Lesson 286: PreAnesthetic Assessment of the Patient With Goodpasture’s Syndrome

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DATE REVIEWED: MAY 2010

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TIME TO COMPLETE ACTIVITY: 2 hours
RELEASE DATE: June, 2010
TERMINATION DATE: June 30, 2011
TARGET AUDIENCE: Anesthesiologists

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Needs statement

Goodpasture’s syndrome (GS), an autoimmune disease, presents challenges for the anesthetic care of patients, particularly because of effects on the respiratory and renal systems. Perioperatively, the anesthesiologist should be able to appropriately manage these patients. Rarely encountered disease states have been identified as important topics for clinical anesthesiologists.

Learning Objectives

At the end of this activity, the participant should be able to:

1. Define GS.
2. Review special problems associated with the administration of anesthetics to patients with GS.
3. Describe the pulmonary and renal manifestations seen in these patients.
4. Explain the pathogenesis of GS.
5. Apply appropriate preoperative testing and evaluation of patients.
6. Discuss the findings of laboratory tests.
7. Present an anesthetic and analgesic plan for the treatment of patients with GS.
8. Discuss treatment options.
9. Cite the incidence and prevalence of GS.
10. Anticipate, recognize, and manage likely perioperative complications associated with GS.

Case History

A 26-year-old man presented with a 5-year history of GS, confirmed by a renal biopsy. Due to his declining renal function, placement of an arteriovenous graft for renal dialysis was scheduled. A review of systems indicated slight dyspnea and occasional hemoptysis. Pulmonary function tests conducted 2 months previously indicated mild restrictive lung disease.

Goodpasture’s syndrome (GS) is characterized by the classic triad of diffuse pulmonary hemorrhage, glomerulonephritis, and circulating anti–glomerular basement membrane (anti-GBM) antibodies. It is an uncommon disorder, with an estimated incidence of 0.3 cases per 100,000 people annually. Males are predominantly affected, at a ratio between 2:1 and 9:1. The disease can develop at any age, but typically appears between the ages of 20 and 30 years.

Ernest W. Goodpasture, MD, a US pathologist, first described the pulmonary-renal syndrome in 1919 during the influenza epidemic. However, it was not until 1958 that Stanton and Tange referenced Goodpasture’s original description in a report about young men with pulmonary hemorrhage and glomerulonephritis. The role of anti-GBM antibodies in the pathogenesis of GS was discovered in 1967. Reported risk factors for the development of GS include exposure to hydrocarbons, cigarette smoking, and a preceding viral illness, especially influenza.

Clinical Manifestations

Although the clinical presentation of GS varies considerably, in most cases the initial symptoms include progressive dyspnea and hemoptysis (80%-95% of cases) that may range in severity from blood-tinged sputum to massive hemorrhage. Additionally, some patients develop alveolar hemorrhage—evident only on biopsy or bronchoalveolar lavage. Between 20% and 40% of patients have only renal disease, and less than 10% have only pulmonary disease.

Patients may present initially with hemoptysis as a sole symptom, and glomerulonephritis may develop months or years later. Alternatively, in some patients with glomerulonephritis, pulmonary hemorrhage might develop later or never develop. Unlike systemic inflammatory disorders, GS typically does not cause clinical signs of inflammation, although prodromal symptoms such as nausea, vomiting, fatigue, and weight loss may develop in some patients.
Continuous pulmonary hemorrhaging can result in hypoxemia and significant iron deficiency, with decreased serum levels of iron and ferritin.\(^1\) If massive hemoptysis develops, blood rapidly floods the alveolar spaces, resulting in respiratory failure.

