Review Article

International Journal of Clinical Pharmacokinetics and Medical Sciences

Published by Pharma Springs Publication Journal Home Page: https://pharmasprings.com/ijcpms/

# A Review Article on Granulomatosis with Polyangitis

Abhirami M T*, Anisha Varghese, Anusha Shaji, Georgina Sarah

KLE College of Pharmacy, Hubli-Dharwad Hwy, Vidya Nagar, Hubli-580031, Karnataka, India

*Article History:*

Received on: 07 Jan 2022
Revised on: 26 Jan 2022
Accepted on: 29 Jan 2022

*Keywords:*

Granulomatosis with Polyangitis, Anti-Neutrophil Cytoplasmic Antibody Associated Vasculitis, PR3, Endothelial Inflammation, Upper Respiratory Tract

Abstract

Wegener's granulomatosis, also known as granulomatosis with polyangitis (GPA), is a rare inflammatory illness characterised by vasculitis and granulomatosis. Upper & lower respiratory tract and kidneys are the organ systems that gets affected in GPA. Granulomatosis with polyangitis is characterised by necrotizing granulomas with pauci-immune vasculitis. GPA prevalence in Asians ranges between 0.37/million to 2.1/million populations. Symptoms usually occur depending on organ systems that get affected. Initial symptoms in the respiratory tract may include mucous membrane ulcers with secondary bacterial infection, chronic runny nose, sinus pain, and chronic middle ear infection, resulting in hearing loss. Clinical features along with physical examination, laboratory tests, X-Ray, MRI or CT scan and biopsy (sometimes) together help to prove diagnosis of GPA. The two stages in the treatment of granulomatosis with polyangitis are inducing remission of symptoms and maintenance therapy. Mainstay of treatment is immunosuppressant's and is selected on the basis of severity of the disease.

*Corresponding Author

Name: Abhirami M T
Phone: 9497014950
Email: Mtabhirami18@gmail.com

eISSN: 2583-0953

DOI: https://doi.org/10.26452/ijcpms.v2i1.262

Production and Hosted by

Pharmasprings.com



## INTRODUCTION

Wegener's granulomatosis, also known as granulomatosis with polyangitis (GPA), is a rare inflammatory illness characterised by vasculitis and granulomatosis. Upper & lower respiratory tract and kidneys are the organ systems that gets affected in GPA [1, 2]. Granulomatosis with polyangitis is characterised by necrotizing granulomas with pauci-immune vasculitis. It is diagnosed clinically by a combination of acute sinusitis or lung inflammation, varied arteritis symptoms, and terminal renal failure [3]. GPA comes under the spectrum of disorder called Anti-neutrophil-cytoplasmic antibody (ANCA) associated vasculitis (AAV). The AAV group includes granulomatosis with polyangitis (GPA), microscopic polyangitis (MPA), and eosinophilic granulomatosis with polyangitis (EGPA) [4].

GPA primarily affects sinuses, nose, trachea, lungs and kidney; however, eyes, ears, skin, joints and other organs also gets affected [5]. Although it can happen at any age, it affects people aged between 40 & 60. GPA primarily affects countries/regions with predominantly European origin population, and it is rarely seen in East Asian countries, while MPA is most commonly seen in Asian countries/regions. The occurrence of GPA is impacted by latitude, with a decreased occurrence near the equator [6, 7]. GPA has a prevalence of 5 cases per 100,000 people in Europe, Northern Europe has a higher incidence [1]. United States reports a prevalence of 3 cases of GPA per 1,00,000 people. On the other hand, UK reports incidence of 10.2 cases and a prevalence of 250 cases per million populations [8]. GPA prevalence in Asians ranges between 0.37/million to 2.1/million populations [9]. GPA occurs in minors, with 8-15 percent of instances occurring in people aged < 19 [10].

