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Véronique Witko-Sarsat, Nathalie Thieblemont

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## **Granulomatosis with polyangiitis (wegener's)**

**Xavier Puéchal<sup>1,2</sup>**

1. Centre de Référence des Maladies Systémiques Auto-immunes rares,

Université Paris Descartes

Hôpital Cochin, Assistance Publique – Hôpitaux de Paris

27, rue du faubourg Saint Jacques,

75014 Paris

2. Institut Cochin, INSERM U1016, CNRS UMR 8104, Paris, France;

Phone: +33 1 58 41 32 41

Fax: +33 1 58 41 29 68

Email: [xavier.puechal@aphp.fr](mailto:xavier.puechal@aphp.fr)

## **Abstract**

Granulomatosis with polyangiitis (GPA) (Wegener) is a necrotizing vasculitis combining inflammation of the vascular wall and peri- and extravascular granulomatosis. Clinically, GPA is characterized in its full form by ENT signs, lung, and kidney involvement. One of the key features of GPA is the presence of ANCA – cytoplasmic in approximately 90% of systemic forms and in 50% of localized forms – directed against proteinase 3 in most cases. PR3-ANCA are highly specific to GPA and therefore have a high diagnostic value. Treatment of GPA is based on a combination of corticosteroids and cyclophosphamide or rituximab, which allows remission to be achieved in more than 80% of cases. Azathioprine was the most widely used maintenance treatment, but low-dose semi-annual rituximab maintenance infusions further decrease relapses with acceptable safety. Nevertheless, relapses occur in more than 50% of cases. One of the biggest treatment challenges is the occurrence of side effects, the severity and frequency of which are often linked to the prolonged treatment course, which is difficult to avoid.

**Key words:** Granulomatosis with polyangiitis; necrotizing vasculitis; ANCA-associated vasculitis; biological response modifiers; biologics; rituximab

Granulomatosis with polyangiitis (GPA) (Wegener) is a necrotizing vasculitis combining inflammation of the vascular wall and peri- and extravascular granulomatosis. Clinically, GPA is characterized in its full form by ENT signs, lung, and kidney involvement. Other systemic symptoms may be present. GPA is a serious disease that may be fatal if not treated. Current therapies can control its progression and cure it in most cases, although relapses are common.

## 1. Pathogenesis of disease

Neutrophils are key players in the pathogenesis of the disease because they produce the proteinase 3 (PR3) autoantigen and their regulation is altered in patients with GPA (1). Patients with GPA have autoantibodies directed against PR3 in neutrophils. When recruited to the inflammation site, these cells have a crucial role in defending against microbes but can also contribute to tissue damage. The PR3 autoantigen expressed in the membrane of apoptotic neutrophils disrupts their elimination by macrophages. PR3 expression in the membrane of activated neutrophils prevents inflammation from resolving and is a major factor in GPA pathogenesis. While the phagocytosis of an apoptotic cell under physiological conditions has an anti-inflammatory effect, PR3 is perceived as a danger signal by macrophages, who alert the immune system. This subversive effect of PR3 contributes to the development of an autoimmune response, in particular by alerting plasmacytoid dendritic cells, who – in turn – completely stop producing CD4+ regulatory T cells; instead, they promote the emergence of activated helper T cells with a Th9/Th2 profile.

## 2. Histopathology

From a histopathology perspective, GPA consists of **layers** of ischemic necrosis, with the formation of non-microbial abscesses and polymorphic granulomatosis involving polymorphonuclear neutrophils, lymphocytes, and multinucleated giant cells. The vasculitis affects small-sized blood vessels (arterioles, capillaries, and venules), and more rarely, medium-sized vessels (**Figure 1**). The granuloma is nonspecific and contains giant cells. Histological proof of the diagnosis can be achieved with guided biopsies (**Box I**).