Acute pulmonary hemorrhage is seen on the chest radiograph as bilateral patchy areas of dense alveolar infiltrates; also, air bronchograms often are seen.\(^2\) The apices and costophrenic angles generally are not involved.\(^3\) In some patients, the chest radiograph may be normal, but computed tomography scan may reveal parenchymal abnormalities.\(^3\)

After an acute episode of pulmonary hemorrhage, serial chest radiographs reveal a predictable change in pattern. Within 2 to 3 days, the initial patchy areas of consolidation disappear, and a reticulonodular pattern becomes evident.\(^3\) The pattern becomes distinctly reticular within 1 week, and the chest radiograph usually returns to normal in 10 to 12 days.\(^3\)

In patients with GS and renal disease, rapidly progressive glomerulonephritis usually develops (Figure). Renal dysfunction causes azotemia, proteinuria, and hematuria; red blood cell casts are seen on urinalysis.\(^1\) Without treatment, end-stage renal failure can develop within days to weeks after the onset of symptoms.\(^2\)

**Pathogenesis**

Genetics likely are involved in the pathogenesis of GS, given that there is a strong association between the disease and human leukocyte antigen DR2 (HLA-DR2). The prevalence of HLA-DR2 is higher in patients with GS than in the general population.\(^6\) However, additional factors also must be involved, as most cases are sporadic.

GS is defined by the presence of antibodies that target the carboxyl-terminal region of the α3 chain of type IV collagen.\(^1\) Only the lungs and kidneys are involved despite the presence of type IV collagen throughout the body. This effect might be explained by the antigen being more accessible to the antibody in the alveoli and glomeruli, or because of the predominance of the α3 chain in the alveoli and glomeruli instead of other tissues.\(^1\)

Structural differences between alveoli and glomeruli may explain why some patients develop only alveolar hemorrhage or glomerulonephritis, but not both pathologies. One such structural difference is the presence of fenestrae in the glomerular endothelium that allow the antibodies greater accessibility to the basement membrane.\(^1\) These fenestrae are absent in the alveolar endothelium.\(^3\)
Diagnosis

Microscopic abnormalities associated with GS include intra-alveolar blood, hemosiderin-laden macrophages in the alveoli and interstitium, interstitial fibrosis, and type II cell hyperplasia.\(^1\) Occasionally, a lymphocytic interstitial infiltrate may be seen.

Electron microscopy findings have been inconsistent, ranging from no abnormalities to a thickening, splitting, discontinuity, or smudging of the basement membrane.\(^1\) None of these findings, however, are diagnostic of GS.

The diagnosis is confirmed by performing a renal biopsy and proving the presence of tissue-bound anti–basement membrane antibodies by enzyme-linked immunosorbent assay (ELISA).\(^3\) If a biopsy is contraindicated, the diagnosis can be made by serologic testing and demonstrating the presence of anti-GBM antibodies with either indirect immunofluorescence or ELISA. Focal or diffuse crescentic and necrotizing glomerulonephritis is seen on light microscopic examination of kidney tissue, and immunofluorescence shows linear staining of immunoglobulin G (IgG) along the glomerular basement membrane.\(^3\) Immunofluorescence of lung tissue reveals diffuse linear staining along the alveolar wall, usually attributable to IgG.

Pulmonary function testing is not useful in diagnosing GS, but may help in monitoring the course of the disease.\(^5\) Generally, a restrictive pattern is demonstrated along with a decreased diffusing capacity and decrease in resting PaO2, which may exist even during remission of the disease.\(^3\) The diffusing capacity of the lung for carbon monoxide (DLCO) may be increased due to intra-alveolar blood binding to carbon monoxide.\(^5\) When measured throughout the course of the disease, DLCO may help to identify an acute pulmonary hemorrhage versus other causes of radiographic opacities.\(^5\)

Prognosis and Treatment

Before the development of immnosuppressive therapy and plasmapheresis, GS was usually fatal, secondary to either lung hemorrhage or renal failure. Corticosteroids, immunosuppressants, and plasmapheresis have greatly improved outcome, although some patients remain dependent on dialysis.\(^1\) Three to 6 months of treatment are usually required, although symptoms begin to resolve within 2 months.\(^6\)

Plasmapheresis rapidly decreases the level of circulating anti-GBM antibody, whereas corticosteroids and immunosuppressants (prednisone and cyclophosphamide) decrease the production of antibody.\(^7\) If irreversible kidney damage has taken place at the time of diagnosis, the patient may receive a kidney transplant only after the anti-GBM antibodies have been cleared from the serum.\(^3\) In contrast, if irreversible kidney damage has not occurred when the diagnosis is made, chronic immunosuppression can prevent progression of renal damage and a kidney transplant often is not necessary.\(^3\)
Anesthetic Considerations

There are significant considerations in the delivery of anesthetics to patients with GS.

