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Ear, nose, and throat involvement in eosinophilic granulomatosis with polyangiitis

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Eosinophilic granulomatosis with polyangiitis (EGPA) is the rarest of the anti-neutrophil cytoplasm antibody (ANCA)-associated small-vessel vasculitides. In Europe, its prevalence ranges from 10 to 15/million and annual incidence from 0.9 to 1.2/million. EGPA affects men and woman equally, with a mean age of 50 years at diagnosis. The most characteristic features include late-onset asthma, pulmonary infiltrates, mono- or polyneuropathy, and peripheral and extravascular eosinophils. Ear, nose, and throat (ENT) manifestations are particularly frequent, occurring in 30–80% of patients and most often early in the disease process. ENT features include allergic rhinitis, chronic sinusitis and polyposis, lacrimal and salivary gland involvement, otitis media and, rarely, cranial nerve involvement. The diagnosis of EGPA may be relatively straightforward in the 30–40% of ANCA-positive patients and in those with biopsies demonstrating vasculitis, but it can be more challenging, or even debatable, in ANCA-negative patients who do not present clear evidence of vasculitis. Because EGPA is a multisystem disease, it requires a multidisciplinary approach for diagnosis and management, including by an otolaryngologist.

Keywords: *vasculitis*; *eosinophilic granulomatosis with polyangiitis*; *Churg-Strauss syndrome*; *hypereosinophilia*; *ANCA*

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Eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg–Strauss syndrome, is the rarest of the three anti-neutrophil cytoplasm antibody (ANCA)-associated small-sized vessel vasculitides (1, 2). In Europe, its prevalence ranges from 10 to 15/million and annual incidence from 0.9 to 1.2/million (3–5). The mean age at diagnosis is 50 years, with no sex preponderance. The etiology of EGPA remains poorly understood, although various triggers for disease flares have been suggested, including exposure to inhaled allergens. The hallmarks of the disease, which distinguish it from the other two ANCA-associated vasculitides (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA]), include eosinophilia and asthma and a lower ANCA-positivity rate, only 30–40% of cases, usually of the anti-myeloperoxidase specificity (MPO-ANCA).

Ear, nose, and throat (ENT) manifestations are extremely frequent in EGPA. They are most often present in the early phase of the disease and usually appear years before the development of the other features, with frequencies ranging from 30 to 80% (6–13). Thus, the otolaryngologist may play an important role in the early diagnosis and management of this rare condition. Here, we review these ENT manifestations, the diagnostic workup and markers of EGPA, and the treatment of EGPA and associated ENT involvement.

Clinical characteristics of EGPA

EGPA usually develops in three phases; each phase may be of variable duration and may overlap (6, 14, 15). The prodromal phase manifests as late-onset asthma with or without 'allergic' rhinitis, nasal polyposis, and rhinosinusitis. The eosinophilic phase is characterized by blood eosinophilia and eosinophilic infiltrates in various tissues and organs, most commonly the lungs. The final phase, which really defines EGPA, is the vasculitic phase, with more typical vasculitis manifestations, such as cutaneous purpura or, more rarely, pauci-immune glomerulonephritis. Peripheral nerve and cardiac involvements are also

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possible during this phase, but these can result from direct toxicity of the eosinophil granule contents rather than from ischemia due to vasculitis (of the vasa nervorum and the coronary arteries and their branches, respectively). In patients presenting in the vasculitic phase with ANCA positivity, the diagnosis can be easy. In patients presenting in the first phases or in the vasculitic phase without ANCA positivity, the diagnosis is more challenging. Therefore, detailed clinical, biological, and radiological assessment to search for other disease manifestations and rule out alternative diagnoses is crucial for promptly establishing the correct diagnosis.

The lungs are the most commonly involved organ system in EGPA. Asthma is present in virtually all patients (6–13, 16, 17). The characteristics of this asthma do not really differ from those of common allergic asthma, but it is most typically late-onset, in people in their 30s and 40s. The interval between the appearance of this late-onset asthma and the definitive vasculitic EGPA manifestations varies, with the average between 4 and 15 years (7, 18). Atopy may be less frequent in patients with EGPA than previously thought, with hypersensitivity to common allergens documented in one-third of patients (18, 19).

