

# Granulomatosis with polyangiitis of sinonasal tract

## Abstract

Granulomatosis with polyangiitis also known as Wegener's Granulomatosis is a granulomatous disease which involves multiple organs as upper and lower respiratory tract, nasal, sinuses, kidneys, parotids are few of them. It is of two types - limited and systemic. Limited type is difficult to diagnose and commonly involves ENT organs as nose, ear and sinuses. ENT involvement as the presentation as the first symptom of the disease ranges from 63% and 72% of cases of patients. This review will thus focus on the sinonasal involvement in granulomatosis with polyangiitis.

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**Abbreviations:** GPA, Granulomatosis with Polyangiitis; WG, Wegener's Granulomatosis; ANCAs, Anti-Neutrophil Cytoplasmic Antibody

## Introduction

Granulomatosis with polyangiitis (GPA) also known as Wegener's granulomatosis (WG) was first identified as a clinical entity by Friedrich Wegener in 1936. It is a granulomatous disease which involves multiple organs. It involves progressive ulceration in the respiratory tract along with signs of widespread inflammatory disease, histological examination show granulomas, frequently in the respiratory tract and kidneys.<sup>1,2</sup>

GPA is an autoimmune disorder of unknown cause, characterised by necrotising granulomatous inflammatory and pauci-immune vasculitis in small and medium sized blood vessels (capillaries, venules, arterioles and arteries). It primarily affects upper and lower respiratory tract and the kidneys with segmental necrotising glomerulonephritis. Organ systems which can also be affected, include nose, paranasal sinuses, eyes, ears, skin, joints, bones, salivary glands, thyroid, heart, liver, colon and intestine.<sup>3,4</sup>

WG can manifest as two forms: limited disease and generalised disease with renal involvement. Limited variety can involve upper respiratory tract with only involvement of sinonasal tract. A delay in its confirmation and start of treatment may lead to varied complications. So early diagnosis is very important thus particular emphasis on sinonasal involvement is needed.

## Epidemiology

The prevalence of WG ranges between 3 cases per 100 000 (USA) to 16 cases per 100 000 (southern Sweden).<sup>5</sup> The most common age of presentation of WG is the sixth and seventh decades, but it can appear at any age.<sup>6</sup> The presence of ENT involvement in patients with WG ranges between 72.3% and 99%.<sup>7,8</sup> ENT involvement and presentation as the first symptom of the disease ranges from 63% and 72% of cases.<sup>9,10</sup>

## Pathology

Histopathologic findings in WG vary with location and type of involvement in the respiratory tract. In sinonasal disease histopathologic examination of nasal and sinus tissue involved

frequently reveals extensive tissue necrosis and infiltration with mixed population of inflammatory cells or occasionally necrotising granulomas. Histopathologic findings of vasculitis are not often seen in pathologic specimens from upper respiratory tract.<sup>11,12</sup>

## Clinical manifestations

Patients with GPA (either classic or limited) may have either upper airway or pulmonary involvement and simultaneous involvement of both may also be seen. They may present with nonspecific or systemic complaints of fever, anorexia, weight loss, and malaise.<sup>13</sup>

Nasal and sinus disease are the most common presenting symptoms and signs of GPA. It includes- nasal crusting, sinus pain, chronic rhinosinusitis, nasal obstruction, olfactory disturbances, purulent or bloody nasal discharge, excessive tearing (epiphora) and formation of sinus mucocele (benign, epithelium-lined cysts filled with mucus). Nasal congestion and purulent nasal discharge fails to resolve with appropriate antibiotic therapy. There may be perforation of nasal septum, saddle nose deformity, serous otitis, and hearing loss.<sup>14,15</sup> Adjacent structures such as orbital pseudo tumor with proptosis and vision impairment, oral ulcers may also get affected.<sup>16</sup>

## Laboratory findings

For patients with nasal ulcerations or a saddle nose deformity, cocaine addiction should also be considered.