Environmental (silica, hydrocarbons, fumes, pes-

ticides, and farming), infectious (*Staphylococcus aureus,* UV light, smoking, solvent and occupational solvent exposure) and some genetic (gene polymorphism in cytokine, chemokine's, adhesion molecules or Proteinase 3) factors are involved in the formation of the GPA. However, no single environment factor appears to be associated with a significant population-attributable risk [7, 11]. In 1936, Wegener established the clinical and pathological entity; however, Klinger documented a case as a form of periarteritis nodosa in 1931 and is thought to be the first instance of Wegener's granulomatosis to be published [12]. Although it is a rare condition and occurs among adults and children; prompt diagnosis and treatment should be done initially in order to avoid the complications and life-threatening condition resulting from delayed diagnosis and management.

**Pathophysiology**

Micro-vascular endothelial swelling leads to extravascular inflammation, increasing damage, tissue degradation, fibrosis, and loss of function are observed in Anti-neutrophil-cytoplasmic antibody (ANCA) associated vasculitis (AAVs). Immunological T and B cell tolerance is lost when one of two neutrophil proteins, PR3 or MPO is overexpressed; this causes Granulomatosis with polyangitis (GPA) and Microscopic polyangitis (MPA). As tolerance declines ANCAs are formed, acts as autoantibodies that activate neutrophils. Neutrophils that have been triggered by ANCA go to susceptible micro-vascular beds, causes injury and liberates auto antigen (see Figure 1), allowing effector T cells to recognise the antigen and mediate further injury [7].

Neutrophils are the most significant effector cells in pathophysiology of AAV. Neutrophils serve as a first line of defence in normally functioning human immune system, engulfing external pathogens, degranulating antimicrobials, and forming Neutrophil extracellular trap (NETs). Neutrophils at rest in the circulation undergoes a process known as "priming" in which they target antigens on their surface membrane (e.g., MPO or PR3) under certain conditions. Reactions to treatments, infections, and alternative complement pathway activation are all potential causes of priming. Concomitant "hits" like infections, silica exposure, or medicines might trigger a reaction like this. Dendritic cells generate TGF-beta and interleukin (IL)-6, which stimulate the development of T helper 17 (Th17) cells from naïve T cells when infectious pathogens are detected. Th17-derived IL-17 then encourages macrophages to create tumour necrosis factor (TNF) and IL-1ß, and these both are known priming factors.

The exposed auto antigens interact with ANCA, causing neutrophils adhering to endothelial cells to become too activated. This hyperactivation is accompanied by abnormal cytokine synthesis, reactive oxygen species release (ROS), and the release of lytic enzymes, all of these things harm vascular endothelial cells. PR3 and MPO are NET components, and prolonged elevations in their levels in the bloodstream cause dendritic cells to recognise them as neoantigens, which are then recognised by T cells and plasma cells. Hyperactivation of neutrophils, inflammatory activity, and vasculitis are all part of a vicious cycle, emerges from lymphocytes' constant synthesis of PR3 and MPO ANCA. As a result, neutrophils, elevated ANCA, altered plasma and T cell tolerance, and overproduction and persistence of NETs all play a role in the pathogenesis of PR3- and MPO-ANCA vasculitis. PR3-ANCA vasculitis is characterised by a predominance of upper respiratory system involvement and less frequently affects the lower respiratory tract and kidneys [13]. This entire pathology was represented in Figure 1.

**Clinical Manifestations**

Symptoms usually occur depending on organ systems that get affected (see Table 1). A region less affected by GPA includes CNS, heart, eye, breast, salivary gland, GI tract, spleen, pituitary & thyroid gland and urogenital tract [15]. Initial symptoms in the respiratory tract may include mucous membrane ulcers with secondary bacterial infection, chronic runny nose, sinus pain, and chronic middle ear infection, resulting in hearing loss. Cough, hemoptysis, shortness of breath, inflammation of thin membrane that lines the exterior of lungs & tissues inside of the lungs, pleural effusion and lung tissue inflammation may be present if lungs are being affected [2, 16]. Some individuals may experience kidney failure, which requires dialysis or kidney transplant. Other symptoms include joint pain, rashes on the skin, redness in the eyes, and/or changes in eyesight, nasal discharge, oral/nasal ulcers, sore throat, fatigue, stridor, dysphonia, wheezing, salivary gland enlargement, subglottis stenosis [17], fever, anorexia, arthritis, arthralgia, peripheral neuropathy, weight loss, nocturnal sweats, and numbness or loss of movement in the fingers, toes, or limbs [2, 15].