Pulmonary infiltrates that are transient and patchy in their distribution are present in 40–75% of patients (Fig. 1). Nodules are rare but possible. Pleural effusions are observed in less than one-third of patients. Examination of fluids from bronchoalveolar lavage or thoracocentesis in patients with pleural effusions can reveal inflammation with predominant eosinophils.

ENT manifestations are common in EGPA (30–80%) associated with lung symptoms or in isolation. 'Allergic' rhinitis has been reported in 15–75% of cases, occurring early, before, or at the onset of asthma in most cases. Chronic sinusitis has been reported in 60–80% of cases, sinusitis and polyposis in about 40%, and 'paranasal sinus involvement' in 75% (6–13, 16, 17, 20–22). Nasal polyps were frequent in some studies, in up to three-quarters of patients, and were usually present before diagnosis (12, 13). Polyps are often diffuse and bilateral (13). Crusting is rarer and more typically a hallmark of GPA, but it can occur in EGPA ($<15\%$), usually associated with polyposis. Epistaxis, anosmia, and hyposmia can also occur. Erosive disease (such as nasal septum perforation) is exceptional in EGPA and should first lead physicians to question the diagnosis. Computed Tomography (CT) of the sinuses can demonstrate thickening of the paranasal sinuses, obstruction and/or opacification of the sinuses, and polyposis (Fig. 2). Sinus and soft-tissue masses or polyps can cause an obstruction or mass effect on adjacent structures, such as the orbits; however, orbital pseudotumor is rarer in EGPA than GPA (23). Rhinitis and sinusitis may be more frequent in ANCA-positive than ANCA-negative patients (52 and 37% versus 25 and 11%), but this is not a reproducible finding across different studies (6–11, 20–22).

Otological manifestations of EGPA are rare and may include conductive, sensorineural, and mixed hearing loss (12, 24, 25). Conductive hearing loss may result from otitis media with effusion or obstruction resulting from eosinophilic granuloma (12, 24, 25). Otitis media with effusion is typically thick and mucoid in nature, and mastoid opacification is commonly seen on CT scan (12, 24, 25). Cochleitis and cochleovestibular-nerve eosinophilic neuropathy have been proposed as the etiology of sensorineural hearing loss (24). Vertigo and facial nerve palsies have also been reported (12, 26). Ear disease in EGPA tends to occur more in the eosinophilic and vasculitic phases and may occur out of sync with other systemic flares (12).

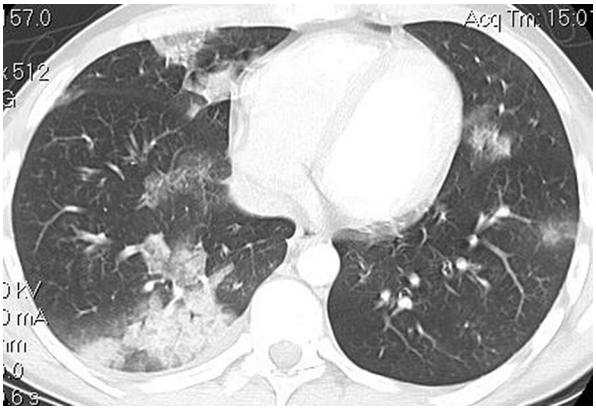

Fig. 1. Computed Tomography (CT) demonstrates lung abnormalities in this patient with EGPA with patchy consolidation areas, ground glass opacities and air bronchograms.

