The Management of Subglottic Stenosis in Patients With Wegener's Granulomatosis

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Wegener's granulomatosis (WG) is a multisystem inflammatory disease characterized by vasculitis, granuloma formation, and necrosis. Among 158 patients treated at the National Institutes of Health during the past 24 years, 145 (92%) had an otolaryngologic manifestation of their disease and 25 (16%) had subglottic stenosis (SGS). SGS varied from asymptomatic to life-threatening. Sixteen (80%) of 20 patients with fixed SGS required surgical intervention, including manual dilations, carbon-dioxide laser resections, and laryngotracheoplasty (LTP). LTP was performed with and without microvascular reconstruction. Thirteen of the patients required tracheostomy and all 13 were ultimately decannulated. Five patients who repeatedly failed dilations and/or endoscopic laser surgery underwent LTP. Since 1987, two patients have undergone LTP with microvascular free flaps. Both patients were subsequently decannulated. The authors' experience demonstrates that management of SGS in WG is complex, requiring individualized frequent multimodality interventions to achieve satisfactory results. Microvascular laryngotracheal reconstruction should be considered in the surgical armamentarium for patients with persistent stenoses.

INTRODUCTION

Wegener's granulomatosis (WG) is characterized by necrotizing granulomatous inflammation and vasculitis of unknown etiology which classically affects the upper airway, lung, and kidneys.[1] The diagnosis requires exclusion of mycobacterial, fungal, or other infectious agents which can cause similar pathologic lesions.[2] When typical clinical and histopathological features of the disease are present in various organ systems but not in the kidney, such patients are said to have "limited WG."[3,4] Isolated involvement of the subglottic larynx may be the single presenting feature of WG.[5]

During the past 24 years, 158 cases of WG have been followed for a minimum of 6 months to a maximum of 24 years at the National Institute of Allergy and Infectious Diseases.[4] Otolaryngologic manifestations of disease were common both at the onset of disease (73% of all patients) as well as through the course of the illness (92% overall) (Fig. 1). An overall incidence of subglottic stenosis (SGS) in WG has been reported at 8.5%.[6] In the present series, 25 (16%) of 158 patients had varying degrees of subglottic narrowing (Fig. 2). In 13 (52%) of those 25 patients, tracheostomy was required. In other reports, decannulation rates of 0% to 86% have been described[7–9] despite multiple interventions and varied treatment modalities. McCaffrey,[9] using open technique, successfully decannulated 6 of 7 WG patients in whom endoscopic methods failed; that report was part of a larger series and did not stratify for endoscopic successes in WG. This report now describes the authors' experience with 25 patients having SGS, including 13 who required tracheostomy (all of whom have been successfully decannulated). Many of the 25 patients had several different procedures.

MATERIALS AND METHODS

Subglottic stenosis of any degree was diagnosed either by flexible fiberoptic examination or by direct laryngoscopy in the operating room. Clinical suspicion alone was not sufficient to establish the diagnosis. Magnetic resonance imaging (MRI) or linear tomography of the trachea confirmed the endoscopic evaluations. Computer-enhanced tomography was of limited value in demonstrating most lesions. Treatment modalities for SGS included the following: observation without surgical intervention, manual dilation, endoscopic carbon-dioxide laser resections, intralesional corticosteroid injections, laryngotracheal reconstruction (anterior and posterior cricoid split) with cartilage augmentation, and laryngotracheal reconstructions with microvascular repair (MVR). Both elective and emergent tracheostomies were performed based on the clinical pre-

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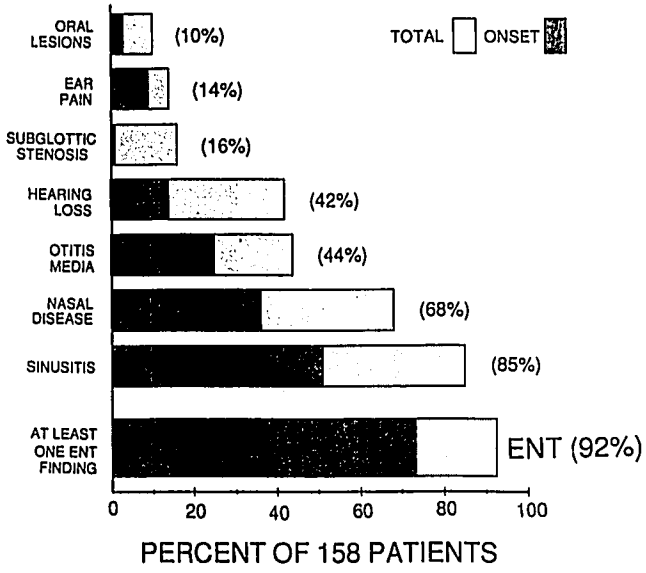

Fig. 1. Otolaryngologic manifestations of Wegener's granulomatosis that were apparent at disease onset and during the course of illness. ENT = ear, nose, and throat.