### 3. Systemic And Localized Forms

During GPA, we can distinguish between:

- systemic/diffuse forms characterized by
  - kidney involvement
  - and/or significant and progressive alveolar hemorrhage
  - and/or involvement of one or more other organs, especially a vital organ, with systemic signs
- limited/localized forms, mainly respiratory (ENT and/or lung without alveolar hemorrhage), without kidney involvement, although sometimes cutaneous, without affecting the patient's overall health or being life threatening (approximately 30% of GPA cases).

During the disease, a localized/limited form can become systemic/diffuse, and vice versa.

### 4. Epidemiology

GPA is a rare disease, with a prevalence estimated at 3/100,000 inhabitants. There is a north-south gradient, with a higher frequency in Nordic countries. GPA affects both sexes. While mean age of occurrence is 45 years, some cases have been described in older adults and in children.

### 5. Clinical Signs

The main clinical manifestations are summarized in **Table I** (2-7).

#### 5.1 ENT manifestations

ENT signs are often the ones that reveal the disease. They may persist for several months and remain unrecognized until new manifestations occur. Chronic sinusitis or rhinitis are common. CT scan may show bone destruction. Sinusitis, epistaxis, and deafness are also common. Subglottic stenosis is rarer. Lastly, an orbital inflammatory pseudotumor is possible with unilateral exophthalmos.

## 5.2 Lung manifestations

Lung signs are nonspecific: cough, dyspnea, chest pain, hemoptysis. Chest x-rays and CT scan show one or multiple unilateral or bilateral nodules, excavated in half the cases (**Figure 2**). Their occurrence parallels the progression of the disease. Pulmonary infiltrates can also be seen in one or both lungs. Bronchoscopy can reveal stenosis due to the granulomatosis. Pseudotumoral granulomatous pulmonary masses are possible. Alveolar hemorrhage is a potentially serious lung manifestations of GPA (**Figure 3**). The diagnosis is confirmed when the bronchoalveolar lavage fluid is red or pink and/or if the lavage fluid is clear, with Perl's staining showing more than 30% siderophages and/or a Golde score higher than 100. It can be complicated by respiratory distress syndrome. The combination of lung signs and kidney failure define the pulmonary-renal syndrome.

## 5.3 Kidney manifestations

The kidney signs are univocal, with rapidly progressing kidney failure and histological findings of extracapillary crescentic glomerulonephritis. Immunofluorescence is negative. It is vital to look for hematuria and proteinuria at the time of diagnosis and at each follow-up visit. If not detected and treated in time, it will progress toward severe kidney failure. It is important to treat it quickly because partly or completely reversal can be achieved with treatment. The kidney failure may have other causes, such as unilateral or bilateral hydronephrosis secondary to ureteral stenosis or an iatrogenic origin.

## 5.4 Joint and/or muscle manifestations

Joint and/or muscle signs occur in more than half the patients and may be the ones that reveal the presence of GPA. This may be genuine polyarthritis.

## 5.5 Other manifestations

The other signs are those observed in other types of vasculitis (**Table I**). Peripheral neurological

manifestations are not specific to the disease and, like cutaneous signs, are evidence of small-sized vessel involvement.

## **6. Laboratory Tests**

GPA has a critical component to its diagnosis and monitoring: the presence of ANCA, with diffuse cytoplasmic fluorescence, directed against PR3 in 75% of cases and much more rarely against myeloperoxidase (7). They are present in about 90% of systemic forms and 50% of localized forms of the disease. They are highly specific, thus have a high diagnostic value. Under certain conditions – in combination with suggestive clinical signs – their presence may be sufficient for diagnosis.

## **7. Progression And Prognosis**

Untreated, GPA has a 1-year mortality of about 70%. With treatment, remission is achieved in more than 80% of cases. Relapses are common and occur in more than 50% of cases. Despite this, the 10-year survival rate is 75% (8).

