GOODPASTURE AND HIS SYNDROME

By Eric C. Ehman

Ask any medical student which disease affects the lungs and kidneys, and he or she is likely to answer Goodpasture’s syndrome. We encountered a case of this fascinating disease on our internal medicine service recently.

Goodpasture’s syndrome is a rare disorder characterized by auto-immune damage to the lungs and kidneys, affecting approximately 1 in 1,000,000 worldwide. The hallmark of Goodpasture’s syndrome is high levels of circulating IgG auto-antibodies to the alpha-3 chain of type IV collagen, causing a type 2 hypersensitivity reaction that results in damage to the glomeruli and alveoli.

The exact stimulus for antibody production is not well understood, but it is currently thought that the transient increase in circulating anti-GBM antibodies may occur after an acute viral infection. The predilection for kidney and lung tissue is due to the limited distribution of the alpha-3 chain found only in alveolar and glomerular basement membranes (anti-GBM). Typically, Goodpasture’s syndrome is used to describe the syndrome of pulmonary and renal involvement while Goodpasture’s disease is used to describe anti-GBM-mediated kidney disease alone.

The classic clinical presentation of Goodpasture’s syndrome is a young man or a middle-aged woman with no history of lung disease or renal dysfunction who notices the abrupt onset of hemoptysis, cough, shortness of breath, peripheral edema, dark urine and oliguria. Kidney biopsy—the current gold standard for diagnosis—reveals crescentic glomerulonephritis, inflammation and interruption of the glomerular basement membrane. Immunofluorescent stains show virtually pathognomonic finding of linear deposition of IgG antibody along the glomerular basement membrane. Laboratory testing of affected patients reveals high levels of circulating IgG or IgM anti-glomerular basement membrane antibodies as well as increased creatinine as a marker of kidney dysfunction. Urinalysis shows proteinuria, and nephritic sediment characterized by dysmorphic red cells, white cells, and red cell and granular casts.

Patients with pulmonary involvement typically have pulmonary infiltrates on chest X-ray and increased carbon monoxide diffusing capability due to hemoglobin in the alveoli. Some patients may also have evidence of iron-deficient anemia if pulmonary hemorrhage has been active long enough to cause significant blood loss. Patients may or may not have anti-neutrophil cytoplasm antibodies (ANCA), but ANCA status should be investigated to rule out additional vasculitides or systemic inflammation that may alter treatment decisions.

The first case of what would later be termed Goodpasture’s syndrome was a young sailor found to have lung and kidney damage after an acute viral illness. This case was described in Dr. Ernest William Goodpasture’s 1919 manuscript detailing the significance of pulmonary lesions in patients infected with the worldwide epidemic influenza virus of the time. Dr. Goodpasture is also known for his work in viral replication. He was the first person to describe a method for growing viruses in fertilized chicken eggs, allowing for production of different virus strains for testing. This technique is used today for large-scale manufacture of viral vaccines, like the seasonal and H1N1 variant of influenza virus.

The most important factors that alter prognosis for patients with Goodpasture’s syndrome are timely diagnosis and initiation of treatment. Treatment has two main goals: removal of existing anti-GBM antibodies and prevention of inflammation causing kidney and alveolar damage. Since the creation of anti-GBM antibodies is transient, successful removal with a short (14-day) course of daily plasmapheresis may be accomplished. Immunosuppression using high-dose oral prednisone, as well as cyclophosphamide, has become the standard treatment. Anti-GBM antibody levels are monitored every two weeks to track disease progression or remission and tailor dosing. In general, treatment lasts between six to nine months or until anti-GBM antibodies have been cleared.

A patient’s prognosis is strongly dependent on her plasma creatinine level at presentation and her requirements for hemodialysis. Studies show that patients with creatinine less than 5.7 mg/dL and no dialysis requirement within 72 hours of presentation have a patient survival of 100% and a renal survival of 95% in the first year, while dialysis-dependent patients with creatinine above 5.7 mg/dL have much poorer outcomes—65% patient survival and 8% renal survival in the first year.

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