

Laryngeal and tracheobronchial involvement in Wegener's granulomatosis

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ABSTRACT

Introduction: Wegener's granulomatosis (WG) is a form of systemic vasculitis that involves primarily the upper and lower airways and the kidneys. The most frequent airway manifestations include subglottic stenosis and inflammation, and tracheal and bronchial stenoses. The endoscopic visualization of the airways is the best tool for assessing, diagnosing and managing those changes. **Objectives:** To describe the endoscopic abnormalities found in the airway mucosa of a group of patients with WG undergoing bronchoscopy at Hospital das Clínicas of the Faculdade de Medicina, Universidade de São Paulo (HC-FMUSP), and to report the therapeutic bronchoscopic interventions used in some cases. **Methods:** The study assessed 15 patients diagnosed with GW from the Vasculitis Outpatient Clinic of the Department of Pulmonology, HC-FMUSP, referred for bronchoscopy at the Service of Respiratory Endoscopy, HC-FMUSP, from 2003 to 2007. **Results:** Fifteen patients were studied [11 females (73.33%)]; mean age, 34 ± 11.5 years. Airway changes were found in 80% of the patients, and the most frequent endoscopic finding was subglottic stenosis ($n = 6$). Therapeutic bronchoscopy was performed in three patients with subglottic stenosis and in other three patients with bronchial stenosis, all showing good results. **Conclusion:** Bronchoscopy allows for diagnosing, monitoring, and treating the airway lesions in WG, being a minimally invasive therapeutic option in selected cases.

Keywords: Wegener's granulomatosis, laryngeal stenosis, bronchoscopy, tracheal stenosis.

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INTRODUCTION

Initially described in 1936,¹ the Wegener's granulomatosis (WG) is characterized by granulomatous inflammation and necrotizing vasculitis, affecting mainly small arteries, arterioles, capillaries, and venules of upper and lower airways and of kidneys.^{2,3} The involvement of the airways is one of the major characteristics of WG, and occurs in 15%–55% of the patients.^{4–7} The symptoms include cough, hemoptysis, stridor, sibilant rales, and dyspnea.^{7,8} The manifestations of WG in the respiratory tract include nasal stenosis, nasal cartilage necrosis, subglottic stenosis, tracheal and bronchial stenosis,

granulomatous nodules and masses, alveolar infiltrates, and cavities.^{9,10} In addition, cutaneous, musculoskeletal, and ocular involvement can occur. Cardiac and central nervous system lesions are rarer.

Regarding the laboratory findings, urinalysis with hematuria and red blood cell casts indicates associated renal lesion. In the presence of active generalized disease, ANCA-c has sensitivity of 90%–95% and specificity of 90%. ANCA-p can be present in 20% of the cases. The inflammatory activity should be elevated. In cases with negative ANCA-c and doubtful diagnosis, tissue biopsy should be performed. Despite their lower sensitivity, biopsies of cutaneous and

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upper airway lesions should be performed prior to lung biopsy, because they are less invasive. In the presence of renal involvement, renal biopsy shows focal necrotizing pauci-immune glomerulonephritis.^{2,3}

The most common radiologic findings are pulmonary infiltrates (67%) and nodules (58%), the latter being usually multiple, bilateral and with cavitation in approximately 50% of the cases. Chest computed tomography reveals infiltrates and nodules not observed on conventional radiography in 43%–63% of the patients. Consolidation and ground glass opacity are seen in up to 50% of the patients and can present the following patterns: peribronchial consolidation, focal consolidation with or without cavitation, parenchymatous bands, peripheral consolidation areas mimicking pulmonary infarctions, and diffuse and bilateral ground glass opacity areas, usually corresponding to alveolar hemorrhage. Less frequent manifestations include pleural effusion (5%–20%), mediastinal masses, and enlarged lymph nodes, usually in association with parenchymal infiltrates.^{2,3}

Respiratory endoscopy allows assessment, diagnosis, and minimally invasive treatment of some airway alterations in WG. Our study aimed at describing the endoscopic changes in the airways of patients with WG undergoing bronchoscopy at our service, and at reporting the bronchoscopic therapeutic interventions used in some cases.

