ORIGINAL ARTICLE

Otolaryngological Manifestations of Wegener’s Disease

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KEYWORDS
Otolaryngology; Wegener’s granulomatosis; Rheumatology

Abstract
Introduction: Wegener’s granulomatosis (WG) is characterised by granulomatous vasculitis of the airway and glomerulonephritis. Since its first description, important advances have occurred in diagnosis and treatment; however, the aetiology remains unknown. Involvement of the head and neck region can often occur as the first and only manifestation. The aim of this study was to determine the frequency of symptoms and signs in the region of the nose, ears and pharynx-larynx in a group of patients with WG.

Materials and methods: We evaluated 17 patients with WG defined by clinical, laboratory and pathology criteria. Detailed histories were taken and an ENT physical examination, audiometry, tympanometry and nasofibrolaryngoscopy were performed in all the patients.

Results: The average age was 41.7 years and the average disease time was 9.12 years, ranging between 1 and 40. In these patients, 9 (53.1%) reported hearing loss and had altered audiometry, and 5 (55.6%) had bilateral sensorineural hearing loss. In the nose, nasal obstruction in 11 (64.8%) and rhinorrhea in 10 (58.8%) were the most prevalent; there was altered endoscopy in 12 (70.2%). In the pharynx-larynx, dyspnoea in 6 (35%) and hoarseness in 7 (41.2%) were the most prevalent and 7 (41%) had an altered laryngoscopy.

Conclusion: The otolaryngologist plays an essential role in diagnosis, treatment and follow-up of these patients. Knowing common symptoms renders diagnosis and treatment easier and earlier.

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PALABRAS CLAVE
Otorrinolaringología; Granulomatosis de Wegener; Reumatología

Manifestaciones otorrinolaringológicas de la granulomatosis de Wegener

Resumen
Introducción: La granulomatosis de Wegener (GW) se caracteriza por una vasculitis granulomatosa de vías aéreas y glomerulonefritis. Desde su primera descripción han surgido importantes avances para su diagnóstico y tratamiento, sin embargo su etiología aún es desconocida. La...
afectación de la región de cabeza y cuello muchas veces puede ocurrir como su primera y única manifestación. El objetivo del estudio es determinar la frecuencia de los síntomas y signos en la región de nariz, oídos y faringe-laringe en un grupo de pacientes con GW.

**Materiales y métodos:** Se evaluaron 17 pacientes con diagnóstico de GW definido por criterios clínicos, de laboratorios y anatomicopatológico. Fueron realizadas anamnesis detallada, un examen físico otorrinolaringológico minucioso, audiometría, impedanciometría y nasofibrolaringoscopia en todos los pacientes estudiados.

**Resultados:** La edad media de los pacientes al diagnóstico fue de 41.7 años, y el tiempo promedio con la enfermedad fue de 9.12 años, variando entre uno y 40 años. De los pacientes estudiados, 9 (53,1%) tenían hipoadacusia y presentaron audiometría alterada, y 5 (55,6%) presentaron hipoadacusia neurosensorial bilateral. A nivel nasal, los síntomas más frecuentes fueron obstrucción en 11 (64,8%) y rinorrea en 10 (58,8%), con endoscopia alterada en 12 (70,2%). A nivel faringo-laringeo, la disnea en 6 (35,2%) y la carraspera en 7 (41,2%), con laringoscopia alterada en 7 (41,2%).

**Conclusión:** El otorrinolaringólogo desempeña un papel esencial para el diagnóstico, seguimiento y tratamiento de estos pacientes. Conocer sus síntomas más comunes facilita su diagnóstico y tratamiento precoz.

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**Introduction**

Wegener’s granulomatosis (WG) is a clinical-pathological syndrome characterised by granulomatous vasculitis of the upper and lower airways and glomerulonephritis, although it can affect virtually any organ. The disease was first described by Heinz Klinger in 1931 and was later reported in greater detail by Friedrich Wegener in 1936 and 1939.

In 1985, significant progress was made for its diagnosis with the discovery of an autoantibody, the antibody against neutrophil cytoplasm, whose presence is correlated with the activity of the disease. The incidence of WG is estimated at about one to three cases per million population. The disease can appear at any age, although the mean age at diagnosis is between 20 and 40 years. It affects both genders in equal proportions and is predominant among white patients, being virtually unknown in other ethnicities. Its aetiology is unknown, although some medications, infections, toxins and genetic factors have been implicated. Infectious agents have been frequently associated as trigger factors in cases of vasculitis. The presence of *Staphylococcus aureus* (*S. aureus*) in the nasal mucosa of some patients with WG has been documented. Furthermore, certain environmental factors, such as exposure to silicon, have been mentioned repeatedly as an aetiological agent in small vessel vasculitis.

Involvement of the head and neck region by WG can often appear as the first and only manifestation of the disease. It is usually the location of the first symptoms in 80%-95% of cases. For this reason, otolaryngologists are crucial in obtaining a rapid and correct diagnosis and treatment, in order to prevent the natural progression of the disease.