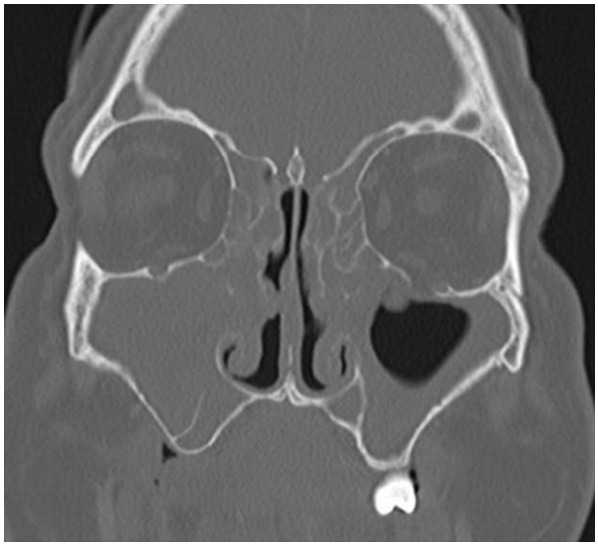

Fig. 2. Computed Tomography (CT) demonstrates paranasal sinus abnormalities in this patient with EGPA with opacification of the maxillary sinuses.

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Less common ENT or oral manifestations of EGPA include salivary gland involvement with a focal mass or enlargement of the salivary glands (27–29) and neurolaryngeal involvement (30), with dysphonia initially intermittent and then persistent. Parotid-, submandibular-, and sublingual-gland involvements are all reported. Salivary gland biopsy demonstrated vasculitis in one case and eosinophilic granulomas in the remaining two cases (27–29). In some of these patients, elevated serum IgG4 levels and infiltration of IgG4-positive plasmacytes in the nasal mucosa were observed, which suggests some common pathogenic mechanisms between IgG4-related disease and EGPA (31, 32).

Other manifestations of EGPA include peripheral-nervous-system involvement in 35–75% of patients, mainly mononeuritis multiplex; gastrointestinal involvement (5–60%), with abdominal pain, nausea, vomiting, diarrhea, bleeding and, rarely, bowel perforation; cardiac manifestations (10–50%), more common in ANCA-negative patients; and skin and joint involvements (0–70% and 15–50%, respectively). Cardiac manifestations include cardiomyopathy (with poor prognostic value), pericardial effusion, conduction disorders, and supraventricular arrhythmia. Myocardial infarctions are rare and can be clinically silent. Skin lesions are variable and include cutaneous nodules, livedo reticularis, purpura, urticarial rash, ulcerations, erythema multiform, scalp erythematous, macular lesions, nail fold-infarctions, digital ischemia, and panniculitis. Constitutional symptoms, including fever, chills, weight loss, or myalgias are also frequent at diagnosis.

Less common EGPA features include renal involvement (5–40%) manifesting as pauci-immune glomerulonephritis with an active urinary sediment; central nervous system (CNS) involvement (0–15%), which occurs most often late in disease; and ocular manifestations (33). Venous thrombosis and pulmonary embolism can occur in up to 8% of patients, especially during active phases of the diseases (34, 35).

Importantly, several studies showed that clinical manifestations differed between ANCA-positive and -negative patients with EGPA (7, 9, 10, 20–22). Constitutional symptoms and vasculitic features, such as renal involvement, palpable purpura, alveolar hemorrhage, and mononeuritis multiplex, and biopsies demonstrating vasculitis are more common for ANCA-positive than -negative patients. Conversely, cardiomyopathy and pericarditis, livedo and pulmonary infiltrates and biopsies demonstrating 'only' extravascular eosinophilic infiltrates are more common for ANCA-negative patients.

Diagnostic approach

There are no validated diagnostic criteria for EGPA. The 1990 American College of Rheumatology classification criteria are the most widely accepted criteria for classification (Table 1) (1). Although intended to be applied to patients with already documented vasculitis, they are often applied to patients with suspected EGPA without clear-cut vasculitic features or hypereosinophilic syndromes (HESs). As a result, many patients without definite EGPA may be classified as having EGPA according to these criteria. Conversely, many patients with EGPA in whom the absolute (histological) confirmation of vasculitis cannot be obtained may not be classified as such.

