Three Cases of Wegener's Granulomatosis: ENT Perspectives and Findings

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Abstract: This article examines three cases of Wegener's Granulomatosis, now referred to as Granulomatosis with Polyangiitis (GPA), with a particular emphasis on ENT (ear, nose, and throat) manifestations and clinical observations. GPA is a rare form of Vasculitis that frequently affects the Upper respiratory tract, making early ENT evaluation vital for accurate diagnosis and treatment. The cases presented here illustrate a range of ENT symptoms, such as Chronic sinusitis, Nasal obstruction, and Epistaxis, which played a key role in the initial diagnosis. The detailed clinical assessments and imaging findings shed light on the disease's progression and the difficulties in distinguishing it from other ENT conditions. This article underscores the essential role of the ENT department in the early detection of systemic diseases, emphasizing the importance of maintaining a high index of suspicion for systemic conditions during ENT evaluations. The case reports highlight the necessity for prompt and comprehensive investigations to ensure accurate diagnosis and timely intervention.

Keywords: Wegener's Granulomatosis, Granulomatosis with Polyangiitis, ENT, Vasculitis, Chronic Sinusitis, Nasal Obstruction, Epistaxis, Upper Respiratory Tract

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Introduction:

Wegener's granulomatosis now named as Granulomatosis with Polyangiitis[1] is a rare systemic disorder of unknown origin, marked by necrotizing granulomatous inflammation affecting both the upper and lower respiratory tracts, along with vasculitis of medium and small arteries, and is often associated with focal or proliferative glomerulonephritis. [2]
Vascular wall inflammation and necrosis are common across primary vasculitic disorders. The defining pathological feature of this condition is the simultaneous presence of vasculitis and granulomas. It typically presents as a triad involving the airway, lungs, and kidneys. [3]
Three diseases of the group causing small-vessel vasculitides, Wegener's granulomatosis, microscopic polyangiitis, and Churg-Strauss syndrome are often linked with antineutrophil cytoplasmic antibodies (ANCA)[4]. These conditions share a common pathological feature of focal necrotizing lesions that impact various vessels and organs. [5]

The present paper presents three case reports of patients who initially presented to the ENT (Ear Nose and Throat) outpatient department and were subsequently diagnosed with Wegener's granulomatosis. It highlights the critical role of the ENT department in the early identification of systemic diseases and underscores the need for a low threshold for diagnosis. The cases demonstrate the importance of considering systemic conditions in ENT evaluations and the necessity for prompt and thorough investigation to ensure accurate diagnosis and timely intervention.

Review of Literature

Vasculitic disorders exhibit a shared pathology characterized by focal necrotizing lesions that can affect various vessels and organs. In the lungs,

this may manifest as capillaritis leading to alveolar hemorrhage; in the kidneys, as crescentic glomerulonephritis causing acute renal failure; and in the skin, as a purpuric rash or vasculitic ulceration. [6]

The 1990 ACR criteria for classifying Wegener's granulomatosis require the presence of at least two of the following four criteria: nasal or oral inflammation (painful or painless ulcers or purulent/bloody discharge), abnormal chest X-ray findings (nodules, fixed infiltrates, or cavities), urinary sediment abnormalities (microhematuria or red cell casts), and granulomatous inflammation on biopsy (granulomas in or around arteries). Meeting two or more of these criteria provides an 88.2% sensitivity and 92.0% specificity for diagnosing the disease.[7]

Wegener's granulomatosis predominantly affects middle-aged individuals and shows no gender preference, being equally prevalent in both males and females. It is a chronic, multisystem autoimmune disease with an unpredictable course, even under immunosuppressive therapy. Most patients initially seek care in Oto-rhino-laryngology clinics, with 95% presenting with symptoms in the head and neck region. [8] Sinonasal involvement is the most common manifestation, occurring in approximately 85% of cases. [9]

Wegener's granulomatosis (WG) is traditionally identified by its impact on three major organ systems: the upper respiratory tract, lungs, and kidneys. The ELK classification system categorizes WG into three types: "E" for ear, nose, and throat involvement; "L" for lung involvement; and "K" for kidney involvement. WG localized to the upper aerodigestive tract (WG-E) is more common in men, though laryngeal involvement is more frequent in women. The sino-nasal tract is most commonly affected, with symptoms including sinusitis, rhinorrhea, nasal obstruction, pain, epistaxis, and headaches. [10]

The disease has varied presentation. Wegener's granulomatosis (WG) presents in three clinical types: [9,11]

Type 1 (Limited Disease): Primarily affects the upper airway with symptoms such as nasal pain, serosanguineous rhinorrhea, and crusting. Systemic involvement is minimal, and symptoms resemble an unresponsive upper respiratory tract infection.