ENT involvement is associated with better prognosis but more relapses. The prognosis is based on the Five Factor Score (FFS) (9), the updated version of which also applies to GPA (10). It takes into account five signs (each one point) associated with increased mortality: age >65 years, specific cardiomyopathy, gastrointestinal manifestations, kidney failure defined by stabilized serum creatinine >150 µmol/L and the absence of ENT manifestations. However, while the FFS is helpful in determining the GPA prognosis, it does not drive treatment decisions, like with the other types of necrotizing vasculitis (11).

At the time of diagnosis, the factors associated with relapse are the presence of anti-PR3 ANCA, cardiac involvement, and creatinine clearance of >60 mL/min (12). Over the course of the disease, persistent ANCA are also associated with increased risk of relapsing (13-15). But the disappearance of ANCA does mean there will be no relapse. A significant increase in PR3 ANCA levels is a reason to be worried about relapse (12). Nevertheless, even if ANCA levels increase, 29% to 60% of patients do not relapse at 1 year (16,17). This means that if we had initiated treatment based on this increase alone, 29% to 60% too many patients

would have been treated. Thus, ANCA levels alone cannot be used as a basis to adjust treatment. An increase in the ANCA titer is a reason to monitor the patient more closely, not to increase treatment.

## **8. Treatment Of Granulomatosis With Polyangiitis**

Treatment of GPA is based on a combination of corticosteroids and immunosuppressants (**Figure 4**) (11). In systemic forms, corticosteroids alone are not sufficient to achieve and maintain remission (18). Cyclophosphamide, in combination with corticosteroid therapy, allows prolonged remissions (2). Nevertheless, relapses occur in more than half the patients. Long-term treatment is needed to control the disease. One consequence is the development of frequent and severe side effects. In older long-term protocols with oral cyclophosphamide, the risk of bladder cancer was multiplied by 33, that of lymphoma by 11, and that of a solid tumor by 2.4 (2).

GPA treatment now consists of an initial induction treatment with the aim of remission, which the vast majority of patients achieve in 3 to 6 months (11). Once this is achieved, a less toxic maintenance treatment is then started with the aim of keeping the patient in remission.

### **8.1 Induction treatment**

#### **8.1.1 Corticosteroids**

Prednisone, initially prescribed at a dose of 1 mg/kg/day, is sometimes preceded by one or more boluses of methylprednisolone (15 mg/kg/day). After an initial 3-week course, the corticosteroid dose is reduced. To reduce the iatrogenic risk, the dose is reduced as much as possible (19-21), for a total duration of 18 to 24 months. The main targets for corticosteroid therapy are approximately 20 mg/day at 3 months, 10 mg/day at 6 months and 5 mg/day at 1 year (14).

The randomized controlled PEXIVAS study evaluated lower-dose corticosteroid therapy in the case of kidney involvement or alveolar hemorrhage in more than 700 patients with ANCA-associated vasculitis. This study showed the lower-dose corticosteroid arm was non-inferior to a standard regimen for controlling vasculitis,

which was evaluated based on a composite criterion associating death or progression to end-stage kidney failure (22). The rates of severe infection were significantly less at 1 year in patients who had received the lower-dose corticosteroid therapy. Since this study, there has been a trend to further reducing the cumulative corticosteroid dose, although additional results on vasculitis control with longer follow-up need to be analyzed. Steroid-induced osteoporosis must be countered with regular physical exercise, a calcium-rich diet, vitamin and calcium supplements, and a bisphosphonate, especially if bone mass is low to begin with.

### **8.1.2 Cyclophosphamide is the traditional induction treatment for systemic/diffuse GPA**

Cyclophosphamide is used as an induction treatment in combination with corticosteroids. The oral form is prescribed at 2 mg/kg/day (2), but needs to be adjusted based on age, kidney function, therapeutic response and the occurrence of side effects. Bolus injections of cyclophosphamide are widely done (23,24). After three infusions of 0.6 g/m<sup>2</sup> at 15-day intervals, cyclophosphamide is given every 3 weeks at a dose of 0.7 g/m<sup>2</sup> until full remission is achieved (11). Typically, six bolus injections are needed over 3 months before switching to maintenance treatment. Intravenous pulse administration achieves the same short-term results as those obtained with oral cyclophosphamide (25), while also being safer since the cumulative dose is lower. The number of long-term relapses remains high and may be greater with intravenous administration than with oral administration.