Unfortunately, we have no reliable biological diagnostic markers, although 30–40% of patients show ANCA positivity (7, 36). Therefore, the diagnosis of EGPA relies in practice on recognition of the clinical and biological features and the exclusion of all differential diagnoses. Whenever possible, the diagnosis of EGPA should be confirmed by biopsy of an involved tissue. The three hallmark histological features of EGPA include 1) predominantly eosinophilic infiltration of vessel walls with fibrinoid necrosis, 2) extravascular eosinophilic infiltrates, and 3) extravascular eosinophilic necrotizing granulomas (37). All three features are rarely identified on a single biopsy. Possible biopsy sites include skin, lung, muscle, and peripheral nerves, which all have high diagnostic yield (7). Other biopsy sites include endomyocardial areas, in the case of cardiomyopathy, and gastrointestinal tract, although such biopsies are considered invasive. In the presence of renal disease, patients have hematuria and proteinuria, and biopsy may demonstrate 'pauci-immune' glomerular nephritis. Biopsy of nasal mucosa, although relatively accessible, has low diagnostic value and sensitivity, with less than 10% demonstrating vasculitis or eosinophilic granuloma. Eosinophilic infiltrates, commonly seen in allergic polyposis, are not specific to EGPA. Deep biopsy of the sinus tissues, under general anesthesia, can improve the diagnostic yield, up to 50%, but is invasive (38).

Biologically, levels of inflammation markers such as erythrocyte sedimentation rate and C-reactive protein are almost always elevated during active phases of the disease but are non-specific. Hypereosinophilia is a hallmark of the disease and usually exceeds $>1{,}500/mm^3$. At diagnosis, the average is about $7{,}500/mm^3$ and can be up to $50{,}000/mm^3$. However, hypereosinophilia is not restricted to EGPA and is present in many other conditions, including HES, allergic bronchopulmonary aspergillosis (ABPA), and parasitic infections. IgE level is elevated but again non-specific (39). ANCAs, which highly support the diagnosis if present, are present only in 30–40% of EGPA patients, usually those with MPO-ANCA.

Other potential diagnostic biomarkers are being studied to help differentiate EGPA from these other causes of hypereosinophilia and, ideally, better assess disease activity. Some of these biomarkers may also be used as therapeutic targets in the future. Levels of T helper 2 cell

Table 1. Comparison of eosinophilic granulomatosis with polyangiitis (EGPA) with hypereosinophilic syndrome (HES): classification/definitions, main clinical features, biological findings and treatments

Diagnosis	Eosinophilic granulomatosis with polyangiitis	Primary/idiopathic hypereosinophilic syndrome (HES)
Classification criteria and definitions		
	1990 American College of Rheumatology – 4/6 of the following (1): 1) Asthma 2) Eosinophilia ≥10% 3) Mono- or poly-neuropathy 4) Pulmonary Infiltrates, non-fixed 5) Paranasal sinus abnormality 6) Extravascular eosinophils 2012 Chapel Hill nomenclature (2): Part of the ANCA-associated small-vessel vasculitis - Eosinophil-rich, necrotizing granulomatous inflammation often involving the respiratory tract - Necrotizing vasculitis predominantly affecting small to medium vessels - Associated with asthma and eosinophilia - ANCA more frequent when glomerulonephritis is present	2011 Consensus Definition – 3/3 of the following (49, 50): 1) Peripheral blood eosinophilia >1,500 cells/μl for ≥1 month 2) Evidence of eosinophil-mediated target organ damage 3) Exclusion of other causes
Clinical features		
ENT	'Allergic' rhinitis, **rhinosinusitis***, polyposis, salivary gland enlargement, **otitis media, cranial nerve palsy**	'Allergic' rhinitis, polyposis
Cardiac	Arrhythmia, pericarditis, myocardial ischemia and/or infarction, eosinophilic infiltration, endomyocardial fibrosis, LV dysfunction, intraventricular thrombosis	Eosinophilic myocarditis, endomyocardial fibrosis, LV dysfunction, **restrictive cardiomyopathy, valvular regurgitation, intraventricular thrombosis**
Pulmonary	**Asthma**, transient and patchy infiltrates, effusions, **pulmonary hemorrhage**, nodules (rare), pulmonary embolism, hilar lymphadenopathies	Asthma, pulmonary infiltrates, nodules, effusions, **pulmonaryembolism**, **hilar lymphadenopathies**
Gastrointestinal	Eosinophilic esophagitis, gastritis, colitis, colon ulcerations, **bowel perforation**	**Eosinophilic hepatitis, cholangitis**, esophagitis, gastritis, colitis, **pancreatitis**, **hepatosplenomegaly**
Renal	**Glomerulonephritis**	–
Eye	**Orbital pseudotumor**, **oculomotor nerve palsy, vision loss**	**Microemboli or thrombosis**
Neurological	**Mononeuritis multiplex**, peripheral sensory neuropathy, pachymeningitis	**Embolic/thrombotic strokes**, **encephalopathy**, peripheral sensory neuropathy, **dementia**, **eosinophilic meningitis**
Dermatologic	**Palpable purpura,** cutaneous nodules, urticarial rash, **livedo reticularis**, nail fold infarcts, erythema multiforme, **ulcerations**, **digital ischemia, panniculitis**	**Eczema, erythroderma,** urticaria**, angioedema, maculopapular nodules**
Other	Venous thrombosis, pulmonary embolism	Arterial thromboses > venous thromboses
Biology		
Eosinophil count	Elevated	Elevated
CRP/ESR	Elevated	Elevated
Ig-E	Elevated	Myeloid variant: normal (usually) Lymphoid variant: elevated
ANCA	**Positive in ~30–40% (mainly MPO-ANCA)**	Negative