Type 2 (Moderate Disease): Features more pronounced systemic symptoms, including persistent nasal discharge, pain, tenderness, and ulceration. Pulmonary involvement is common, with cough, hemoptysis, and cavitary lesions on chest radiography.

Type 3 (Disseminated Disease): Involves widespread systemic disease, affecting both upper and lower airways, skin, and progressing renal involvement. Symptoms are more severe, with nasal ulcerations and extensive systemic effects.

Wegener's granulomatosis (WG) can present with a variety of symptoms depending on the affected system. Common symptoms include persistent fever, fatigue, chest pain, and hematuria. The disease often first manifests through head and neck symptoms, such as nasal bleeding, obstruction, and loss of smell, occurring in 80-95% of cases. These early signs may be localized to the respiratory tract, with advanced stages leading to more severe systemic issues. Differential diagnoses for sino-nasal symptoms include granulomatous conditions like Tuberculosis and Leprosy. [12]

Symptomatic Presentation in ENT outpatient department of Wegener's granulomatosis (WG) can be both acute and chronic symptoms. Acute symptoms often include nasal bleeding, crusting, and disturbances in smell.

Chronic manifestations can lead to conditions like chronic rhinosinusitis, septal perforation, and nasal deformities. The nasal cavity and paranasal sinuses are frequently affected, with symptoms ranging from obstruction and discharge to severe structural damage. [13,14]

Pathology

Wegener's granulomatosis (WG) is marked by focal necrotizing lesions affecting various organs and vessels. It presents with ulcerative and crusted lesions with tissue destruction. [15]

Histopathology

The key histopathological features of Wegener's granulomatosis (WG) include vasculitis, granulomas (which may or may not exhibit fibrinoid necrosis), and multinucleated giant cells. For diagnosis, Sørensen and colleagues have proposed criteria based on the Chapel Hill Consensus Conference (CHCC) definitions.[16] These criteria for WG include: Granulomatous inflammation confirmed by biopsy or surrogate markers in the respiratory system, necrotizing vasculitis verified through biopsy or positive PR3-ANCA, and absence of eosinophilia in blood and biopsy samples. The features commonly affect small to medium-sized blood vessels. [15,16]

Diagnosis [2,5,8,13,14]

The diagnosis of Wegener's granulomatosis (WG) is primarily clinical, relying on findings suggestive of vasculitis and granulomatous inflammation. However, histological confirmation should be pursued whenever possible. If a biopsy from the head and neck region is inconclusive, other organs with active disease, such as the kidneys, lungs,

or skin, should be considered for biopsy. A comprehensive examination of various organ systems is essential for detecting and assessing disease manifestations.

An interdisciplinary approach, involving rheumatologists, neurologists, radiologists, ophthalmologists, and otorhinolaryngologists, has proven to be the most effective method for diagnosis and management.

Laboratory findings typically show signs of acute-phase reaction, raised c-ANCA, and imaging (CT, MRI) is used to assess involvement of the nasal cavity, paranasal sinuses, and lungs. [17,18]

Case Reports

Case Report 1-

A thirty-year-old female attended ENT Outpatient department with history of treatment at some other hospital. Previously she had complaints of Fever, difficulty breathing, cough with expectoration, weakness, nasal blockage, blocked sensation in ears, tinnitus, ear discharge, decreased hearing, and bilateral facial weakness.

Initially Treatment started was for ear discharge and facial weakness. When the disease progressed, she developed painful diffuse swelling in bilateral parotid and submandibular regions, painful ulcers in bilateral retromolar trigone.
Biopsy were taken which showed Chronic granulomatous disease with no malignancy. Differential diagnosis included Tuberculosis, sarcoidosis, and Wegener's granulomatosis.

Then she presented to us with a wide range of symptoms affecting multiple organ systems.
On Examination she was Conscious, oriented, pale, febrile.