### **8.1.3 Methotrexate is recommended in limited/localized forms of GPA**

Methotrexate is less effective than cyclophosphamide. In induction treatment, methotrexate is an alternative to cyclophosphamide in forms of GPA that are not life-threatening (26,27). Only one controlled study has been done; it compared administration of methotrexate or cyclophosphamide for 12 months – in addition to corticosteroid therapy – in patients with vasculitis that was not life-threatening (28). At 6 months, there was no difference in the frequency of remission. However, patients relapsed more often after receiving methotrexate than cyclophosphamide. This study confirms the benefits of not continuing immunosuppression past 12

months and that some patients respond to methotrexate alone. Nonetheless, this strategy can be used only in initially mild cases of GPA, with normal or below-normal kidney function and with very close monitoring.

#### **8.1.4 Rituximab has revolutionized induction treatment of severe refractory or relapsing GPA**

In combination with corticosteroid therapy, this anti-CD20 monoclonal antibody has revolutionized the treatment of severe GPA, especially refractory or relapsing forms. It is an effective alternative to cyclophosphamide. It received marketing authorization for severe GPA, in combination with corticosteroid therapy, as infusions of 375 mg/m<sup>2</sup> for 4 consecutive weeks. Preliminary open-label studies mainly enrolled patients with refractory GPA (29,30). All were positive except one (31). Full remission was reported in 75% to 83% of treated patients (29,30). It may take 3 months to obtain the maximum therapeutic effect. Patients with retroorbital granulomas do not always respond, nor do those with subglottic stenosis (29,31,32). Maintenance treatment is necessary once remission is achieved. Looking at B-cell repopulation and/or for renewed increase in ANCA is not enough to determine the best time to consider retreatment with rituximab (29). Two controlled studies compared rituximab with cyclophosphamide as an induction treatment in combination with standard corticosteroid therapy. The remission rate was not less with rituximab than with conventional cyclophosphamide treatment, while the short-term safety profile was comparable (19,33,34). On the other hand, in the event of relapse, rituximab is associated with a significantly better remission rate than cyclophosphamide (34). Thus, rituximab is preferable to cyclophosphamide for induction treatment of severe active forms in relapsing patients or in women of childbearing age. Post-hoc analysis showed rituximab was more effective than cyclophosphamide for achieving remission in patients with anti-PR3 ANCA (35). It is also very promising in cases of refractory GPA – when cyclophosphamide induction treatment fails – as it leads to remission in a large majority of cases (36). Pneumocystosis prophylaxis is essential.

#### **8.1.5 Mycophenolate mofetil**

Mycophenolate mofetil was the subject of a noninferiority study against cyclophosphamide as an induction

treatment for ANCA-associated vasculitis (37). There were no fewer remissions at 6 months in patients receiving mycophenolate mofetil, but there were more relapses later on, especially in patients with anti-PR3 ANCA. Consequently, it is little used in patients with GPA.

### **8.1.6 TNF inhibitors are not used**

Infliximab has sometimes been prescribed as an induction treatment for refractory GPA (38-41). Its efficacy, however, is only suspensive. Severe infectious complications have also been reported when infliximab and cyclophosphamide were used in combination (42).

A controlled study compared etanercept with a placebo, in addition to conventional treatment, in patients with GPA (20). There was no benefit of using etanercept as a maintenance treatment nor potentially as an induction treatment. On the other hand, patients who received etanercept in combination with cyclophosphamide developed more solid tumors than those who received the placebo.