Table 1 (*Continued*)

Diagnosis	Eosinophilic granulomatosis with polyangiitis	Primary/idiopathic hypereosinophilic syndrome (HES)
Other	***Eotaxin-3***	Myeloid variant: ***FIP1L1/PDGFRA/B, JAK2*, elevated serum levels of tryptase and/or vitamin B12** Lymphoid variant: **Clonal T-cell population**
Treatments		
Glucocorticoids	Responsive, but often glucorticoid-dependent	Often Refractory, partially or transiently responsive
Induction therapy	*FFS* = 0: First-line: glucocorticoids alone. Second line: glucocorticoids + methotrexate, azathioprine, or mycophenolate. *FFS* ≥ 1: First line: glucocorticoids + cyclophosphamide	*No organ threatening disease*: simple monitoring? *Organ threatening disease:* - Myeloid Variant: 1st line: glucocorticoids ± hydroxyurea, interferon-alpha, tyrosine kinase inhibitor (imatinib) - Lymphoid Variant: 1st line: glucocorticoids ± interferon-alpha 2nd line: chemotherapeutic agents
Alternative therapies/ under investigation	Rituximab, omalizumab, mepolizumab, interferon-alpha	Mepolizumab, reslizumab, alemtuzumab

In bold are features that are more characteristic, albeit not totally, of EGPA, especially in ANCA-positive patients, or HES, depending on the column.
FFS, Five Factor Score; LV, left ventricle; PDGFRA, platelet derived growth factor receptor A; PDGFRB, platelet derived growth factor receptor B.

cytokines such as interleukin 4 (IL-4), IL-5 and eotaxin-3, IL-25, vascular endothelial growth factor, and tumor necrosis factor-related apoptosis-inducing ligand receptor 3 are increased in EGPA (40–46). However, none has emerged as entirely specific or sensitive enough. A combination of some of these markers may be of interest.

Differential diagnosis

The differential diagnosis for EGPA is broad and includes reactive causes such as parasitic infections, drug reaction, and allergy but also idiopathic HES, neoplastic HES (lymphoid and myeloid variants, and eosinophilic leukemia), and eosinophilic lung diseases such as eosinophilic pneumonia and ABPA (6, 47, 48).

