Treatment of Subglottic Stenosis, Due to Wegener's Granulomatosis, with Intralesional Corticosteroids and Dilation

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ABSTRACT. ***Objective.*** To determine the longterm efficacy of intralesional long-acting corticosteroid injection plus dilatation (ILCD) for subglottic stenosis (SGS) in Wegener's granulomatosis (WG).

Methods. Since November 1994, all patients with WG who presented with SGS of more than 50% or symptoms of airway compromise were treated with intralesional injection of methylprednisolone acetate, injected directly into the stenotic segment, followed by microsurgical lysis of the stenotic ring and serial dilatation with Maloney bougies or Fogarty catheter balloon. The procedure was repeated at a later date if re-stenosis occurred. Patient outcome was evaluated over a period of 7 years.

Results. Twenty-one patients underwent 64 procedures. Mean followup was 40.6 months. Patients who did not have scarring from prior procedures required a mean of 2.4 procedures at mean intervals of 11.6 months to maintain subglottic patency. Patients with established laryngotracheal scarring required a mean of 4.1 procedures at mean intervals of 6.8 months to maintain patency. None of the 21 patients required a new tracheostomy. Only 2 significant complications occurred, both pneumothoraces. There were no adverse longterm sequelae.

Conclusion. ILCD is effective therapy for SGS due to WG. Best results are obtained when these endoscopic techniques are performed prior to other forms of surgery, which may produce extensive scar formation. Based on this experience, the authors recommend ILCD as the preferred therapy in WG-SGS. (J Rheumatol 2003;30:1017–21)

Key Indexing Terms:
WEGENER'S GRANULOMATOSIS SUBGLOTTIC STENOSIS TREATMENT

The subglottic region is one of the narrowest parts of the airway. In normal adults, the transverse diameter is about 14 mm in women and 18 mm in men[1,2]. Wegener's granulomatosis (WG) has a peculiar tendency to affect this segment. Subglottic stenosis (SGS) is encountered in 17–23% of patients with WG (WG-SGS). WG-SGS is due to or follows tracheal inflammation[3,4]. The glottic segment of the larynx is usually spared[5]. WG-SGS is not uniformly responsive to systemic immunosuppressive therapy and may persist despite adequate disease control in other organ systems[3]. In addition, localized SGS may occasionally be the first or only presentation of WG. Persistence of focal disease makes it difficult to justify the use of systemic corticosteroid and cytotoxic drug therapy.

Intralesional corticosteroid injections have been employed to treat non-WG largyngotracheal stenosis[6-10]. However, these results have been inconsistent. The majority of non-WG-SGS lesions are secondary to post-intubation scarring and laryngotracheal trauma[11]. These strictures may be fibrotic or calcified[2] and difficult to treat in a conservative fashion. However, in one study of WG-SGS, intralesional corticosteroid injections were remarkably effective. Langford, *et al*[3] reported 20 cases treated over 5 years, in which intralesional injection of methylprednisolone acetate together with mechanical dilation (ILCD) preserved laryngotracheal patency in all patients. In addition, 6 patients who previously required tracheotomy were decannulated. Prior to the use of this technique, the large variety of methods employed (e.g., instrumental dilation, laser resection and evaporation, stenting, and reconstructive surgery) led to unsatisfactory results[12], and tracheotomy rates of about 50%[12-15].

The report in the literature of only one systematically collected cohort treated by ILCD prompted us to analyze our experience employing similar techniques in 21 patients with WG-SGS.

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MATERIALS AND METHODS

Since November 1994, all patients with clinically significant SGS (> 50% obstruction or < 4 mm intraluminal diameter) due to WG at our institution underwent intralesional corticosteroid injection and dilation (ILCD) as first-line surgical therapy. Fiberoptic laryngoscopy was performed every 1–3 months and whenever symptoms such as cough, wheeze, stridor, dyspnea, or voice changes were reported.

Patients continued to receive systemic immunosuppressive agents based on extratracheal disease activity. The presence of SGS alone was not deemed to be an indication for systemic immunosuppressive therapy.