## **8.2 Maintenance treatments**

**8.2.1 Azathioprine** previously was the standard first-line treatment since it is effective and well-tolerated. After achieving remission with cyclophosphamide and corticosteroids, there were not more relapses at 18 months when patients were switched to azathioprine than when cyclophosphamide was continued (21). Azathioprine induces fewer long-term side effects than cyclophosphamide. The initial dosage is 2 mg/kg/day. Relapses remain common, generally after azathioprine is discontinued. They are less common when immunosuppressants are used for 4 years after diagnosis than when maintenance treatment is discontinued after 2 years (13).

**8.2.2 Methotrexate** is another potential maintenance treatment – at 0.3 mg/kg/week – once remission is achieved (43-46). It maintains remission in more than 80% of cases (43); however, relapses still occur in more than half the patients after it is discontinued (45). In the only controlled randomized trial that has been done up

to now, azathioprine and methotrexate had comparable efficacy as a maintenance treatment for 12 months after remission was achieved with corticosteroid therapy and cyclophosphamide bolus (46). The results were also comparable after 10 years' follow-up (8).

### **8.2.3 Rituximab has emerged as the best maintenance treatment**

In late 2018, its marketing authorization was extended for this indication in Europe and the United States based on data from the MAINRITSAN trial (47). Rituximab is initiated once remission is achieved, within the month following the last cyclophosphamide infusion or 4 to 6 months after the start of induction treatment with rituximab. It is administered at 500 mg on D1 and D15 then every 6 months for 18 months (5 infusions in 18 months). This represents a real advance in treatment. In a controlled study, after remission was achieved with cyclophosphamide and corticosteroids, the likelihood of a severe relapse was reduced six-fold at the 28<sup>th</sup> month relative to the standard maintenance treatment with azathioprine continued for 22 months (47). This reduced relapse rate was maintained at 5 years (15). It is also possible to administer rituximab – only when the ANCA titer is increased or B-cell repopulation occurs – without significantly increasing the number of relapses compared with standard systemic infusion every 6 months (48). The D15 infusion is likely not essential and four infusions administered over 18 months may be sufficient (49). In practice, after induction treatment with rituximab, its efficacy and safety as a maintenance treatment for GPA are also satisfactory in the medium term: 2 years from diagnosis or relapse, the relapse-free survival is 85% and therapy maintenance level for rituximab is 78% (32).

### **8.2.4 Neither leflunomide nor mycophenolate mofetil are prescribed as a first-line treatment**

They have been tried in a limited number of patients. Mycophenolate mofetil was found to be less effective than azathioprine in maintaining remission during a controlled trial (50). Their use cannot be recommended as a first-line treatment.

### **8.3 Immunoglobulins**

Intravenously, immunoglobulins are mainly used in relapsing patients with some indication of efficacy and a decrease in ANCA titer. Nevertheless, the number of patients who relapse once the infusions are stopped limits the benefits of this therapy, which is well-tolerated overall. This treatment may be useful for helping certain patients who have active vasculitis and severe immunodepression get through a difficult period. Immunoglobulins are administered intravenously at a dose of 2 g/kg per month; the dose is spread over 4 days, especially in patients with kidney failure.

### **8.4 plasma exchanges**

Plasma exchanges were readily used severe forms of ANCA-associated vasculitis with rapidly progressive kidney failure. In a randomized controlled study, they were significantly better than a bolus of methylprednisolone in patients with initial serum creatinine  $>500 \mu\text{mol/L}$  as they reduced the number of patients requiring dialysis at 3 and 12 months (51). Nevertheless, they did not affect overall survival, and the kidney benefit was not maintained over the long term. The PEXIVAS study, a randomized controlled trial evaluating the benefit of plasma exchanges in cases of kidney involvement or alveolar hemorrhage in more than 700 patients with ANCA-associated vasculitis, showed no benefit of these exchanges based on a composite criterion combining death and progression toward end-stage kidney failure (52). Since the results of this study were published, there has been a trend toward recommending exchanges only in severe forms that have not responded to well-conducted medical treatment (as second-line therapy) or in cases of massive alveolar hemorrhage.