HES is likely the most difficult mimicker of EGPA to rule out. HES can present cardiac, pulmonary, gastrointestinal, central and peripheral neurological, and dermatologic manifestations similar to EGPA (Table 1) (49, 50). However, mononeuritis multiplex, ENT manifestations, and necrotic purpura are less common in HES than EGPA. Conversely, a more frequent feature of HES is arterial and venous thrombotic disease, including cardiac thrombosis, embolic or thrombotic cerebral vascular accidents, pulmonary embolism, Budd–Chiari syndrome, and digital gangrene (51). However, all these thrombotic events have also been reported in EGPA (34, 52–54). Biopsy of an affected organ or bone marrow may show eosinophilic infiltrates, like in EGPA, but vasculitis features are absent. In some cases, only the patient's follow-up and response to treatments will help with the final diagnosis. The 2008 World Health Organization definition emphasizes the need to exclude reactive causes and classifies HES into different subsets, including myeloproliferative neoplasms associated with different genetic changes (*FIP1L1-PDGFRA* or *ETV6-PDGFRB* gene fusions, or other rearrangements of *PDGFRB* gene), myeloproliferative neoplasm or acute leukemia associated with *FGFR1* rearrangement, chronic eosinophilic leukemia not otherwise specified, and finally, idiopathic HES (50, 55, 56). In addition to the search for these gene fusion rearrangements, the detection of a circulating T-cell clone, a clonal *TCR*-gene rearrangement, or both, can favor the diagnosis of (a lymphocytic variant of) HES, although they can also be detected, transiently, in patients with active EGPA (57, 58).

Treatment and prognosis

Overall, the mortality of EGPA patients is now estimated at 10–15% at 5 years (7, 11, 59, 60). The original 1996 Five Factor Score (FFS) indicated that the presence of cardiac, CNS, or gastrointestinal involvement, peak creatinine ≥ 140 µmol/L, and/or proteinuria > 1 g/24 hour as the five most important predictors of poor outcome (death) in EGPA as well as in MPA and polyarteritis nodosa (61). From these findings, it has been proposed that patients

with a FFS = 0 could initially receive prednisone alone, whereas those with any of these poor-prognosis factors should receive a combination of glucocorticoids and another immunosuppressant, mainly cyclophosphamide.

The revised FFS is the updated version of this tool for predicting patient survival and remains applicable to patients with EGPA, MPA, or polyarteritis nodosa but also now with GPA (59). It includes age >65 years at diagnosis, presence of cardiac symptoms, gastrointestinal involvement, stabilized peak creatinine ≥150 μmol/L, and the absence of ENT involvement (for EGPA and GPA only). Risk of mortality increases with each of these five items. Hence, the presence of ENT manifestations in patients with EGPA constitutes a marker of good prognosis (better survival). Importantly, as compared with the original FFS, the revised FFS is not validated and therefore must not be used to guide treatment decisions.

Several studies suggest that relapse rate is increased but mortality rate reduced for EGPA patients with MPO-ANCA positivity (60, 62). Patients with eosinophilia <3,000/mm^3 may also have increased risk of relapse (7, 60, 62). Mononeuritis multiplex could also be a predictor of treatment response; in a recent study, 45% of patients with FFS = 0 but mononeuritis multiplex ultimately required an immunosuppressant in addition to glucocorticoids (62). Finally, most EGPA patients continue to have asthma; greater than 75% require prolonged use (years) of anti-asthma medications, including puffers, and, frequently, low-dose glucocorticoids (7).

Systemic treatments

Glucocorticoids play a key role in inducing remission of EGPA, along with the common treatment against asthma (i.e., inhaled bronchodilators and glucocorticoids). Prednisone should be initiated at high doses depending on the disease severity (i.e., at 0.5–1 mg/kg/day, with a maximum daily dose of 60–80 mg), followed, after 2–4 weeks, if the disease is under control, by a gradual tapering over a minimum of 6 months. As mentioned above, patients with a FFS ≥1 require an additional immunosuppressant (59–63). Cyclophosphamide is generally used in such cases to induce remission (orally at 2 mg/kg/day or intravenously at 15 mg/kg every 2 weeks for the first 3 doses, then every 3 weeks, with dose adjustment according to the patient's age and renal function), switched 3–6 months later to azathioprine (2 mg/kg/day) or methotrexate (0.3 mg/kg/week) for maintenance therapy for 1–2 years at least. In patients with an initial FFS = 0 but whose disease does not respond to glucocorticoids alone or relapses, azathioprine or methotrexate can be considered as glucocorticoid-sparing agents, in cases of no major organ involvement that would indicate the use of cyclophosphamide. The optimal regimens and duration of the maintenance therapy for EGPA are unknown and remain based on studies of GPA or MPA.

