauleda M.D., coordinator of respiratory medicine department, Hospital Universitari Son Dureta, Palma Mallorca, Spain. "Our findings provide further support for the hypothesis that the pathogenesis of COPD involves an auto-immune component."

The researchers recruited 328 patients with clinically stable COPD three months after hospitalization for the first time with an exacerbation of the disease at nine participating hospitals in Spain, and 67 healthy volunteers from primary care clinics, blood donors and hospital workers. They collected information on current and past smoking habits, comorbidities, and data such as body mass index, degree of dyspnea and six-minute

walk distance. They tested lung function with spirometry.

They then took blood samples and tested the blood for antinuclear antibodies (ANA), anti-tissue antibodies (AT) including mitochondrial (AMA), liver-kidney microsomal (LKM), smoothmuscle (SMA), and parietal gastric cell (PGC) antibodies. The serum levels of C-reactive protein were also tested in patients.

"We wanted to quantify the levels of auto-antibodies in COPD with respect to the patients' lung function and disease severity. By doing so, we hoped to determine whether in fact COPD had an auto-immune aspect," said Dr. Sauleda. "COPD is the fourth-leading cause of death in the world, and is becoming increasingly common in the developing world as generations of heavy smokers age. Understanding its pathogenesis is key to developing effective treatments that go beyond symptom palliation."

The researchers found that, overall, 34 percent of COPD patients had abnormally high levels of ANA titer—a prevalence 11 times higher than seen in the control group, and 7 times higher than reported in healthy subjects in previous studies. Furthermore, 26 percent of the patients were positive for AT, a prevalence 4.5 times higher than in the controls, and 4 times higher than reported in healthy subjects in other studies.

Patients with AT tended to be younger and active smokers, and the level of these auto-antibodies was related to impairment of lung function. There were no other associations between auto-antibodies and other patient characteristics.

The much higher prevalence of auto-antibodies in COPD patients has several implications and possible explanations. Other studies have found that patients with "severe bronchitis" (which would probably be characterized as COPD today) had high levels of circulating ANA, and

these results confirm those earlier findings. Recent reports have also suggested that circulating antibodies are directed against components of the lung matrix and epithelium in patients with COPD.

"We can only speculate on the mechanisms underlying the observed associations," said Dr. Sauleda. "The prevalence of ANA and AT may be non-specific markers of an ongoing auto-immune response or may be directly involved in the pathogenesis of the disease. However, these alternatives are not mutually exclusive. "Future longitudinal studies in general population evaluating the relationships between these auto-antibodies and lung function during several years can help us to unravel this issue."

Dr. Sauleda continued, "If future research confirms the suspected auto-immune component of COPD, it raises the possibility of future clinical trials evaluating possible new therapies for this disease, for instance, immunomodulators."

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