Hearing loss, permanent loss of vision, glaucoma, cataract, peripheral ulcerative keratitis (PUK); ischaemic optic neuropathy, optic nerve oedema, optic atrophy, corneal melt [15]; saddle nose deformity [18], acute hypoxic respiratory failure resulting from diffuse pulmonary haemorrhage,

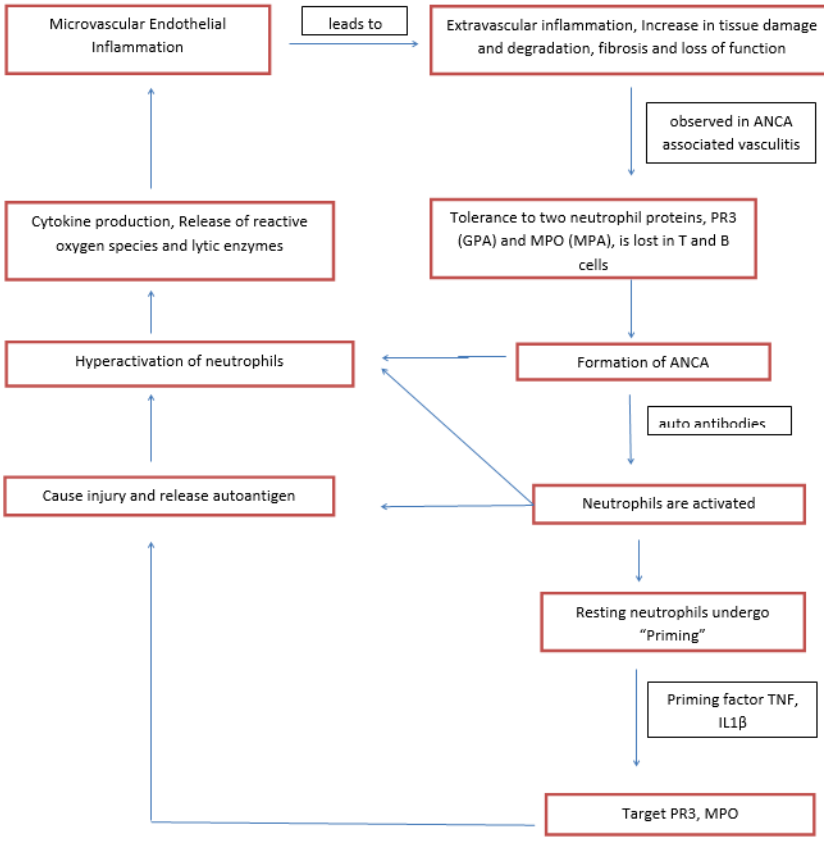


**Figure 1: Pathophysiology of Granulomatosis with Polyangitis**

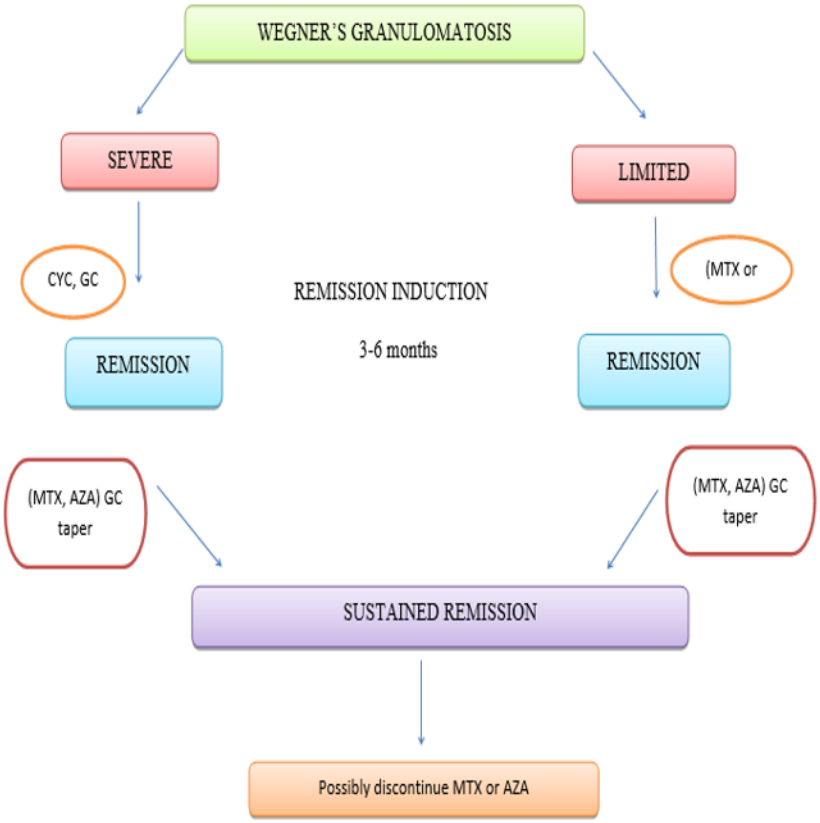


**Figure 2: Algorithm for Managaement of Granulomatosis with Polyangitis**

**Table 1: Clinical Manifestations of Granulomatosis with Polyangitis**

| Organ | Clinical Manifestations |
|---|---|
| General | Fever, malaise, myalgia, anemia, anorexia, weight loss |
| Ear | Sensorineural hearing loss, conductive hearing loss, otitis media [1]. |
| Eye | Pain, diplopia, proptosis, visual loss, orbital cellulitis [14], limited movement of extraocular muscles, erythematous edema of eyelids, conjunctivitis [11], xanthelasma, dacryoadenitis, scleritis, episcleritis, entropion, trichiasis [15]. |
| Nose | Nasal congestion, purulent nasal discharge, facial pain/pressure, loss of smell [14], epistaxis, sinusitis, epiphora, crusting, mucosal ulceration [1]. |
| Oral | Oral ulcers in buccal, lingual mucosa, floor of the mouth, posterior pharynx, tonsils & labial mucosal nodules, ulceration, delayed healing of extraction wounds, strawberry-like gingivitis, erythema, petechiae, bleeding, necrosis, loss of teeth, osteonecrosis of palate, oral-antral fistulae, swelling and desquamation of lips and salivary gland enlargement [15]. |