ILCD for subglottic stenosis. (1) The patient is positioned supine with a shoulder roll and head donut to achieve the optimal position for visualizing the larynx, through a rigid suspended articulating, expandable laryngoscope. (2) Intravenous (IV) dexamethasone (10 mg) is provided preoperatively to reduce postoperative edema and tracheobronchospasm. General IV anesthesia and chemical paralysis are provided in conjunction with laryngoscope placement. (3) The articulating expandable laryngoscope is advanced to bring the larynx and subglottic region into view. The laryngoscope is then suspended on a Mayo stand via a Lewy C arm over the patient's chest (suspension laryngoscopy). (4) Jet ventilation is a convenient way to achieve effective oxygenation without an endotracheal tube and allows for binocular, microscopically enhanced visualization and bimanual manipulation of the narrowed airway. Minimal air pressures, adequate expiratory time, and low ventilatory rates are used. Total procedure time is kept to a minimum to reduce laryngeal irritation and the risk of pneumothorax. Oxygen saturation generally remains at 99–100% throughout the procedure. (5) The subglottic stenosis is visualized, usually 3 to 10 mm below the true vocal cords. Methylprednisolone acetate 40 mg/ml is injected submucosally into the stenotic area and scar tissue, using a 1 ml tuberculin syringe attached to a 20G long laryngeal needle. Typically, 4 quadrants of the stenotic ring are injected, administering proportionately more to hypertrophic ridges of tissue if present. A total of 40–120 mg is utilized for the entire procedure. About half the dose (20–60 mg) may leak into the tracheal lumen. (6) Lysis of the stenotic ring is performed after corticosteroid injection and before dilation. A laryngeal microsickle knife is used to create radial incisions through the subglottic scar. The surgical microscope is used to provide magnification for this delicate maneuver. Two to 6 incisions were placed within the stenotic lesion circumferentially, especially where there were thickened ridges of tissue. These cuts extended to a depth of 2–3 mm into the submucosa and scar tissue. Care was taken not to injure the true vocal cords or disrupt the inner perichondrium of the laryngeal cartilage during this maneuver. Epinephrine 1 mg/ml (1:1000 dilution) soaked cotton patties on an applicator were held over these incisions for hemostasis. (7) The stenosis is then serially dilated using flexible Maloney bougies that are well lubricated with sterile aqueous gel. The size chosen at each stage is such that these dilators could pass safely without undue resistance. Dilators range from 22 French, for pinpoint stenoses, to as large as 46 French. Great care is taken not to cause tissue damage with excessive force. (8) The vocal cords and subglottic area are sprayed with topical lidocaine. An endotracheal tube (#6–6.5) is then introduced through the articulating laryngoscope, which is then withdrawn gently over the endotracheal tube. Jet ventilation is discontinued and the patient is ventilated through the endotracheal tube until fully awakened.

The entire process including the additional modification noted below takes about 45 minutes. Blood loss is typically less than 5 ml. A patency of at least 6 mm is usually achieved.

Modification. The alkylating agent mitomycin C, isolated from *Streptomyces caespitosus*, inhibits fibroblast activity while sparing epithelial growth[16]. It has been used to prevent scar formation in various ophthalmic procedures[16-18] and in laryngotracheal cicatrix[17-20], including one case of WG[17]. From 1999 to the present, mitomycin C has been applied to lesions. Merocel® pledgets soaked in mitomycin C, held with long cupped alligator forceps, are held against the subglottic area for roughly one minute. Pregnancy constituted a contraindication to the use of mitomycin.

Precautions. Desaturation, hypotension, or cardiac arrhythmias may indicate respiratory compromise from either airway obstruction or pneumothorax. Airway reexamination and suctioning of secretions may be required. Temporary insertion of an endotracheal tube may be indicated. A chest radiograph is urgently obtained if pneumothorax is suspected. Mild transient laryngeal spasm may occasionally cause some delay in extubation. Laryngobronchospasm can also occur as a result of the manipulations or due to irritation from blood and medications propagated to distal airways by the jet ventilation.

If patient is stable, discharge is feasible on the day of the procedure. However, in recent years we have preferred to observe patients overnight for respiratory distress, occult pneumothorax, and excessive production of secretions. During this period of observation, aerosol treatments and incentive respiratory exercises are encouraged to expand atelectatic segments and clear secretions. If not already using corticosteroids, the patient is discharged with a short course of corticosteroids to minimize manipulation-induced mucosal edema. A postoperative radiograph before discharge should be done to document the absence of pneumothorax.

Special situations. Whenever the diameter of the glottic chink did not accommodate adequate size Maloney bougies, a Fogarty balloon catheter was used instead for dilation. This was passed uninflated beyond the vocal cords, then inflated with saline to dilate the stenotic segment. This avoids stretching and trauma to the true vocal cords by the large Maloney bougies. The applied pressures are manometrically monitored.

Life-threatening pinpoint critical stenosis of less than 2 mm diameter should ordinarily be immediately treated by tracheotomy. However, we elected to treat these patients with emergent ILCD because extensive personal experience and operating room readiness allowed for emergency tracheotomy if necessary.

The potential contribution of concomitant reflux to laryngeal inflammation is recognized, and patients with reflux were treated with proton pump inhibitor prophylaxis.