The objective of this study is to show which were the otolaryngological manifestations identified and their frequency among a group of 17 patients with a previous diagnosis of WG.

**Materials and Methods**

We studied a group of 17 patients diagnosed with WG, defined according to clinical criteria, laboratory tests and anatomopathological studies. The evaluations of these patients were carried out prospectively in 2011 at the Department of Otolaryngology and Head and Neck Surgery of Hospital de Clínicas de UNICAMP in Campinas, Brazil.

The following tests were performed in all patients studied: detailed history, thorough ENT physical examination, audiometry, impedanciometría/tymanometría y nasofibrolaringoscopia. The evaluations were always performed by the same otolaryngologist.

Hearing loss was considered in cases with mean tonal laminar values above 25 dB for at least three consecutive frequencies, being conductive when the difference between the bone and air pathways was greater than 10 dB for the mean of the altered frequencies.

**Results**

We evaluated 17 patients with WG. The mean age of the patients studied was 41.7 years, ranging from 22 to 70 years, and the mean duration of the disease was 9.12 years, ranging from 1 to 40 years.

Of the patients studied, 9 (52%) presented some degree of hearing loss in the audiogram. The most common type was bilateral sensorineural hearing loss, which was present in 5 (55%) of these patients.

Regarding rhino logical symptoms, nasal obstruction in 11 (65%) patients and rinorrea in 10 (59%) patients were the most prevalent, with compatible alterations being present in the endoscopy in 12 (70%) cases, among which the most relevant were nasal crusts, septal perforations (Fig. 1), mucosal oedema and turbinate hypertrophy.

Of the pharyngolaryngeal symptoms, dyspnôea in 6 (35%) patients and hoarseness in 7 (41%) patients were the most...
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Figure 1  Endoscopic image showing a nasal septal perforation by WG in the right nostril (black arrows: edges of the perforation; grey arrow: septal perforation; white arrow: nasal crusts).

prevalent. A further 7 (41%) cases presented abnormalities upon physical examination, including hyperemia of the posterior pharynx, inter-arytenoid oedema and 1 (6%) case of subglottic stenosis (Fig. 2).

The frequency of the signs and symptoms observed among studied patients is summarised in Tables 1–3.

Discussion

Our findings regarding the main manifestations of WG in the head and neck region were similar to those described in the literature.

Figure 2  Endoscopic image showing a subglottic stenosis by WG.

Table 1  Frequency of Nasal Signs and Symptoms.

<table>
<thead>
<tr>
<th>Nose</th>
<th>Number, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered rhinoscopy</td>
<td>12 (70)</td>
</tr>
<tr>
<td>Nasal obstruction</td>
<td>11 (65)</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>10 (59)</td>
</tr>
<tr>
<td>Sneezing</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Scabs</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Nasal pruritus</td>
<td>6 (35)</td>
</tr>
<tr>
<td>Hyposmia</td>
<td>6 (35)</td>
</tr>
<tr>
<td>Postnasal drip</td>
<td>5 (29)</td>
</tr>
<tr>
<td>Septal perforation</td>
<td>3 (18)</td>
</tr>
<tr>
<td>Headache</td>
<td>3 (18)</td>
</tr>
<tr>
<td>Anosmia</td>
<td>2 (12)</td>
</tr>
<tr>
<td>”Saddle nose” deformation</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Cacosmia</td>
<td>1 (6)</td>
</tr>
</tbody>
</table>

Table 2  Frequency of Otological Signs and Symptoms.

<table>
<thead>
<tr>
<th>Ear</th>
<th>Number, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Otalgia</td>
<td>8 (47)</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Altered otoscopy</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Sensorineural hearing loss</td>
<td>5 (29)</td>
</tr>
<tr>
<td>Otorrhea</td>
<td>4 (23)</td>
</tr>
<tr>
<td>Conductive hearing loss</td>
<td>4 (23)</td>
</tr>
<tr>
<td>Aural fullness</td>
<td>3 (18)</td>
</tr>
<tr>
<td>Vertigo</td>
<td>1 (6)</td>
</tr>
</tbody>
</table>

Table 3  Frequency of Pharyngolaryngeal Signs and Symptoms.