| Skin | Palpable purpuria, skin ulcer, vesicles, papules, subcutaneous nodules [15], digital necrosis, pustules, palpebral xanthoma, necrotic papules, gingival hyperplasia, pustules, livedo reticularis petechiae, bullae, maculae, and erythema [11]. |
| Upper Respiratory Tract | Subglottic stenosis/ tracheal stenosis [1]. |
| Lower Respiratory Tract | Cough, breathlessness, wheezing, hoarseness, stridor, pleuritis, pleural effusion, pulmonary infiltration, pulmonary infiltrates, alveolar capillaritis, pulmonary hemorrhage, respiratory failure, cavitating lung lesion, small air way obstruction, pulmonary nodules [1]. |
| CNS | Mononeuritis multiplex, neuropathy, headache, vomiting, stroke, seizure, cerebritis, meningitis, paraesthesia, numbness, burning pain, paresis, impaired sensation of pain, touch, vibration, temperature; muscular atrophy, asthenia [11, 15]. |
| Cardiovascular | Pericarditis, valvular lesions, myocardial infarction, coronary artery disease, cardiomegaly, endocarditis, pericardial tamponade, pericarditis, pericardial effusion, heart failure [11, 15]. |
| Gastrointestinal | Abdominal pain, gastrointestinal bleeding, dyspepsia, vomiting, diarrhea, haematochezia, melena, hematemesis [11]. |
| Kidney | Glomerulonephritis, urinary abnormalities, elevated serum Creatinine, haematuria, proteinuria, renal impairment (AKI, CKD/ ESRD) [1]. |
| Spleen | Fever, left upper quadrant pain, nausea, splenomegaly [11]. |
| Musculoskeletal | Myalgia, arthralgia, inflammatory arthritis, muscle enzyme elevation [15]. |