Preoperative Assessment

Elective surgery in a patient with GS should be delayed until the disease is inactive. Chest radiography, pulmonary function studies, and arterial blood gas estimations may be used to evaluate pulmonary status; renal studies, urinalysis, and blood chemistry results indicate kidney function. Causes of renal insufficiency, other than glomerulonephritis, should also be sought. Prerenal factors such as hypovolemia and decreased cardiac output can compound GS-induced renal dysfunction, and should be corrected to avoid further kidney damage.

Dialysis-dependent patients should undergo dialysis shortly before surgery to correct volume overload, hyperkalemia, and acidosis. Renal failure often demands that drug selection and dosing be modified. In general, the technique of choice when applicable would be the use of local anesthetics for local or regional blockade.

Pulmonary

Because of the alveolar hemorrhage that occurs in GS, oxygenation of the patient during surgery is the principal challenge for the anesthesiologist. Blood in the alveoli makes gas exchange difficult. Furthermore, continuous alveolar hemorrhaging results in anemia, which plays an additional role in diminishing the delivery of oxygen to tissues. A larger than normal-sized endotracheal tube should be used to allow better pulmonary suction. Care should be taken to avoid elevated airway pressure, increased oxygen tension, and other stressors on the lungs, all of which can worsen antibody-mediated lung injury.

Renal

Renal failure in GS—as in all cases of renal failure—can affect the volume of distribution, metabolism, and excretion of certain anesthetic drugs. Water-soluble metabolites that are minimally active may accumulate and prolong the effects of the parent drug. The elimination half-life of drugs that are excreted unchanged by the kidneys can be prolonged in cases of renal failure. The protein loss and uremia that occur in renal failure may potentiate the effects of drugs that are typically protein-bound. For induction with thiopental, a reduced dose is administered because the free fraction of the drug is nearly doubled in patients with renal failure. The dosing of ketamine, in contrast, does not need to be altered because it is not highly protein-bound and the free fraction is minimally affected by renal failure. Etomidate exhibits less protein binding in patients with renal failure than in patients with normal renal function, but the larger free fraction does not appear to alter its clinical effects. Propofol is quickly metabolized by the liver into inactive metabolites that are then excreted by the kidney; thus, in patients with renal failure the clinical effects of propofol are not extended.

The free fraction of benzodiazepines in plasma is increased by renal failure because these drugs are normally highly protein-bound. Additionally, benzodiazepines have active metabolites that can accumulate after repeated doses in renal failure and lead to prolonged sedation. Midazolam is metabolized to an active α-hydroxy compound, and 60% to 80% of the drug is excreted in this form. The metabolite accumulates after long-term infusions in patients with renal failure, therefore causing a
longer period of sedation. Compared with individuals with normal renal function, patients with renal failure are more sensitive to the sedative effects of alprazolam because of reduced protein binding and an increased free fraction. Dexmedetomidine undergoes hepatic metabolism. When volunteers with impaired renal function were given dexmedetomidine, sedation was longer than in those with normal renal function, likely due to reduced protein binding in the presence of renal dysfunction.

In the patient with chronic renal failure, the pharmacokinetics of a single dose of morphine are unaffected; however, long-term morphine administration causes the active metabolite morphine-6-glucuronide to accumulate and exert potent analgesic and sedative effects. Thus, the dose of morphine should be decreased in the presence of renal dysfunction.

Meperidine, which is metabolized to the neurotoxic compound normeperidine which must be excreted by the kidneys, should not be administered to patients with renal failure. The active metabolite of hydromorphone, hydromorphone-3-glucuronide, also accumulates in patients with renal failure and can cause cognitive dysfunction and myoclonus.

Oxycodone has a longer elimination time in patients with renal failure, and thus repeated dosing prolongs its effects. Codeine is not recommended for long-term use in patients with renal dysfunction because it also can prolong narcosis.