On ENT examination - Necrotic tissue with granulation was seen in both external auditory canals. Right tympanic membrane intact but congested; left tympanic membrane with central perforation. Facial weakness was noticed bilaterally: Right side grade IV, Left side grade II.

On Audiologic assessment- Bilateral profound mixed hearing loss was noticed.
On Nasal endoscopy- Slough-covered necrotic tissue was seen on septum and turbinate with granulation and septal perforation.
Oral Examination- Painful ulcers were seen in both side Retromolar trigone.
Neck on palpation found to have Diffuse, tender enlargement of bilateral parotid and submandibular glands. No other palpable lymphadenopathy was noted.

On Systemic Examination:
Patient on examination found to have Tachypnea, diminished chest movement, crackles, and wheezes.
On per Abdomen examination she was found to have Hepatomegaly 2 cm below the right costal margin, splenomegaly 1.5 cm below the left costal margin.
On Ophthalmologic Examination- There was Normal fundus and vision, but bilateral episcleritis were noted.

On Radiology Findings noted are-
X-ray Chest: Right upper and left lower zone haziness.

HRCT Chest: Multifocal patchy nodular consolidations with ground-glass opacities in bilateral lung fields.
USG Abdomen: Mild hepatosplenomegaly.
CT Scan PNS: Mucosal thickening in left maxillary and bilateral post-ethmoid sinuses, erosion of anterior nasal septum, hypertrophy of bilateral inferior turbinates.

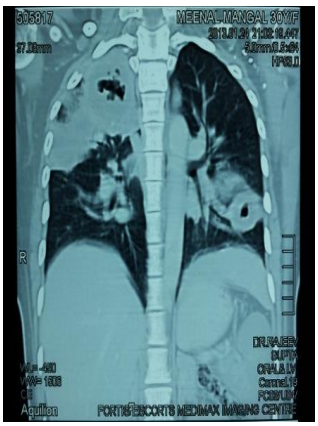

Figure 1: **HRCT Chest** showing multi-focal nodular consolidation

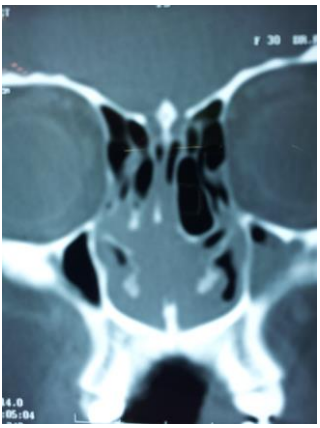

Figure 2: **Coronal Section CT Nose with PNS** Mucosal thickening with Septal erosion

Laboratory Investigations following findings were noted-
Sputum AFB: Not detected.
Urine Analysis: High protein levels, elevated urine protein (24 hrs).
ANA: Negative.
C-ANCA: Strongly positive.
ACE: Normal (38).
RF: Negative.
CRP: >96 mg/L (raised).
ESR: 125 (raised).
LFT: Raised.

Gamma Interferon: Not detected.

Histopathology of Nasal Biopsy showed Necrotizing granulomatous inflammation suggestive of Wegener's granulomatosis.

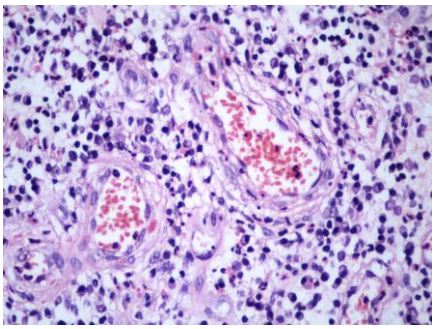

Figure 3: Histopathologic image (magnification 10x) Hematoxylin and eosin (H&E) stain

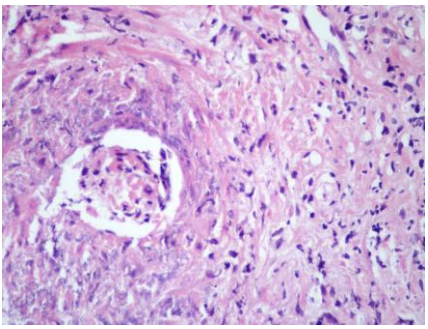

Figure 4: Histopathologic image (magnification 10x) Hematoxylin and eosin (H&E) stain

(Section shows mixed inflammatory infiltrate in the fibro collagenous stroma comprising of lymphocytes, plasma cells and polymorphs. There is involvement of small to medium size vessels with presence of fibrinoid necrosis. The blood vessels are congested with fibrosis in the wall. Morphologic findings favours clinical diagnosis of vasculitis)

Case Report 2-

A 28-year-old female attended ENT OPD with Initial Complaints of Intermittent nasal bleeding, pain over the nose, excessive watering from the left eye for 6 months.