**Table 2: The American College of Rheumatology Criteria for GPA Diagnosis**

| Classification Criteria | |
|---|---|
| Inflammation of nose or mouth | Oral ulcers that are painful or not, and nasal discharge that is purulent or bloody |
| Abnormal chest radiograph | Pulmonary nodules, fixed pulmonary infiltrates or pulmonary cavities |
| Abnormal urinary sediment | Haematuria with or without red cell deposits on a microscopic scale |
| Granulomatous inflammation | A granulomatous inflammation in a biopsy of an artery or perivascular region. |

**Table 3: Therapeutic Option for Granulomatosis with Polyangitis**

| Drug | Monitoring parameters | Route & Dose | Long term adverse effects |
|---|---|---|---|
| Cyclophosphamide + corticosteroids | CBC, CrCl, Urine analysis, RFT, serum glucose every 2-4 weeks, annual bone density. | PO: 2–3 mg/kg pulse 0.5–0.7 g/mon | Hemorrhagic cystitis, bladder carcinoma, Infertility, lymphoma, bone marrow suppression, alopecia |
| Methotrexate + Corticosteroids | Weekly CBC, Cr, AST, ALT for first month of starting drug | PO: 0.3 mg/kg | Hepatic toxicity, bone marrow suppression, pneumocystic jiroveci, transient medullary hypoplasia |
| Azathioprine | Weekly CBC, Cr, AST, ALT for first month. Test for TPMT allele mutations or enzyme activity prior to initiation. | PO: 2 mg/kg pulse 1200–1800 mg/mon | Thrombocytopenia, Pancytopenia, Hypersensitivity, Infectious diseases |
| Leflunomide | ESR, CRP, ALT, CBC, LFT | PO: 30 mg/day | Thrombocytopenia, Anaphylaxis, Peripheral Neuropathy |
| Cotrimoxazole | CBC, serum K+ levels | Trimethoprim 160 mg + sulfamethoxazole l00 mg | Hyponatremia, Neutropenia. Anaphylaxis, Rhabdomyolysis |
| Mycophenolate | Weekly CBC | PO: 2 g/day | Anemia, Neutropenia, Pancytopenia, Opportunistic infections |
| Cyclosporine | CrCl, BUN/Creatinine ratio | PO: 5 mg/kg/day | Nephrotoxicity, Infectious disease |
| Rituximab | CBC weekly to monthly, RFT. | IV: 75 mg/M2 once weekly for 4 weeks | ALT level raised, Nephrotoxicity, Toxic epidermal necrolysis |

CKD, mononeuritis multiplex are the complications associated with Granulomatosis with polyangitis [4, 10, 11].

Palpable single/multiple nodules, multifocal skin ulceration, breast masses, thickening of breast skin, retraction of nipple, clear nipple discharge are the symptoms if GPA involves breast. Endocrine manifestations include subacute granulomatous thyroiditis, diabetes insipidus, hyperprolactinemia, and pan-hypopituitarism [15].