<table>
<thead>
<tr>
<th>Larynx</th>
<th>Number, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoarseness</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Dyspnkea</td>
<td>6 (35)</td>
</tr>
<tr>
<td>Cough</td>
<td>4 (23)</td>
</tr>
<tr>
<td>Dysphonia</td>
<td>3 (18)</td>
</tr>
<tr>
<td>Stenosis</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Foreign body sensation</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Pyrosis</td>
<td>1 (6)</td>
</tr>
</tbody>
</table>

Nose and Paranasal Sinuses

Involvement of the nasal cavity and paranasal sinuses takes place in 60%–90% of cases.13,14 Thus, the head and neck region is the most frequent anatomical location of the manifestations of WG. Up to 30% of patients only present nasal symptoms,15 with the most common being nasal obstruction and rhinorrhea.16 Other signs and symptoms include epistaxis, pain in the nasal dorsum, anosmia, hyposmia, epiphora, septal perforations and “saddle nose” deformity. Chronic sinusitis appears in up to 50% of patients with nasal involvement.15

Rasmussen et al. studied a group of 124 patients and found the following as common nasal symptoms: nasal crusts (56%), nasal obstruction (54%) and bloody rhinorrhea (50%).17
Cannady et al. studied 120 patients with nasal manifestations of WG. Their most frequent findings were: nasal crusts (69.2%), chronic sinusitis (60.8%), nasal obstruction (58.3%), bloody rhinorrhea (51.7%), septal perforation (32.5%) and "saddle nose" deformity (22.7%).

Regarding nasal symptoms, we found that nasal obstruction and rhinorrhea were the most common (65% and 59%, respectively). This correlated with the alterations found on endoscopy, which were mainly nasal crusts in 74% of cases, as well as turbinate hypertrophy, erythema and swelling of the nasal mucosa and presence of granulation tissue, especially in the region of the turbinates and nasal septum, which were secondary to the characteristic vasculitis and chronic inflammation of the disease.

Septal perforations were also common in these patients, due to vasculitis in the Kiesselbach plexus, with consequent necrosis and cartilage resorption. There are few studies which quantify this finding in the literature. Jennings et al. reported this finding in 3 of 49 (6%) patients studied. In our work, 3 (18%) of the 17 patients presented it. Regarding "saddle nose" deformity, this is described in 10%-25% of patients with nasal involvement. We observed this deformity in 1 (6%) patient.

These alterations, along with chronic sinusitis which does not improve despite conventional treatment, should make us consider WG.

We believe that our findings were similar to those described in the literature, with some variations which were probably secondary to differences in the number of patients and the type of study (retrospective in most cases and prospective in our case).

Ear

Ear involvement may occur in 20%-70% of cases and often also represents the first sign of the disease. Involvement of the outer ear is rare, with the most common cases being external otitis secondary to chronic otitis media. The middle ear can be affected in 40%-70% of cases. Otitis media with effusion is the most common otological manifestation of WG, secondary to dysfunction of the Eustachian tube. Chronic suppurative otitis media is present in 24% of cases and may be complicated by contiguity with mastoiditis, which is associated with facial nerve palsy in 8%-10% of cases.

Regarding otological manifestations, the incidence of hearing loss in our study was 53.1%, of which 29.4% cases were sensorineural. The specific aetiology of each case was not investigated. Conductive hearing loss is mainly due to serous otitis media secondary to the presence of granulation tissue in the Eustachian tube, causing its malfunction. Sensorineural hearing loss is found in 5%-35% of cases, according to the literature. We consider this range variability probably due to the difference in disease progression times. Hearing loss can develop rapidly or gradually over several days or weeks. Although the exact cause still remains unknown, some theories link it to deposits of immune complexes in the cochlea, granulomatous compression of the cochlear nerve and vasculitis of the vasa nervorum and cochlear vessels.

Larynx and Pharynx

The most frequent symptoms at the level of the pharynx and larynx were cough and dyspnoea. All of our patients presented at least one of the following signs on direct laryngoscopy: mucosal oedema, erythema and subglottic stenosis. We did not differentiate between laryngeal and pulmonary causes in cases of dyspnoea. However, in the only case of stenosis, we ruled out a pulmonary cause through bronchoscopy, chest computed tomography (CT) scan and lung tissue biopsy.

Stenosis is the most important finding in the region of the larynx due to its potential to threaten the life of patients. The most common symptom is progressive difficulty for breathing, although patients may present acute stridor and require an urgent tracheotomy. The findings in direct laryngoscopy are a circumferential narrowing of the subglottis, with an erythematous and friable mucosa, which may extend up to 4cm towards the trachea. Up to 50% of patients with laryngeal involvement will require a tracheotomy. Subglottic and/or tracheal stenosis appear in approximately 5%-20% of patients and are associated with the generalised form of the disease, although they may also appear in isolation as the first symptom. In our study, the incidence was 6%.

Rottem et al. have reported that subglottic stenosis is five times more common in patients diagnosed with WG before the age of 19 years.

Conclusion

WG is an idiopathic, granulomatous disease with a potential for multiple manifestations in the head and neck region. Diagnosis is often delayed because of its nonspecific symptoms. Otolaryngologists play an essential role in the multidisciplinary team involved in the diagnosis, monitoring and treatment of these patients. Knowing the most common symptoms will help in obtaining an early diagnosis and treatment.

The most frequently identified otolaryngological abnormalities are: nasal obstruction, nasal crusts, rhinorrhea, otalgia, tinnitus, hoarseness and dyspnoea.

Conflict of Interests

The authors have no conflict of interests to declare.

Acknowledgement

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