In contrast, fentanyl which has no active metabolites, an unchanged free fraction, and a short redistribution phase, is well tolerated and a good choice in patients with GS. Alfentanil exhibits decreased protein binding in the presence of renal disease, but because its elimination half-life and clearance are unaffected, the total dose should be similar to that for patients without renal disease. Muscle relaxants, with the exception of succinylcholine, atracurium, cisatracurium, and mivacurium, rely heavily on renal excretion and therefore result in prolonged effects in patients with chronic renal failure. In renal failure, most nondepolarizing muscle relaxants either must be excreted by the liver or metabolized to inactive forms. Some muscle relaxants, such as vecuronium, are metabolized to active compounds that must be excreted by the kidneys, and result in prolonged effects in patients with GS. Because succinylcholine does not significantly prolong clinical effects, it may be used for rapid-sequence intubation.

Because of a shorter duration of action, the intermediate-acting atracurium, cisatracurium, and rocuronium are preferred over the long-acting muscle relaxants in patients with renal failure. Atracurium and cisatracurium are recommended because the metabolites do not depend on renal clearance, and the elimination half-life, clearance, and duration of action are not affected by renal failure.

Vecuronium exhibits prolonged effects in patients with renal dysfunction because of a decrease in plasma clearance and an increase in elimination half-life. In addition, the clinical duration of vecuronium is lengthened because of its metabolism to 3-desmethylvecuronium, an active compound that accumulates in renal failure.

Management of the Case Presented

After a review of the patient’s medical history and laboratory test results that revealed a potassium level of 4.9 mmol/L and a creatinine level of 3.6 mg/dL, the anesthesia options were discussed. Because of the challenges presented by GS and documentation of pulmonary involvement, it was
agreed to perform an axillary block with 40 mL of 1.5% mepivacaine. Bleeding was minimal, and additional sedation was facilitated with IV midazolam (3.5 mg), IV fentanyl (100 mcg), and IV propofol (total dose, 170 mg).

**Conclusion**

Although uncommon, GS is a disease that anesthesiologists may encounter and that poses many clinical challenges. The extensive renal involvement dictates which drugs should be administered and which avoided. Complex pulmonary manifestations require that special care be taken in management of the airway. Patients should be treated with corticosteroids, immunosuppressants, and plasmapheresis to render the disease dormant before elective surgery is performed.

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REFERENCES


Post-test

1. The diagnosis of Goodpasture’s syndrome (GS) is confirmed by:
   a. demonstrating a linear pattern of immunofluorescence with lung or kidney biopsy
   b. electron microscopy showing thickening, splitting, discontinuity, or smudging of the basement membrane
   c. microscopic observation of focal or diffuse crescentic and necrotizing glomerulonephritis
   d. the presence of hemosiderin-laden macrophages within alveoli seen on microscopy

2. Initially, the most common presentation of GS is:
   a. fatigue
   b. chest pain
   c. hemoptysis
   d. hematuria

3. Which best describes the typical age and gender of patients with GS?
   a. Elderly woman
   b. Young adult man
   c. Adolescent girl
   d. Adolescent boy

4. In an acute episode of pulmonary hemorrhage, the typical pattern observed initially with chest radiography is:
   a. patchy, dense alveolar infiltrates bilaterally
   b. lobar consolidation unilaterally
   c. blunting of the costophrenic angles
   d. perihilar lymphadenopathy

5. Microscopic abnormalities associated with GS include all of the following, except:
   a. intra-alveolar blood
   b. hemosiderin-laden macrophages in alveoli and interstitium
   c. interstitial fibrosis
   d. atrophy of type II cells
6. In patients with GS, all of the following are possible treatments, except:
   a. plasmapheresis
   b. cyclophosphamide
   c. corticosteroids
   d. trimethoprim-sulfamethoxazole

7. Which anesthetic is not associated with the complication of impaired renal clearance in patients with GS?
   a. Vecuronium
   b. Atracurium
   c. Pancuronium
   d. Rocuronium

8. Which is the best opioid to administer to patients with renal failure?
   a. Fentanyl
   b. Morphine
   c. Meperidine
   d. Hydromorphone

9. In GS, why are the effects of propofol not prolonged in patients with renal dysfunction?
   a. It exhibits increased protein binding.
   b. It is rapidly redistributed.
   c. It undergoes hepatic metabolism to inactive compounds.
   d. It is excreted in the bile.

10. In GS, which substance is a target of antibodies?
    a. Type IV collagen
    b. Proteinase 3
    c. Fibrilllin 1
    d. Reticulinoccurs