## Diagnosis

Early diagnosis is important for effective and success treatment. Clinical features along with physical examination, laboratory tests, X-Ray, MRI or CT scan and biopsy (sometimes) together help to prove diagnosis of GPA. Because several non-specific symptoms of WG, including as persistent rhinorrhoea, dyspnea, mouth ulcers, chronic sinusitis, and arthralgia, can also be found in other disorders, early diagnosis may be challenging. If these symptoms do not disappear quickly, suspicion of WG should be raised. The American College of Rheumatology criteria for GPA diagnosis was given in Table 2.

## ANCA Blood Test

ANCA can be used in two ways: either as a diagnostic test or as a disease activity marker [1]. A positive ANCA blood test does not confirm disease diagnosis, it indicates the need for further examination. In the majority of cases with granulomatosis with polyangiitis and microscopic polyangiitis, anti-neutrophil cytoplasmic antibodies (ANCAs) directed against either leukocyte proteinase 3 (PR3) or myeloperoxidase are detected (MPO). Antibodies are detected by indirect immunofluorescence (IIF) and other antigen-specific immunoassays, the most common of which are enzyme-linked immunosorbent assays (ELISAs). In IIF, diluted patient serum samples are incubated with ethanol-fixed, permeabilized neutrophils from healthy donors (often pre-attached to glass slides). Using a fluorescent secondary anti-human IgG antibody, fluorescence

microscopy is utilised to assess the presence, titre, and pattern of fluorescence in bound ANCAs [7].

**X-ray/CT**

Although GPA often affects the lungs, patient may show no lung symptoms. In such patients imaging tests like X-Ray or CT scan helps in detecting lung abnormality. A chest X-ray can aid in the diagnosis of underlying disease in patients with pulmonary symptoms, but CT has a higher sensitivity in detecting pulmonary nodules, cavities, and alveolar opacities, as well as masses in the retro-orbital region, paranasal sinuses, and mastoids. A high-resolution CT scan of the chest can reveal interstitial pneumonia [7].

**ESR/CRP**

The acute-phase markers C-reactive protein and erythrocyte sedimentation rate are of limited use in detecting disease activity due to their lack of specificity. The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are both elevated in GPA patients, but ESR corresponds with disease activity better than CRP [10].

**Glomerulonephritis**

Glomerulonephritis is diagnosed by abnormal laboratory findings such as proteinuria, an active urine sediment with microscopic haematuria and red cell casts, and maybe a decline in renal function as evidenced by an increase in serum creatinine or a decrease in creatinine clearance [17].

**Biopsy**

Biopsy of an affected area should be performed to confirm vasculitis. It is recommended for patients with organ sites abnormality found during examination, lab tests and imaging. Scleral biopsy findings may include granulomatous foci, polymorphous inflammation (plasma cells, lymphocytes, and neutrophils), collagen necrosis, and vasculitis. The most common place for biopsies is lung tissue. A biopsy of the kidneys may reveal necrotizing glomerulonephritis [15].

**Other Tests**

Other tests like full blood cell count, differential white cell, LFT, RFT, urinalysis, cryoglobulins, HIV, hepatitis B and C viruses should be done to rule out any disease that could be confused for GPA [15].

GPA classification standards have been proposed by the American College of Rheumatology (see Table 2). If two or more of these criteria are present, the sensitivity is 88 percent and the specificity is 92 percent.

**Management**

The primary goal of treatment is to prevent all injury occurring from GPA. The two stages in the treatment of granulomatosis with polyangitis are inducing remission of symptoms and maintenance therapy. Induction therapy aims to achieve remission in three months and keep it for the next three months. Remission that lasts longer, early return, or refractory disease are all linked to poorer outcomes [7]. It is usually treated using powerful agents that are lifesaving, since it is a life-threatening disease. Any concurrent infections or risk of infection, including chronic viral infections (which should be screened) or immunodeficiency, as well as conditions like diabetes, osteoporosis, and psychiatric disorders, which increase the risk of glucocorticoid-related adverse events, should be assessed before starting [7].