Hematologic abnormalities in GPA includes a leukocytosis, thrombocytosis (>400,000/mm<sup>3</sup>), and elevation of the erythrocyte sedimentation rate.<sup>17</sup> The plasma creatinine and urinalysis are normal in sinonasal GPA.

Generally, in patients with sinonasal GPA involvement have normal ANCAs levels in the serum.

## Imaging

### Sinus computed tomography

Multi planar sinus CT scan is the preferred imaging modality for evaluating chronic rhinosinusitis and suspected rhino sinus involvement by WG.<sup>18,19</sup> Common findings on sinus CT are mucosal thickening in the nasal cavity and paranasal sinuses, bony destruction of the nasal cavity and paranasal sinuses, and bony thickening of the paranasal sinuses.

## Nasal or sinus biopsy

Nasal and sinus biopsies are performed for evaluation and treatment of nasal obstruction due to soft tissue masses and chronic sinusitis.<sup>14,20</sup> Special stains and culture should also be sent for ruling out infections as fungal, mycobacterial. Histopathological infection should also be done.

**Table 1** Summarizes various investigations that should be done to evaluate sinonasal GPA

Investigations of Patients with Sinonasal GPA	
Blood Investigations, Liver Function Tests	C & PANCA, Complete Blood Count, Creatinine, Viral Markers
Urine Tests	Urine Routine, Urine Phase Contrast
Otoscopy	Serous Otitis/ Granulation Tissue In Middle Ear
Anterior Rhinoscopy/ Nasal Endoscopy, Tissue/ Sinusopathy	Nasal Crusts/Septal Perforation/ Granulomatous
Exploration of Oral Cavity/ Oropharynx	“Strawberry” Gingivitis, Deep Ulcers
Laryngotracheal Exploration	Subglottic/ Tracheal Stenosis
Radiography of Sinuses	Sinusopathy
Tone Audiometry	Conductive/ Mixed/ Sensorineural Hypoacusis
Biopsy of Sinonasal/ Ear/ Subglottic, Granulomatous Tissue	In Non-Confirmed GPA Cases

CT: computed tomography, MRI: magnetic resonance imaging

## Differential diagnosis of destructive lesions of sinonasal tracts

- I. Trauma: Accidental or self-induced (Rhinotillomania)
- II. Infection
  - i. Bacterial: mycobacteria, syphilis, leprosy, actinomycosis.
  - ii. Fungal: aspergillosis, rhino mucormycosis.
- III. Toxic substance: Cocaine abuse,<sup>21</sup> Chromium salts.
- IV. Inflammatory: Sarcoidosis, foreign-body granuloma, Wegener’s granulomatosis, polyarteritis nodosa.
- V. Neoplastic: Basal cell carcinoma, squamous cell carcinoma, rhabdomyosarcoma, lymphoma.

## Treatment

In general, limited or sinonasal manifestations of patients with GPA usually respond well to immunosuppressive therapy (methotrexate or cyclophosphamide) along with tapering glucocorticoids. Maintenance therapy with methotrexate and azathioprine is useful. Frequent boluses of glucocorticoids to control reactivations can be used when required. Refractory disease may be treated with rituximab -anti CD20 monoclonal antibody.<sup>22</sup>

Surgical treatment does not change the course of the disease. It can ameliorate the consequences of tissue destruction in the head and neck region. Surgery should be done when the disease is under remission.

## Conclusion

Patients with GPA often present sinonasal manifestations. It is important to perform a systematic and ENT exploration of patients with suspected or confirmed diagnosis of GPA in order to contribute to an early diagnosis of these manifestations so as to prevent secondary complications which would worsen the quality of life of these patients.

## Acknowledgments

None.

## Conflicts of interest

None.

Patients with limited or sinonasal GPA, would not fulfill the American college of Rheumatology criteria 1990 classification criteria for GPA. So a high suspicion and regular follow up should be done to look for other organ involvement (Table 1).

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