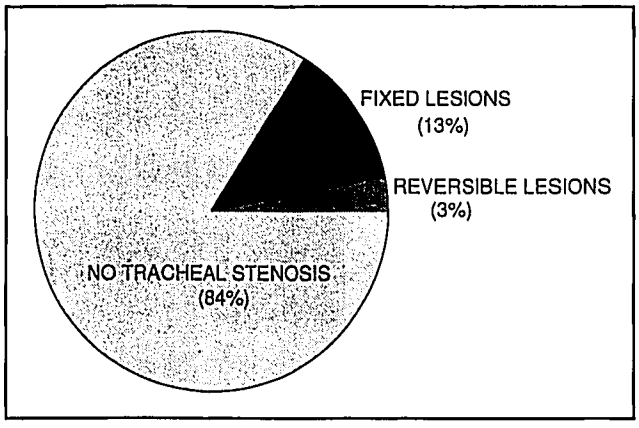

Fig. 2. Subglottic stenosis in 158 Wegener's granulomatosis patients. Reversible lesions: lesions that resolved with either cytotoxic or steroid therapy only.

sentation, fiberoptic laryngeal evaluation, and estimates of subglottic airway diameter. During periods of active inflammatory disease, patients received immunosuppressive therapy with glucocorticoids and/or cytotoxic medication, *e.g.*, cyclophosphamide, azathioprine, or methotrexate as directed by the responsible physicians.[2–4]

The authors' method of tracheal rehabilitation is progressive. New patients with WG and SGS undergo complete otolaryngologic and medical examination. MRI or linear tomography are performed prior to operative endoscopy (and biopsy, if appropriate). Depending on the gross appearance of the lesion, gentle manual dilation may be performed, especially in noninflamed lesions. The dilator is coated with 1% triamcinolone cream as lubricant. Ulcerated, friable tissue is biopsied, after which manual dilation is performed.

During the last 1½ years, friable and polypoid-appearing subglottic tissue has been injected with 15 mg of long-acting (depo)methylprednisolone in four patients. In these four patients, endoscopy was repeated about 1 month after the injections. Carbon-dioxide laser therapy was performed in eight patients and was abandoned because of uniformly poor results. If after 6 months no appreciable progress was made in improving the airways of SGS patients, an open procedure was planned.

RESULTS

Of the 25 patients with SGS, 15 were female and 10 were male (Table I). Eleven of the patients were less than 20 years old and 14 ranged from 21 to 63 years old when first diagnosed with WG. Twenty-three of the total 158 patients were less than 20 years old at the onset of WG. Thus, 11 (48%) of the 23 pediatric/adolescent patients had SGS, compared to 14 (10%) of the 135 adults (Fig. 3). This greater incidence of SGS in juveniles as compared with adults was statistically significant ($P<.001$, Fisher exact test). SGS preceded a diagnosis of WG in 1 patient, a 14-year-old girl, and was observed after the diagnosis of WG in the remaining 24 patients. Five patients with lesions of SGS responded to cytotoxic and/or glucocorticoid therapy alone and did not require surgical intervention. Of the remaining 20 patients, 13 required tracheostomy at some point in their management. Four of 20 patients with persistent subglottic lesions had mild circumferential narrowing of their airways. The mucosa did not appear grossly inflamed, and the patients were asymptomatic with subglottic lumens 6 to 7 mm in diameter. These patients have been followed at regular intervals and, to date, have not required surgical intervention despite the presence of mild narrowing which persisted both during disease remission (2 patients) and flares of WG (2 patients).

In the eight patients who underwent carbon-dioxide laser resections, subglottic scarring recurred rapidly and was more extensive after each laser procedure. This usually became clinically apparent between 10 and 21 days. All of these patients ultimately required other therapy to adequately manage the stenosis. Five (31%) of the surgical patients underwent laryngotracheoplasty (LTP) after endoscopic methods failed. This procedure consisted of an anterior and posterior cricoid split with cartilage augmentation of the subglottic larynx. The airway was stented with a Montgomery Safe-T-tube® for 3 to 6 months; a soft stent was used on one occasion.

Two female patients, similar in age and in presentations for both WG and SGS, initially failed both laser resections and manual dilations. They ultimately underwent LTP. A microvascular free flap was performed in conjunction with LTP in one patient but not in the other. The patient who initially underwent a microvascular repair (MVR) has been decannulated for 2½ years and is doing well. The other patient required periodic additional interventions, ultimately leading to a repeat LTP with MVR. As of this writing, she has been decannulated for 2 months and is doing well.