Alveolar hemorrhage is usually treated with a combination of corticosteroids and cyclophosphamide or rituximab, or even plasma exchanges if the hemorrhaging is severe or there is no improvement with well-conducted medical treatment. In relapsing or refractory vasculitis, it is advised that each case be discussed with recognized centers of excellence.

## **8.5 role of trimethoprim-sulfamethoxazole**

In addition to pneumocystosis prophylaxis, trimethoprim-sulfamethoxazole could be useful for reducing the overall frequency of severe infections in patients on rituximab (53). It may also have a modest role in maintaining remission. In a short, controlled double-blind study, taking 800-mg tablets of sulfamethoxazole two times per day for 2 years was accompanied by a reduction in the relapse rate, mainly ENT, compared with placebo, in patients in full remission (54).

## **8.6 adjuvant measures**

Prevention and detection of thromboembolic complications is part of the initial disease care. Cardiovascular complications are also increased during ANCA-associated vasculitis, requiring screening and management of cardiovascular risk factors (55,56). During treatment, certain side effects may occur such as infections in the short term and malignancies in the long-term with the development cyclophosphamide-induced cystopathy, lymphomas, and solid tumors. Prophylaxis for infections is justified. Regular skin monitoring is important because patients develop more non-melanoma cancers than the controls, possibly because of the prolonged exposure to immunosuppressants (57). They may be less frequent with the use of rituximab (58).

## **9. Conclusion**

GPA remains a severe, chronic, and easily recurring disease. However, with appropriate long-term treatment, its prognosis has improved, and the 10-year survival rate reaches 75%. One of the major problems is treatment-related side effects; their severity and frequency is often a consequence of prolonged treatment, which is difficult to avoid.

### **Conflicts of interest:**

X.P. is an investigator in academic therapeutic trials evaluating rituximab in ANCA-associated vasculitis, in which the rituximab is supplied by Roche. X.P. is an investigator in therapeutic trials evaluating avacopan

(ChemoCentryx) and IFX 1 (InflaRx) in ANCA-associated vasculitis. X.P. was an investigator in clinical trials evaluating mepolizumab in eosinophilic granulomatosis with polyangiitis (GSK). X.P. has received payments for consulting assignments (Sanofi) and scientific presentations (Boehringer Ingelheim), and to cover expenses for conference participation/registration (Sanofi).

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**Box I.** What sites must be biopsied to make the diagnosis?

- The lung biopsy can be taken from a nodule or the parenchyma of a patient with alveolar hemorrhage. Biopsy of these nodules reveals a palisading granuloma in which the vessels show arteriolar vasculitis. Capillaritis is mainly found in those with alveolar hemorrhage. The lung biopsy is guided by bronchoscopy. Thoracotomy is a highly invasive procedure, with non-negligible mortality and morbidity. The need for such a procedure should be discussed, particularly in a patient with a strongly suggestive clinical presentation and anti-PR3 cytoplasmic ANCA on ELISA.
- A nasal and sinus biopsy is easy to do but requires good technique with numerous samples being collected from the granulomatous area, as opposed to the necrotic area. It is less informative than a lung biopsy.
- A kidney biopsy must be done as soon as abnormalities in urinary sediment, proteinuria, and/or a change in kidney function (even a moderate one) are found. It is used to look for extracapillary glomerulonephritis and direct signs of vasculitis. It is used to evaluate the degree of parenchymatous involvement and previously formed fibrous lesions, as well as any associated tubular necrosis, thus providing information on the prognosis for recovery.
- Muscle or neuromuscular biopsy is useful and highly informative in patients with peripheral neuropathy.
- Temporal artery biopsy provides important information in patients with headaches. However, its routine use has not been validated.