Mainstay of treatment is immunosuppressant's and is selected on the basis of severity of the disease. Prior to the introduction of immunosuppressive medications, the prognosis for WG was terrible, with a five-month median survival time and an 82 percent 1-year mortality rate [13]. More than 90% of the patient with severe disease responds to combination therapy (Cyclophosphamide 2mg/Kg/day and Prednisone 1mg/Kg/day). However, GPA is a disease in which frequent relapses occur, requires repeated course of immunosuppressant's [19].

Any patient with an immediately life-threatening illness or rapidly developing glomerulonephritis should be treated with daily cyclophosphamide and a glucocorticoid unless there is a substantial contraindication. Despite the treatment advantages, 50 percent of patients experienced illness recurrence, and 42 percent experienced morbidity from drug-related toxicity [17]. Relapse is now the most common clinical issue. It can happen as early as the first 18 months of treatment and affects up to 50% of patients after 5 years of follow-up [20]. Infections, cancer (lymphoma, myelodysplastic syndrome), infusion reaction and death are complications associated with use of immunosuppressant's [4].

Another commonly used combination agents are Cyclophosphamide and Rituximab. Corticosteroids and Methotrexate are used initially for managing GPA in patients who have less severe GPA. Once patient's condition gets better/ improves doctors slowly reduce the dose of steroids and may discontinue it completely. Cyclophosphamide is given for duration of 3-6months and is later switched to immunosuppressant agents such as Methotrexate, Azathioprine, and Mycophenolate mofetil for 2years or more to maintain remission. Because of its toxicity, cyclophosphamide is not utilised for mainte-

nance therapy. Rituximab was approved in 2011 by FDA for the treatment of granulomatosis with polyangitis and is used along with glucocorticoids. In 2019, FDA approved the use of Rituximab in children > 2years of age. Algorithm for management of Granulomatosis with Polyangitis was represented in Figure 2 and the treatment chart was given in Table 3.

## CONCLUSION

Granulomatosis with polyangitis is a rare disorder that causes vasculitis, which involves the upper and lower respiratory tracts, as well as the kidneys. GPA has an unknown case, but it's thought to be caused by a variety of factors that causes immune system to develop inflammation and necrosis of respiratory tract and kidney. The pathophysiology of GPA is unknown, despite the fact that an immunological response appears to be involved in the disease's progression. A more integrated treatment strategy and greater outcomes would arise from a multidisciplinary team (otolaryngologists, oral & maxillofacial surgeons, physicians, rheumatologists, nephrologists, pulmonologists and ophthalmologists). Discovery of ANCA has made it easier to diagnose the condition, but histological evaluation of the lesional tissue is nearly always required to confirm the diagnosis. Induction agent is selected considering risk of adverse events and cost of treatment. Drugs like Azathioprine, rituximab and low dose steroids helps in maintaining remission. Despite its rarity, every healthcare professional should be aware of the existence of Granulomatosis with Polyangitis.

## ACKNOWLEDGEMENTS

The author thanks KLE College of Pharmacy, Hubballi for all the support.

### Conflict of Interest

The author declares no potential conflicts of interest with respect to research, authorship, and/or publication of this article.

### Funding Support

The authors declare that there is no funding support for this study.

## REFERENCES

[1] A Greco, C Marinelli, M Fusconi, G F Macri, A Gallo, A De Virgilio, G Zambetti, and M De Vincentiis. Clinic manifestations in granulomatosis with polyangiitis. *International Journal of Immunopathology and Pharmacology*, 29(2):151–159, 2016.

[2] NORD. Granulomatosis with Polyangiitis, 2021. National Organization for Rare Disorders, Accessed on: 05 Dec 2021.

[3] J L Fahey, E Leonard, J Churg, and G Godman. Wegener's Granulomatosis. *The American Journal of Medicine*, 17(2):90255–90262, 1954.