MATERIALS AND METHODS

This study was approved by the Medical Ethics Committee of the Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (HC-FMUSP).

This study retrospectively assessed the medical records of patients diagnosed with WG (based on clinical, radiological, serological, and anatomicopathological criteria proposed by the American College of Rheumatology). The patients were on follow-up at the Vasculitis Outpatient Clinic of the Discipline of Pulmonology, HC-FMUSP, and were referred for bronchoscopy at the Service of Respiratory Endoscopy, HC-FMUSP, from 2003 to 2007. The major indications for endoscopy were persistent or progressive dyspnea, investigation of pulmonary infiltrate, and hemoptysis.

All patients underwent flexible bronchoscopy with 5-mm bronchoscope and 2.0-mm working channel (Olympus, P20D), under intravenous sedation with midazolam and fentanyl, topical anesthesia with 1% lidocaine, supplementary oxygen, and monitoring of hemoglobin oxygen saturation.

The nasal cavities, larynx, and tracheobronchial tree were assessed.

Patients with indication for endoscopic treatment underwent therapeutic bronchoscopy under general anesthesia and received monthly follow-up until resolution or stability of the findings, when they were assessed only clinically.

Suspension laryngoscopy and metal tubes were used to dilate the subglottic stenoses. Bronchial stenoses were dilated with metal tubes and balloon-catheter.

Statistical analysis was performed by using the SPSS program, version 12.0, and descriptive statistics by using frequency distribution. The continuous variables were expressed as mean \pm standard deviation (SD), and the categorical variables as percentages.

RESULTS

This study assessed 15 patients diagnosed with WG (11 women; mean age, 34 ± 11.5 years).

Table 1 shows the frequency and characteristics of the airway lesions. In the nasal cavities occurred complete nasal destruction with extensive areas of necrosis in five patients (33.3%), severe mucosal inflammation in four patients (26.7%), and bilateral stenosis of the nasal fossae, treated with dilation and placement of a nasal silicone prosthesis, in one patient (6.7%).

In the larynx, subglottic stenosis was the most frequent alteration ($n = 6$; 40%). One patient underwent three sessions of mechanical dilation with intralesional corticosteroid injection (dexamethasone, 2 mg), with complete resolution of the stenosis in the following endoscopic assessments. Two patients with complex subglottic stenosis refractory to the treatment with mechanical dilation with Chevalier Jackson dilators received silicone endoprostheses, a Dumon stent and a Montgomery T tube. The other patients had mucosal inflammation ($n = 1$) and ulceration ($n = 2$).

In the tracheobronchial tree, the most common manifestation in our patients was inflammation. Four patients (26.7%) had edema and erythema areas, glandular duct dilation, and mucosal atrophy; four (26.7%) showed an exuberant inflammatory process of the bronchial mucosa, diffuse ulcerations, and raised “cobblestone” appearance of the mucosa. Bronchial stenosis was observed in three patients (20%), who were treated with mechanical dilation with metal olive-tipped dilators (Figures 1–3). One patient underwent complementary bronchial dilation with balloon-catheter of a bronchial subsegment of the right inferior lobe.

