Patient

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Goodpasture's syndrome

Synonyms: antiglomerular basement membrane disease, anti-GBM disease

What is Goodpasture's syndrome?

Goodpasture's syndrome is the co-existence of acute glomerulonephritis and pulmonary alveolar haemorrhage, of which Goodpasture's syndrome is one cause.[1]

Goodpasture's syndrome is a specific autoimmune disease caused by a type II antigen-antibody reaction leading to diffuse pulmonary haemorrhage, glomerulonephritis (and often acute kidney injury and chronic kidney disease). There are circulating antiglomerular basement membrane (anti-GBM) antibodies.[2]

How common is Goodpasture's syndrome? (Epidemiology)[3]

- Goodpasture's syndrome is uncommon. Frequencies vary from 0.5 to 1 cases per million per year.[4]
- In adults, Goodpasture's syndrome is more common in men.
- It is rare in children.[5]
- Most patients have both renal and pulmonary disease. In a minority of patients, the kidneys alone or only the lungs are affected, but more often only the kidneys.

Risk factors

Insults to the lungs are probably required to produce both the renal and pulmonary disease.

- There is a strong genetic linkage to HLA-DRB1.[4] [6]

- Exposure to organic solvents or hydrocarbons.
- Smoking.
- Infection - eg, influenza.
- A case in a heavy smoker who had taken to using crack cocaine is described.
- Exposure to metal dusts.
- It can occur after renal transplantation in Alport's syndrome.[7]

Presentation of Goodpasture's syndrome[3]

Typically presents as acute kidney injury caused by a rapidly progressive glomerulonephritis, with or without pulmonary haemorrhage that may be life-threatening.[2]

Symptoms

- Chills and fever, nausea and vomiting, weight loss, chest pain.
- Anaemia, which may result from persistent intrapulmonary bleeding.
- Massive pulmonary haemorrhage, which can cause respiratory failure.
- Haematuria.
- There is a rapidly progressive glomerulonephritis that may lead to acute kidney injury and volume overload.
- Arthralgia.

Signs

- Tachypnoea.
- Dyspnoea, which can be severe.
- Inspiratory crackles over lung bases.
- Cyanosis.
- Hepatosplenomegaly (sometimes).

- Hypertension.
- Skin rash.
- There may be gross haematuria and pallor from anaemia.

Differential diagnosis

- Pulmonary haemorrhage with renal failure can also occur in collagen vascular diseases like systemic lupus erythematosus and rheumatoid arthritis, idiopathic rapidly progressive glomerulonephritis, microscopic polyarteritis, granulomatosis with polyangiitis, and essential mixed cryoglobulinaemia.
- All these diseases have specific laboratory features. In Goodpasture's syndrome the essential feature is antibody to the glomerular basement membrane (GBM).

Diagnosing Goodpasture's syndrome (investigations) [4]

The diagnosis of anti-GBM disease relies on the detection of anti-GBM antibodies in conjunction with glomerulonephritis and/or alveolitis.

Blood tests

- FBC: iron-deficiency anaemia from intrapulmonary bleeding, leukocytosis.
- Renal function and electrolytes: watch for renal failure. Azotemia (abnormally high blood levels of nitrogen-containing compounds, such as urea, creatinine and other nitrogen-rich compounds) is often present.
- Erythrocyte sedimentation rate (ESR) is raised in vasculitis but not in Goodpasture's syndrome.
- Urinalysis is typical of acute glomerulonephritis, with low-grade albuminuria, gross or microscopic haematuria, and red blood cell casts.
- Assess antinuclear antibodies and complement levels.

- Anti-GBM antibodies are diagnostic: assays for antibodies are valuable for confirming the diagnosis and monitoring therapy. Radioimmunoassays or enzyme-linked immunosorbent assays (ELISAs):[4]
- ELISAs for anti-GBM antibodies are highly sensitive and specific.
- Antineutrophilic cytoplasmic antibodies (ANCAs) may be present in addition to anti-GBM antibody.