**Table I - Characteristics of granulomatosis with polyangiitis (Wegener's granulomatosis) from key published studies**

Author	Hoffman	Anderson	Matteson	Guillevin	Reinhold-Keller	Iudici
Year	1992	1992	1996	1997	2000	2019
Reference	(2)	(3)	(4)	(5)	(6)	(7)
Number of patients	158	265	77	50	155	795
Male/female	50/50	55/45	64/36	30/20	49/51	445/350
Age at diagnosis, years	41	50	45	54	48	53
Year of diagnosis	1966–1990	1975–1985	1978–1987	1990–1993	1966–1993	1983–2018
Localized form at diagnosis	NI	22	NI	0	15	55
cANCA positive/anti-PR3 positive (%)*	88	NI	NI	86	84	75
ENT	73/92	75/NI	NI/NI	43/50	93/99	80 %
Lungs	45/85	63/NI	NI/53	41/50	55/66	68 %
Joint pain	32/67	20/NI	NI/NI	32/50	61/77	52 %
Kidney	18/77	60/NI	NI/73	37/50	54/70	56 %
Eye	15/52	14/NI	NI/NI	14/50	40/61	27 %

Skin	13/46	25/NI	NI/NI	15/50	21/33	33 %
Peripheral nerve	NI/15	NI/NI	NI/	7/50	21/40	51 %
Heart	NI/8	NI/NI	NI/14	2/50	13/25	15 %
CNS	NI/8	NI/NI	NI/	NI	6/11	3 %
Digestive	NI/NI	NI/NI	NI/19	NI	3/6	11 %
<hr/>						
Mean follow-up (years)	8	NI	7.1	2.33	7	3.5
Mortality (%)	20	56	36	38	14	10
Death due to GPA or treatment	13	NI	NI	30	12	2.7
Death due to infection	3	12	10	18	3	3.2
<hr/>						

\*Antineutrophil cytoplasmic antibodies (ANCA) with diffuse cytoplasmic fluorescence against proteinase 3 (PR3) in most cases.

ENT = Ear, nose, and throat; CNS = Central nervous system, NI = No information

## FIGURE LEGENDS

Figure 1. The 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides based on the size of the main vessels affected in systemic vasculitis. ANCA-associated vasculitis is one of the forms that primarily affects small blood vessels and that is not accompanied by immune complexes on histological samples (pauci-immune).

GPA: granulomatosis with polyangiitis (Wegener's); MPA: microscopic polyangiitis; EGP: eosinophilic granulomatosis with polyangiitis (Churg-Strauss)

Figure 2. Excavated pulmonary lesion in a patient with granulomatosis with polyangiitis.