Table 1
Frequency and characteristics of airway lesions

Location	Characteristic (n = 15)	Frequency (%)
Nasal cavities	Normal	n = 5 (33.3)
	Nasal destruction/necrosis	n = 5 (33.3)
	Inflammation	n = 4 (26.7)
	Stenosis	n = 1 (6.7)
Larynx	Normal	n = 6 (40)
	Subglottic stenosis	n = 6 (40)
	Ulceration	n = 2 (13.3)
	Inflammation	n = 1 (6.7)
Tracheobronchial tree	Normal	n = 3 (20)
	Mucosal edema and erythema	n = 4 (26.7)
	Ulceration/cobblestone	n = 4 (26.7)
	Bronchial stenosis	n = 3 (20)
	Bronchial cavity	n = 1 (6.7)

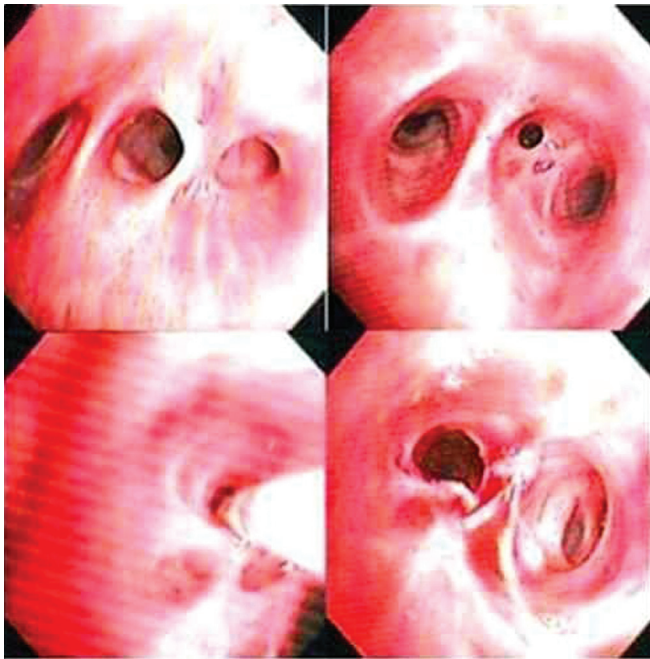


Figure 1
Bronchial stenosis dilated with balloon-catheter, resulting in lumen opening and good airway flow.

DISCUSSION

Impairment of the respiratory mucosa can occur along all the extension of the lower and upper airways in 15%–55% of the patients with WG.⁴⁻⁷ In approximately 25% of the patients with WG, involvement of the airways can be the only manifestation of the disease.¹¹

Young patients under the age of 30 years are prone to develop airway manifestations.¹² The mean age of our patients was 34 ± 11.5 years. Such manifestations are also more

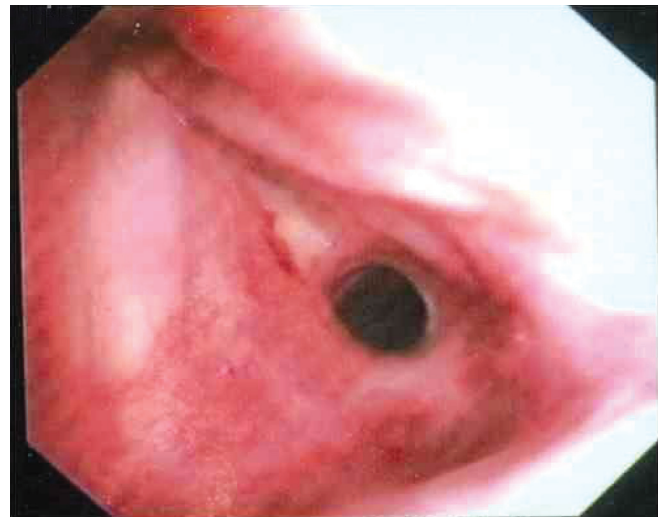


Figure 2
Subglottic stenosis.

