Diffuse Alveolar Hemorrhage Due to Antibasement Membrane Antibody Disease Appearing With a Polyglandular Autoimmune Syndrome

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We describe a patient with type 3-C polyglandular autoimmune syndrome who presented with diffuse alveolar hemorrhage and normal renal function. The diagnosis of antibasement membrane antibody disease was established by immunofluorescent staining of transbronchial biopsy specimens. We suggest the incorporation of antibasement membrane antibody disease into the spectrum of diseases that define the polyglandular autoimmune syndromes.

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ANTIBASEMENT MEMBRANE ANTIBODY (ABMA) disease is recognized by the presence of antibodies directed against alveolar and glomerular basement membranes. In its classic form, Goodpasture's syndrome, patients develop both diffuse alveolar hemorrhage and a rapidly progressive glomerulonephritis. However, cases of ABMA disease limited either to the kidneys or lungs have been reported. We present a case of ABMA disease with normal renal function presenting as diffuse alveolar hemorrhage in a patient with type 3-C polyglandular autoimmune syndrome (PGAS). To our knowledge, ABMA disease has not been previously described in this setting.

CASE REPORT

A 34-year-old woman with a diagnosis of type 3-C PGAS presented to the emergency department with a 7-day history of progressive cough, fatigue, malaise, and dyspnea. The night before hospital admission her dyspnea worsened and minimal hemoptysis was reported.

In 1983, the patient developed myasthenia gravis, underwent a thymectomy, and was treated with prednisone, cyclophosphamide, and pyridostigmine. Over the next 5 years, she experienced several exacerbations requiring mechanical ventilation. In 1984, the patient was diagnosed as having Hashimoto's thyroiditis and has had persistently elevated antithyroglobulin antibody levels.

Her medications at the time of hospital admission were pyridostigmine and levothyroxine. She denied exposure to hydrocarbons, was a one pack per day smoker for 20 years, and had a remote history of intravenous drug abuse but denied use for the last 15 years.

She was afebrile with a blood pressure of 100/60 mm Hg. Her sinuses were nontender. Lung examination was clear to auscultation, and the heart examination was without murmur or extra

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sounds. No skin eruptions, petechiae, or purpura were found. Her
hospital admission arterial blood gas breathing ambient air at a
barometric pressure of 628 mm Hg revealed a PaO₂ of 51 mm Hg,
oxxygen saturation of 86 percent. PaCO₂ of 30 mm Hg, and pH of
7.42. Her hemoglobin was 8.8 g/dl, and the serum creatinine was
1.0 mg/100 dl. Sputum Gram stain contained oral flora. Urinalysis,
including microscopic examination, was negative and subsequent
urinalyses remained normal. The admission chest radiograph is
shown in Figure 1.

The following serum studies were negative: human immunodefi-
ciency virus antibody, antinuclear antibody, antineutrophil cyto-
plasmic antibody, and IgG and IgA antibasement membrane anti-
body. Results of the serum complement and coagulation studies
were normal. The diffusing capacity for carbon monoxide corrected
for alveolar volume was elevated to 125 percent of predicted.
Bronchoscopy with bronchoalveolar lavage and transbronchial bi-
opsies were performed. Bronchoalveolar lavage samples were
negative for acid-fast bacilli, Pneumocystis, fungal and routine
bacterial cultures, and direct fluorescent antibody against Legion-
ella. The transbronchial biopsy specimen showed filling of the air
spaces with red blood cells and hemosiderin-laden macrophages
(Fig 2). Although there was mild diffuse interstitial inflammation,
capillaritis was not present. Immunofluorescent staining of the
tissue with IgG revealed linear staining of the alveolar walls
indicative of ABMA disease (Fig 3).

She was treated with methylprednisolone, 125 mg intravenously
every 6 h and four cycles of plasmapheresis. The patient was
discharged from the hospital on the 16th hospital day on a regimen
of prednisone, 60 mg/d. Her room air oxygen saturation was 92
percent, and the chest radiograph had cleared. The patient has had
no recurrence of diffuse alveolar hemorrhage at 6 months.

**Discussion**

This case demonstrates two interesting features: the
presentation of ABMA disease limited to the lungs, and its
previously unreported association with a type 3-C polyglan-
dular autoimmune syndrome.

In the majority of ABMA disease, alveolar hemorrhage
typically precedes the development of overt renal disease by
weeks and sometimes years. However, in 83 percent of
patients, microscopic hematuria is present. Twenty-seven
cases of ABMA disease with normal serum creatinine,
proteinuria less than 1.5 g/24 h, and fewer than 10 percent
crescents on renal biopsy specimen have been described.
In only four of these cases, a completely normal urinalysis,
as was present in our patient, was recorded. The diagnosis
of ABMA disease is established after the demonstration of
circulating or tissue-bound ABMA. Many authors believe
that a renal biopsy should be the diagnostic procedure of
choice in patients with suspected ABMA disease, and even
patients with normal renal function will demonstrate positive
glomerular linear immunofluorescence on renal biopsy spec-
imen. The potential problem with renal biopsy is the lack of
specificity since several other kidney diseases can cause
a similar deposition of IgG within the glomeruli. These
include idiopathic crescentic glomerulonephritis, systemic
lupus erythematosus, polyarteritis nodosa, poststreptococcal
glomerulonephritis, minimal change disease, and diabetic
nephropathy.