CXR

- Patchy consolidation, usually bilateral, symmetrical, perihilar, and bibasilar.
- The apices and costophrenic angles are usually spared.
- 18% may have a normal CXR.
- Recurrent pulmonary haemorrhage causes new opacities.

Other tests

Pulmonary function tests are not usually helpful but spirometry may show some restriction.

Procedures

- Percutaneous kidney biopsy is the preferred invasive procedure to substantiate the diagnosis.
- Sometimes transjugular renal biopsy is performed. Renal biopsy is not required if anti-GBM antibodies are present.
- Lung biopsy: either transbronchial or open lung biopsy may be performed in cases where renal biopsy cannot be performed.

Management of Goodpasture's syndrome[6]

Treatment aims to rapidly remove pathogenic autoantibody, typically with the use of plasma exchange, along with steroids and cytotoxic therapy to prevent ongoing autoantibody production and tissue inflammation.[8]

Non-drug

- Intubation, assisted ventilation, and haemodialysis are often required in the acute phase.
- Repeated plasma exchange removes anti-GBM antibodies from the circulation.[9]
- End-stage renal disease can be managed by long-term haemodialysis or renal transplantation.

Drugs

- High-dose corticosteroids (intravenous methylprednisolone 7 to 15 mg/kg/day in divided doses) with cyclophosphamide or azathioprine are of benefit. Intravenous steroids are then converted to oral prednisolone.
- Duration of immunosuppressive therapy varies considerably and may be necessary for longer than 12 to 18 months in some patients.
- Usually, cyclophosphamide is given for three months and then the prednisolone is tailed off. Early use of these measures in combination may preserve renal function.

Surgical

- Cessation of pulmonary haemorrhage has been described after bilateral nephrectomy.
- Renal transplantation has been used and, although there are immunoglobulin G (IgG) deposits in the graft, it does not appear to damage the kidney.

Complications of Goodpasture's syndrome[3]

Acute respiratory failure, acute kidney injury and chronic kidney disease are the most common complications. Other complications include:

- Pulmonary haemorrhage with respiratory failure is the most common cause of death.
- An early relapse within two months may occur when circulating antibodies are still present. This typically presents as alveolar haemorrhage. The risk factors for relapse include infection, volume overload, and cigarette smoking.

- Pneumocystis jirovecii has an annual incidence of 1% but is a potentially deadly complication of immunosuppressive therapy in patients with Goodpasture's syndrome. Prophylaxis with co-trimoxazole may be useful.
- If Goodpasture's syndrome occurs in pregnancy it may produce hypertension and associated intrauterine growth restriction requiring premature delivery. Both mother and baby are at risk.[10]

Prognosis[8] [11]

- In the past, the disease was almost invariably fatal, and sometimes rapidly so.
- Aggressive therapy with plasma exchange, corticosteroids, and immunosuppressant drugs has dramatically improved prognosis, with the one-year survival rate of 70-90%.[6]
- Alveolar haemorrhage is usually responsive to treatment, and long-term respiratory sequelae are uncommon.
- Renal prognosis is more variable, but, with aggressive treatment, independent renal function is maintained at 1 year in more than 80% of patients not requiring renal replacement therapy at presentation.
- Presentation with severe renal failure requiring dialysis or a high proportion of glomerular crescents at biopsy are associated with poor renal outcome.[12]
- Relapse is uncommon, but some people may have recurrent disease. Goodpasture's syndrome can recur in a transplanted kidney.[3]

Prevention of Goodpasture's syndrome

There is no known prevention, but avoid associated environmental risk factors such as cigarette smoking and hydrocarbon exposure - eg, sniffing glue and siphoning petrol.

Further reading

- Pedchenko V, Kitching AR, Hudson BG; Goodpasture's autoimmune disease - A collagen IV disorder. Matrix Biol. 2018 Oct;71-72:240-249. doi: 10.1016/j.matbio.2018.05.004. Epub 2018 May 12.

Authored by:	Peer Reviewed by: Dr Doug McKechnie, MRCGP	
Originally Published: 20/11/2023	Next review date: 23/05/2023	Document ID: doc_1497