Rituximab is an anti-CD20 antibody that works mainly via depletion of B cells, although other mechanisms are also involved. The drug is not inferior to cyclophosphamide for inducing remission of both GPA and MPA, and several retrospective case reports and series suggest a possible place for rituximab in the treatment of EGPA, at least for patients with refractory or relapsing disease (64–68). Prospective controlled studies are needed to further determine its role for EGPA.

Omalizumab is a monoclonal antibody for IgE that has been beneficial for treating severe allergic asthma (69–73). Exploratory data suggest that it may also be effective for EGPA, but several cases of EGPA developing under omalizumab treatment have also been reported. Although concerning, similar cases have been described with leukotriene inhibitors, such as montelukast (74–76). These latter drugs can indeed lead to reduced glucocorticoid anti-asthma therapy, which can unmask EGPA manifestations previously controlled with the glucocorticoids. Omalizumab has been investigated in patients with chronic rhinosinusitis with nasal polyposis (1–3, 77–79). Gevaert et al. demonstrated reduced endoscopic and radiographic nasal-polyp findings and improved health-related quality of life as measured by the Medical Outcomes Study Short Form 36 in patients with chronic rhinosinusitis with polyposis and asthma (77). However, these reports had small sample sizes and did not specifically investigate patients with EGPA.

Mepolizumab is an anti-IL-5 antibody currently under study for refractory or glucocorticoid-dependent EGPA (MIRRA trial; ClinicalTrials.gov Identifier: NCT00527 566), after promising results in a two open-label studies (80–82). It has been found efficacious for conditions such as hypereosinophilic asthma and HES (83–86).

Despite a frequent atopic background, desensitizations are not recommended for EGPA because they can trigger severe EGPA flares (63).

Local treatments for ENT manifestations

Management of ENT manifestations in EGPA can be challenging (12, 13, 38). For patients with chronic sinusitis, multiple daily nasal rinses with normal saline may provide some symptomatic benefit but are unlikely to provide lasting relief. Nasal sprays of mometasone furoate monohydrate can also provide transient relief in patients with 'allergic' rhinitis but are unlikely to be sufficient in patients with more severe disease.

Functional endoscopic sinus surgery is the mainstay of therapy for common nasal polyposis, but its role in treating EGPA with polyposis is less definitive. Surgical removal of nasal polyps can provide transient symptomatic relief and may facilitate the application of nasal saline rinses and topical steroids. However, in a case series by Bacciu et al., patients who underwent polypectomy before diagnosis of EGPA experienced early recurrence

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of polyps (13). In this reports, these patients responded to systemic immunosuppression.

Local treatments for the rare otologic manifestations of EGPA do not differ from those used in other more common contexts. Antibiotics are indicated for secondary infections. Placement of pressure equalization tubes may temporarily relieve conductive hearing loss secondary to otitis media with effusion. However, tube placement can be associated with thick mucoid discharge, which may be troublesome to patients and warrants pre-operative counseling (25). The chronic nature of ear disease in EGPA and temporal bone findings on radiography may lead to surgical management with cortical mastoidectomy. In the absence of infectious complications involving surrounding structures (temporal bone or intracranial), surgery is not recommended.

Salivary gland involvement may persist after the initiation of medical management. However, with time, salivary gland swelling appears to improve (25, 27–29).

Conclusions

EGPA is a rare form of ANCA-associated vasculitis characterized by eosinophil-rich granulomatous inflammation with preponderance in airways. Besides classical late-onset asthma, ENT manifestations are extremely common. Diagnosis and management often require a multidisciplinary team, with the otolaryngologist as an important player. Diagnosis involves recognition of clinical manifestations and, ideally, biopsy. However, the utility of ENT biopsy is limited by low diagnostic yield. Prognosis is variable and depends on clinical manifestations and the prompt diagnosis and initiation of adequate treatments. Importantly, the presence of ENT involvement generally suggests a better survival rate. Local treatment of ENT manifestations remains useful but has limited and transient benefits. Therefore, systemic therapy is always required and includes glucocorticoids with or without additional immunosuppressants, depending on the disease severity and initial response to first-line treatments. Several studies found it promising to include rituximab and mepolizumab, which are both under further investigation.

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