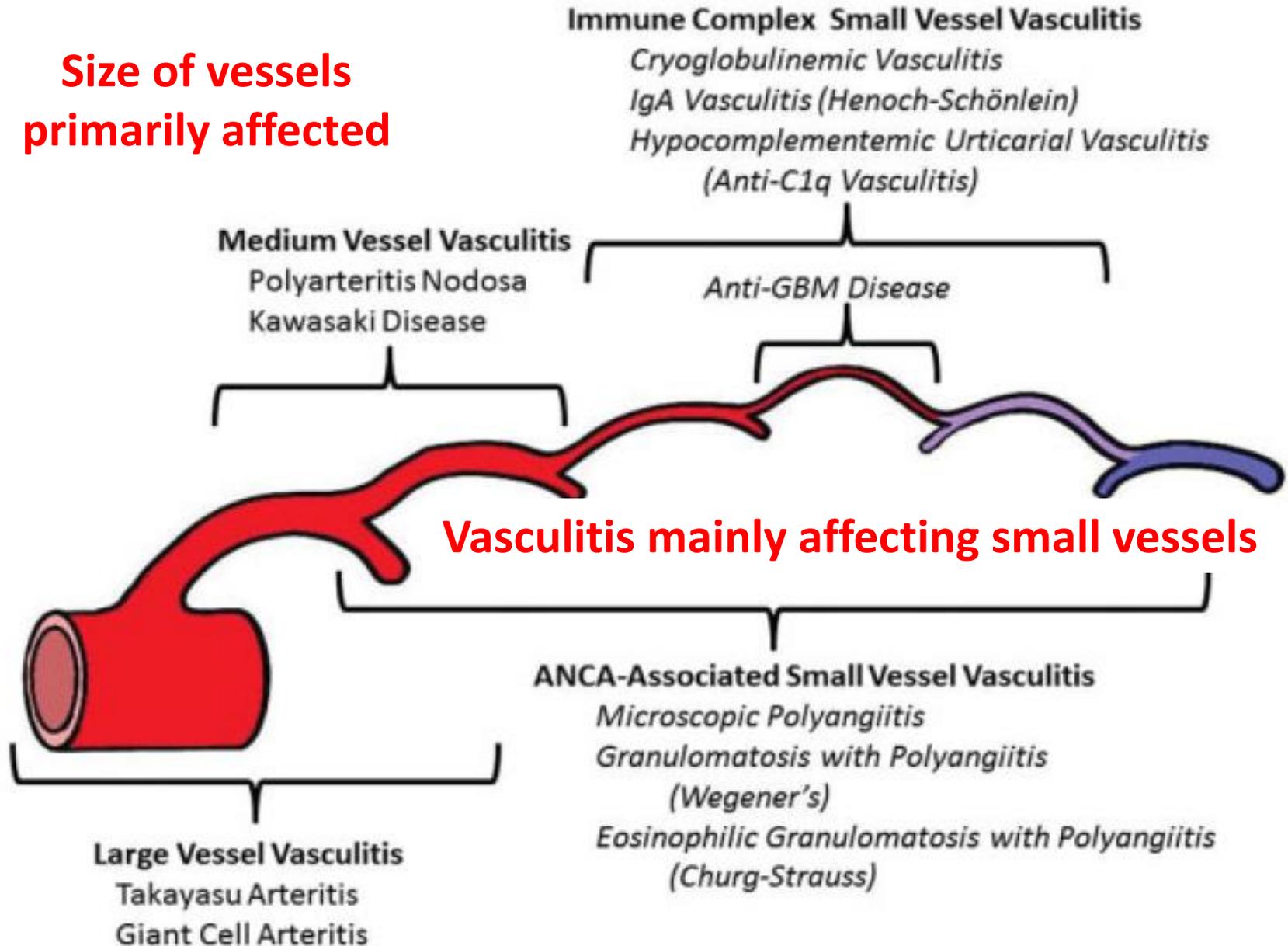
Figure 3. Alveolar hemorrhage in the form of extensive bilateral alveolar and ground-glass opacities.

Figure 4. Treatment of ANCA-associated vasculitis according to the 2019 French National Diagnosis and Treatment Protocol (PNDS).

GPA: Granulomatosis with polyangiitis (Wegener's); MPA: microscopic polyangiitis; EGPA: eosinophilic granulomatosis with polyangiitis (Churg-Strauss)

# 2012 REVISED CHAPEL HILL CONSENSUS CONFERENCE NOMENCLATURE

**Size of vessels  
primarily affected**





3

1  
2  
1

120  
240

age  
16/04/15 00:00



**GFEV** | GROUPE FRANÇAIS  
D'ÉTUDE DES  
VASCULARITES





# Treatment of ANCA-associated vasculitis

	<b>GPA or MPA or EGPA FFS <math>\geq 1</math></b>	<b>MPA or EGPA FFS=0</b>
<b>INDUCTION</b>	<b>Corticosteroids 1 mg/kg/day <math>\pm</math> MP bolus x 1-3 (15 mg/kg) + CYC IV x 6 (600-700 mg/m<sup>2</sup>) or RTX (375 mg/m<sup>2</sup>) x 4 weeks</b>	<b>Corticosteroids 1 mg/kg/day</b>
<b>MAINTENANCE</b>	<b>Corticosteroids + RTX 500 mg/6 mo. x 18 mo. or AZA (2 mg/kg/day) or MTX (0.3 mg/kg/week) (total of 18-24 months)</b>	<b>Corticosteroids (total of 18-24 months)</b>