[4] P Garlapati and A Qurie. Granulomatosis with Polyangiitis. 2021. Updated: 2021 May 15. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, Accessed on: 05 Dec 2021.

[5] Cleveland Clinic. Granulomatosis with Polyangiitis (GPA, formerly called Wegener's), 2021. Accessed on: 05 Dec 2021.

[6] Rheumatology.org. Granulomatosis with Polyangitis (Wegner's), 2021. Accessed on: 05 Dec 2021.

[7] A R Kitching, H. J Anders, N Basu, E Brouwer, J Gordon, D R Jayne, J Kullman, P A Lyons, P A Merkel, C O S Savage, U Specks, and R Kain. ANCA-associated vasculitis. *Nature Reviews Disease Primers*, 6(1):71, 2020.

[8] Emedicine.medscape.com. Granulomatosis with Polyangiitis (GPA, formerly Wegener Granulomatosis): Practice Essentials, Background, Etiology, 2021.

[9] G S R S N K Naidu, D P Misra, M Rathi, and A Sharma. Is granulomatosis with polyangiitis in Asia different from the West? *International Journal of Rheumatic Diseases*, 22:90–94, 2019.

[10] B Kubaisi, K Abu Samra, and C S Foster. Granulomatosis with polyangiitis (Wegener's disease): An updated review of ocular disease manifestations. *Intractable and Rare Diseases Research*, 5(2):61–69, 2016.

[11] J Miłkowska-Dymanowska, P Laskowska, M Rzuczkowski, A J Białas, W J Piotrowski, and P Górski. Untypical Manifestations of Granulomatosis with Polyangiitis-A Review of the Literature. *SN Comprehensive Clinical Medicine*, 1(8):616–626, 2019.

[12] J B Mcdonald and R W Edwards. Wegener's granulomatosis-a triad. *JAMA*, 173(11):1205–1209, 1960.

[13] A Kronbichler, K H Lee, S Denicolo, D Choi, H Lee, D Ahn, K H Kim, J H Lee, H Kim, M Hwang, S W Jung, C Lee, H Lee, H Sung, D Lee, J Hwang, S Kim, I Hwang, D Y Kim, and J I Shin. Immunopathogenesis of ANCA-Associated Vasculitis. *International Journal of Molecular Sciences*, 21(19), 2020.

[14] J O Cleary, N Sivarasan, C Burd, and S E J Connor. Head and neck manifestations of granulo-

matosis with polyangiitis. *The British Journal of Radiology*, 94, 1119.

[15] H A Almouhawis, J C Leao, S Fedele, and S R Porter. Wegener's granulomatosis: a review of clinical features and an update in diagnosis and treatment. *Journal of Oral Pathology and Medicine*, 42(7):507–516, 2013.

[16] M K Ramsey and D Owens. Wegener's Granulomatosis: A Review of the Clinical Implications. *Diagnosis, and Treatment. Laboratory Medicine*, 37(2):114–116, 2006.

[17] C A Langford and G S Hoffman. Rare diseases bullet 3: Wegener's granulomatosis. *Thorax*, 54(7):629–637, 1999.

[18] A Woywodt, M Haubitz, H Haller, and E Matteson. Wegener's granulomatosis. *The Lancet*, 367(9519):1362–1366, 2006.

[19] A Masiak, J Fijałkowska, S Nowakowski, ˙Z Smoleńska, and Z Zdrojewski. New lung mass in a patient with granulomatosis with polyangiitis. *Rheumatology International*, 41(2):493–499, 2021.

[20] P A Bacon. The Spectrum of Wegener's Granulomatosis and Disease Relapse. *New England Journal of Medicine*, 352(4):330–332, 2005.



**Cite this article:** Abhirami M T, Anisha Varghese, Anusha Shaji, Georgina Sarah. **A Review Article on Granulomatosis with Polyangitis**. Int. J. of Clin. Pharm. Med. Sci. 2022; 2(1): 24-31.