In this case, the diagnosis of ABMA disease was estab-
lished by the demonstration of linear IgG deposition along
alveolar walls. The linear staining of the alveolar basement
membrane with immunoglobulin is considered to be highly
specific, but it may not be a sensitive test in the lung due to
sampling error. Patients with ABMA disease and normal
renal function appear to have a relatively favorable progno-
sis, and spontaneous remissions are not unusual. Therapeu-
tic options include combinations of corticosteroids, cy-
clophosphamide, and plasmapheresis.
The PGASs are characterized by the gradual development of multiple endocrine gland dysfunction. Neufeld et al. classified PGAS into three categories, defined by various patterns of organ-specific autoimmunity. Type 1 PGAS, which is more commonly diagnosed during childhood, is defined by the presence of at least two of the following: chronic mucocutaneous candidiasis, hypoparathyroidism, and adrenal insufficiency. Type 2 PGAS, also known as Schmidt’s syndrome, has a peak age of onset of 30 years. In the majority of cases, adrenal insufficiency and autoimmune thyroid disease define the type 2 syndrome; however, diabetes mellitus, gonadal failure, pernicious anemia, and myasthenia gravis can also occur. Patients with type 3 PGAS have autoimmune thyroid disease and another associated autoimmune disease but without adrenal insufficiency. Type 3-A is associated with diabetes mellitus, type 3-B with pernicious anemia, and type 3-C with another organ-specific autoimmune disorder. The present case is classified as a type 3-C PGAS: autoimmune thyroid disease and myasthenia gravis.

To our knowledge, this is the first report of a patient with PGAS as defined by the combination of Hashimoto’s thyroiditis and myasthenia gravis, and an associated ABMA disease. Also to our knowledge, ABMA disease limited to the lungs has not been reported with any type of PGAS. We would suggest that the PGAS definitions may need to be expanded to include ABMA disease.

REFERENCES

Acute Reversible Cardiomyopathy Associated With the Systemic Inflammatory Response Syndrome

In the absence of ischemic heart disease, severe acute reversible myocardial dysfunction is uncommon, with sepsis most often being implicated in the ICU. We report a 38-year-old woman who developed profound transient myocardial depression due to nonseptic systemic inflammatory response syndrome caused by a necrotic kidney. Hemodynamic parameters and echocardiographic findings improved dramatically following nephrectomy. Other causes of acute myocardial suppression, including electrolyte abnormalities, drugs, catecholamine excess, and endocrine disease were excluded.

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Severe acute reversible myocardial dysfunction without ischemic heart disease is a relatively uncommon clinical entity. In the ICU, sepsis is often implicated, related perhaps to cytokines such as tumor necrosis factor (TNF) and interleukin 2. Although not widely recognized, a number of other causes have been described that may require specific interventions.

We describe a patient who developed severe transient myocardial depression resulting in pulmonary edema, in the absence of sepsis. The various mechanisms of “reversible cardiomyopathy” are reviewed.

CASE REPORT

A 38-year-old woman was admitted to the hospital for management of right renal cell carcinoma. She had donated her left kidney 6 years previously to her sister. Several months prior to referral, she had developed symptoms initially attributed to renal calculi. Subsequent investigation, however, demonstrated renal cell carcinoma in the lower pole of her right kidney. She underwent right partial nephrectomy with subsequent apparent good perfusion of the remaining kidney intraoperatively.

Postoperatively she was noted to be oliguric (10 to 20 ml/h) with a creatinine level rising at anaphylactic rates. Diethylene triamine pentaacetic acid renal scan done on the second postoperative day showed no perfusion or function of the remaining right kidney. On the third postoperative day, the patient developed respiratory distress. Oxygen at a concentration of 80 percent was required to maintain oxygenation and her chest radiograph was compatible with pulmonary edema. Hemodialysis was performed with removal of 4 L of fluid. The following day, her respiratory function deteriorated further and she required endotracheal intubation and mechanical ventilation despite dialysis and ultrafiltration. Bronchoscopy with bronchoalveolar lavage was noncontributory and no evidence of infection was documented. Several sets of blood cultures drawn at this time were negative. A pulmonary artery catheter was inserted, demonstrating a pulmonary capillary wedge pressure of 17 mm Hg and cardiac index (CI) of 2.8 L/min/m² (Table 1).

By the fifth postoperative day, she was noted to have a temperature...