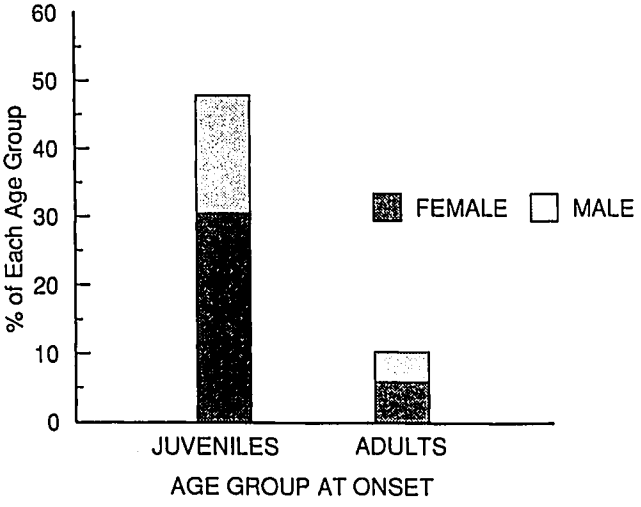

Fig. 3. Subglottic stenosis (SGS) in juveniles and adults. The occurrence of SGS in 11 patients with juvenile-onset Wegener's granulomatosis (WG) was fivefold greater than that in 14 patients with adult-onset WG ($P<.001$). There was no significant difference in the occurrence of SGS in males and females. Juveniles: patients under 20 years of age at time of WG onset.

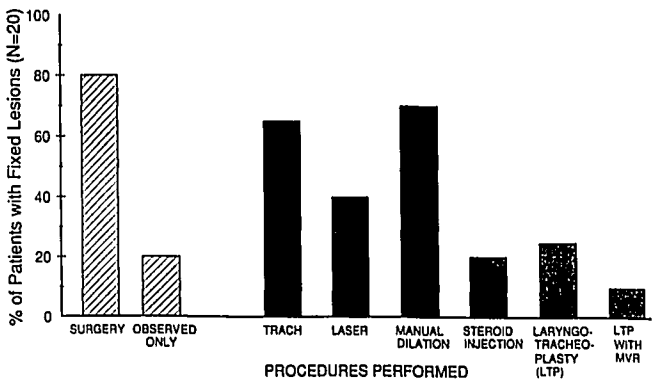

Fig. 4. Treatment modalities used in 20 Wegener's granulomatosis patients with fixed subglottic lesions. MVR = microvascular reconstruction.

Three patients underwent LTP without MVR and have stable airways. At present, all 13 tracheostomy patients have been decannulated with adequate voice (Table I). Treatment modalities for all patients with SGS are shown in Figure 4.

DISCUSSION

Wegener's granulomatosis is a granulomatous vasculitis whose etiology is unknown but which is believed to be immunologically mediated.[2–5,10] Inflammatory events have an unusual affinity for ciliated respiratory epithelium of the nasal cavity, paranasal sinuses, and upper or lower tracheobronchial tree. The reason(s) for the increased incidence of SGS in patients 20 years old or younger is unclear. Treatment of SGS in WG requires determination of whether stenosis is due to active inflammation, noninflammatory scar tissue, or both. One must also consider whether SGS is due to other causes, such as prolonged endotracheal intubation, intubation for elective surgery, or infectious processes of the upper airway. In certain cases multiple factors may play a role. In some patients, the subglottic airway may be clinically or subclinically inflamed and therefore hyperreactive to even minimal trauma. Intralesional glucocorticoid injections are well-known to diminish inflammation and to impair both fibroblast production of collagen and scar formation. Glucocorticoids suppress cytokine-mediated fibroblast stimulation. This modality has been shown to be effective in the treatment of other causes of laryngeal stenosis.[11]

Two patients underwent LTP with a microvascular free flap. The posterior augmentation was inserted as in previous surgical procedures; however, a rib graft was harvested with the intercostal arteries attached. In so doing, it seemed reasonable to bring in healthy tissue (cartilage and periosteum) with an independent blood supply perfusing a normal microcirculation. Another reason that this appeared prudent was that the hallmark of WG is vasculitis (most commonly small vessels). In the canine model, successful laryngotracheal reconstruction had been accomplished with a composite vascularized free-rib transfer which had objectively demonstrated healthy metabolizing bone 6 weeks postoperatively.[12,13]

One patient, a 25-year-old woman (now decannulated 2½ years), underwent an MVR without complication. Another patient, a 24-year-old woman, underwent a standard LTP. The MVR patient was decannulated within 6 months; the patient who had a standard LTP required almost monthly dilations for 3 years. She later underwent a second open repair, during which a microvascular free flap was placed; 6 months after that second open repair, she also was decannulated. In another patient, an MVR was abandoned intraoperatively because vasculitis had resulted in inadequate donor and recipient vessels. She was an unusual WG patient in that her disease also affected larger vessels including the pulmonary artery; right-sided heart failure necessitated thoracotomy for treatment.