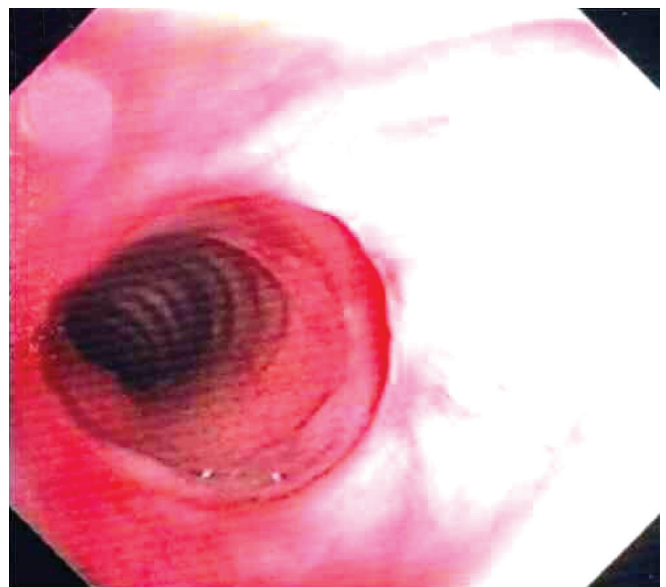


Figure 3
Subglottic stenosis after metal tube dilation.

common in women,^{6,13} in accordance with our case series, in which 73.3% were female patients.

Respiratory endoscopy helps in the diagnosis and follow-up of such alterations, also enabling, through therapeutic bronchoscopy, the re-establishment of the functional airway patency.¹⁴

The nasal cavities, frequently affected in patients with WG, deserve special attention. In our study, 10 patients (66.7%) had nasal lesions.

Fauci *et al.*¹⁵ have reported endobronchial abnormalities in 12 (15%) of 80 patients with WG and lung disease. Cordier *et al.*⁷ have reported either endobronchial abnormalities or hemorrhage in 41 (55%) of 74 patients with WG.

Subglottic stenosis was the most commonly found manifestation in our case series ($n = 6$; 40%), which is in accordance with the findings of the literature.^{14,16,17} Fibrotic scarring stenosis found in WG does not respond to immunosuppressive therapy,¹⁸ with the endoscopic treatment being a good alternative. Other causes of subglottic stenosis, such as post-intubation stenosis, post-infectious stenosis, and other systemic diseases (eg, Crohn's disease, sarcoidosis, and Behcet's syndrome) should be ruled out.^{19,20} Our study identified lower airway inflammation in four patients (26.7%), ulceration and "cobblestone" mucosa in the tracheobronchial tree in four patients (26.7%), and bronchial stenosis in three patients (20%).

Options for the treatment of stenoses are: intralesional injection of corticosteroids, balloon dilation, dilation by use of metal tubes, laser, endoprosthesis, tracheostomy, surgical resection, and reanastomosis.^{8,16,18,21-27} In the study by Gluth *et al.*,⁵ of the 27 patients with WG and subglottic stenosis, 11 (40.7%) required tracheostomy and 13 (48.1%) required multiple surgical procedures. The endoscopic diagnosis of laryngeal tracheobronchial stenoses allows, in some cases, minimally invasive treatment as an alternative

for the surgical treatment. In our study, all stenoses were endoscopically managed as follows: one subglottic stenosis, treated with mechanical dilation with metal tubes and intralesional corticosteroid injection, with complete resolution of the stenosis; two complex subglottic stenoses, treated endoscopically with mechanical dilation with metal tubes and endoprosthesis placement; three bronchial stenoses dilated with metal olive-tipped tubes, one of which, because of being subsegmental, required complementary dilation with balloon-catheter.

No complications related to the dilation procedure occurred. All patients remained under observation during post-anesthetic recovery, being discharged after two hours.

The major limitation of the study is that all patients included had indication for endoscopic assessment, mainly due to progressive or persistent dyspnea. The lack of patients with WG and without airway complaints prevents us from extrapolating the results to all patients with WG.

Wegener's granulomatosis can cause alterations in any segment of the airways, including inflammation, ulceration, pseudomembranes, tracheobronchomalacia, destruction of cartilages, endobronchial masses, and laryngeal tracheobronchial stenoses. Respiratory endoscopy allows for the diagnosis and treatment of several manifestations in a minimally invasive way, avoiding surgical procedures.

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