On Examination Findings are-

Nose: Dorsum of nose depressed.

Nasal Endoscopy: Large septal perforation with florid granulation tissue.

Other Systemic Examination- Unremarkable.

Investigations
CT Scan PNS: Septal Perforation with ethmoid sinusitis.

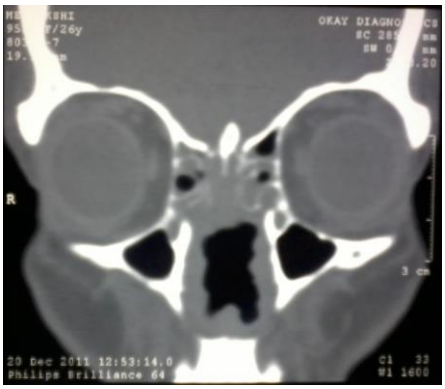

Figure 5: Coronal Section CT Nose with PNS showing Septal Perforation with Ethmoid Sinusitis

X-ray Chest PA View**:** Normal.
C-ANCA: Weakly positive.
ESR**:** 50 (elevated).
Urine Routine and Microscopy: Normal.
Nasal Biopsy HPE: Results showing features consistent with granulomatous inflammation.

Case Report 3 –
A 45 years old male presented with Complaints of Bilateral submandibular and parotid swelling for 2 months.

On Examination Findings
Nose: Crusts on the right side.

Nasal Endoscopy Crusts on the right inferior turbinate.

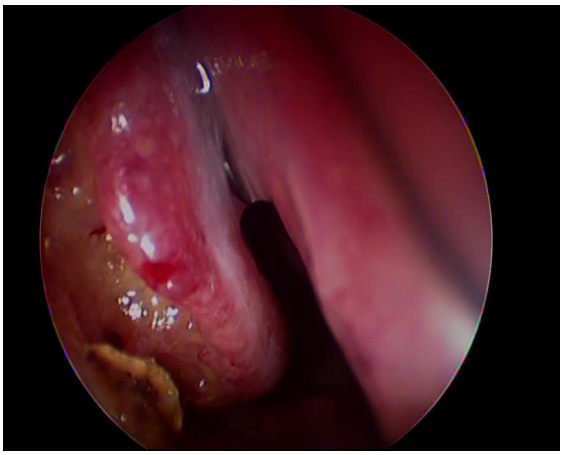

Figure 6: Nasal Endoscopy with Zero degree Nasal endoscope showing Crusts on Right Inferior Turbinate

On Investigations
HRCT Lung: Normal.
C-ANCA: Weakly positive.
Urine Routine and Microscopy: Presence of RBC casts.
Biopsy
Nasal Biopsy HPE: Results likely showing features consistent with granulomatous inflammation.

Summary of Cases

Case 1: Diagnosed with Wegener's Granulomatosis based on clinical presentation, strongly positive c-ANCA, nasal biopsy showing necrotizing granulomatous inflammation, and multifocal lung lesions.

Case 2: Presents with classic nasal symptoms and a large septal perforation. Weakly positive c-ANCA and elevated ESR suggest Wegener's Granulomatosis, though biopsy results and further diagnostic confirmation are needed.
Case 3: Features suggestive of Wegener's Granulomatosis with bilateral salivary gland swelling, nasal crusting, weakly positive C-ANCA, and RBC casts in urine. HRCT lung normal, indicating possible limited or localized disease.
These cases highlight the variability in clinical presentations and the importance of combining clinical, serological, and histopathological findings for accurate diagnosis.

Wegener's granulomatosis, confirmed by clinical presentation, strongly positive c-ANCA, HRCT findings, and histopathology. Treatment was started with Oral Prednisolone (1 mg/kg body weight) and Oral Cyclophosphamide (2 mg/kg body weight)
Follow-Up and Regular monitoring of disease activity, response to treatment, and management of complications.
To conclude a continuous low threshold of suspicion should be there to establish the diagnosis at the earliest opportunity.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.