Most of the 16 surgical patients have had several interventions, with 1 patient having more than 30 procedures during a 4-year period (dilations and/or steroid injections) prior to repeat LTP with MVR. Thirteen (81%) of the surgical patients have had a tracheostomy at some time during their therapy. The question of management with or without tracheostomy is based on individual clinical circumstances. Some patients present in extremis with airway obstruction, while others have only mild dyspnea. In lesions with airways larger than 4 mm, endoscopic interventions can be performed safely with jet ventilation anesthesia and perioperative glucocorticoids. Tracheostomy facilitates future surgical interven-

TABLE I.
Treatment Modalities.

Patient	Sex	Age at Wegener's Onset	Surgery Any Type	Tracheostomy	Laser	Manual Dilat.	Steroid Injection	LTP	LTP With MVR	Decannulated With Adequate Voice
Subglottic Stenosis (Fixed)										
1	F	11	Y	Y	Y	Y	N	Y	Y	Y
2	F	12	Y	Y	Y	Y	Y	N		Y
3	M	14	N	N	N	N	N	N		N/A
4	F	14	N	N	N	N	N	N		N/A
5	M	15	Y	Y	N	Y	N	N		Y
6*	F	16	Y	Y	Y	Y	Y	Y	Y	Y
7	M	18	Y	Y	N	N	N	N		Y
8	F	19	Y	Y	N	Y	N	N		Y
9	F	21	Y	Y	Y	Y	N	N		Y
10	M	23	Y	N	N	Y	Y	N		N/A
11	M	23	N	N	N	N	N	N		N/A
12	F	24	Y	N	N	Y	N	N		N/A
13	M	24	N	N	N	N	N	N		N/A
14	F	25	Y	Y	Y	Y	Y	Y	N	Y
15	M	29	Y	Y	Y	Y	N	Y	N	Y
16	M	29	Y	Y	Y	Y	N	N		Y
17	F	34	Y	Y	N	Y	N	N		Y
18	F	37	Y	Y	Y	N	N	Y	N	Y
19	F	61	Y	N	N	Y	N	N		N/A
20	M	63	Y	Y	N	Y	N	N		Y
Subglottic Stenosis (Reversible, Medical Therapy Only)										
21	F	13	N	N	N	N	N	N		N/A
22	F	16	N	N	N	N	N	N		N/A
23	M	17	N	N	N	N	N	N		N/A
24	F	22	N	N	N	N	N	N		N/A
25	F	25	N	N	N	N	N	N		N/A

*Patient underwent standard laryngotracheoplasty and was redone 3 years later with laryngotracheoplasty and microvascular reconstruction.

LTP = laryngotracheoplasty; MVR = microvascular reconstruction; Y = yes; N = no; N/A = not applicable.

The median age at onset of Wegener's granulomatosis for these 25 patients with subglottic stenosis was 22 years; the median age at onset for the 133 patients without subglottic stenosis was 43 years.

tions but is not always necessary. Decannulation following tracheostomy is individualized and is delayed until there is subjective and objective evidence of a stable airway.

Management of SGS in patients with WG is complex, often requiring frequent multimodality interventions and a team approach. At the National Institutes of Health, an immunologist directs the medical therapy so that the inflammatory process may be suppressed or eliminated concurrent with or prior to surgical treatment of the upper airway. In patients failing endoscopic therapy, an open procedure is advised to facilitate decannulation. Pathologic interpretations of biopsy specimens from the trachea can be difficult since diagnostic features of granulomatous inflammation, parenchymal necrosis, and vasculitis may be inconspicuous and are found in the minority of specimens. In patients with previous procedures, the possibility of a foreign body giant cell reaction should be considered when granulomas are observed.[14]

CONCLUSION

Otolaryngologic abnormalities occur in almost all patients with WG. SGS in its full spectrum was present in 16% of these WG patients. Patients who present with WG at 20 years of age or younger are at significantly increased risk for developing SGS. Management is complex and often frustrating; several modalities of treatment may be required to maintain a stable airway. Those patients with more severe SGS may need a tracheostomy during part of all of their management. If LTP is indicated, MVR should be considered in the surgical armamentarium of the otolaryngologist if adequate donor/recipient vessels are present.

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