We reviewed the clinical outcomes of all patients who underwent this procedure from November 1994 until February 2002. The results were further analyzed after patients were separated into 2 groups: (1) patients whose airways were undamaged by previous procedures and (2) patients with airway trauma and scarring from previous surgical procedures.

RESULTS

A total of 21 patients with significant stenosis underwent ILCD. Cohort characteristics and followup are presented in Table 1. Results of procedures are summarized in Table 2. Six patients had prior tracheotomies. New tracheotomies were not required in any patient. The longest period of post-dilatation sustained patency to date was 81 months. The mean period of sustained laryngeal patency has been about 24 months.

Morphology of stenosis ranged from circumferential, anterior, or posterior ridges to a corkscrew pattern. Severe, extensive, thickly fibrotic corkscrew-like lesions extending both cephalad and caudally were encountered in patients

Table 1. Profile of Wegener's granulomatosis/subglottic stenosis cohort.

Total no. of patients	21
Total no. of procedures	64
Males:females	5:16
Mean age at diagnosis of WG, yrs (range)	39.1 (21–68)
Age range at time of intralesional therapy, yrs	21–73
Mean followup, mo (range)	40.6 (7–87)

Table 2. Wegener's granulomatosis and subglottic stenosis: outcomes.

	Group 1, No Prior Manipulation	Group 2, Subglottic Scar from Prior Instrumentation
No. of patients	12	9
No. of patients with prior tracheostomy	0	6
No. of patients decannulated after intralesional corticosteroid therapy and dilatation	Not applicable	4
Mean no. of procedures	2.4 (range 1–6)	4.1 (range 1–11)
No. of patients who required 1–3 procedures	10	4
No. requiring > 3 procedures	2	5
Mean interval between procedures, mo (range)	11.6 (2–36)	6.8 (1–21)
Mean period of patency since last procedure, mo (range)	25.2 (1–81)	21.4 (1–48)

treated in other institutions by various other approaches, especially laser resection.

Group 1 outcome. Twelve patients had ILCD as their first-ever procedure. These individuals did not have extensively scarred subglottic tissue. Patients in this group had the greatest improvement and the most enduring asymptomatic intervals and required fewer procedures. Ten of 12 required 3 or fewer procedures (4 required one procedure). The eleventh patient was transferred to our institution with severe stridor and pinpoint stenosis. She required 6 procedures over 55 months before her airway became stable. The twelfth patient had very active disease and required 4 procedures over 60 months.

Group 2 outcome. Nine patients were referred to our center after prior surgical procedures, which included laser resection of subglottic tissue in 6 (Figure 1). Three patients had multiple rigid bronchoscopic dilations. Nevertheless, ILCD was able to improve and stabilize the outcome in this group.

The most difficult lesions were found in the 6 patients with tracheotomies, presenting with multilevel laryngotracheal stenoses, cicatrix formation, vocal cord fixation, and arytenoid cartilage damage. Widening the subglottic region alone was not sufficient. Four patients achieved decannulation by means of various laryngotracheoplastic techniques[21,23].

Complications and problems. Two patients developed right side pneumothorax during the procedure. One had a right main stem bronchus stenosis in addition to subglottic stenosis. This caused a one-way valve-like entrapment of the air within her right lung. The other patient had a bronchopulmonary fistula that required thoracotomy and wedge resection of the affected lung. This patient had a previous open-lung biopsy for the diagnosis of WG.

DISCUSSION

Our experience corroborates the favorable results of Langford, *et al*[3] for ILCD treatment for WG-SGS. We have demonstrated that in airways undamaged by previous surgical interventions, extended periods of patency can be achieved in some instances even with a single treatment. Conversely, scarring and cicatrix formation from prior traumatic therapeutic instrumentation, especially laser therapy, had a significant adverse affect on outcome. Every surgical intervention induces scar formation and fibrous scars tend to recur[1]. Further fibrosis with each traumatic procedure creates a cycle. Prior endotracheal intubations and use of curved indwelling tracheotomy tubes have a cumulative effect on airway damage through pressure necrosis, mucosal ulceration, secondary infection, and eventually intractable stenosis[1,6]. Severe airway compromise results, especially if the vocal cords are immobilized by damage to the posterior commissure and the cricoarytenoid joints[23].

Some scar tissue deposition is inevitable even with controlled minimally traumatic techniques. There is direct correlation between the severity of stenosis at presentation and the need to perform more procedures subsequently. ILCD should be undertaken as soon as signs of airway compromise are observed, rather than delaying until obstruction is near complete.

Laryngotracheomalacia from repeated steroid injection causing airway collapse is a theoretical concern, but was not encountered in this series.

There were 2 occurrences of pneumothorax among our 64 procedures. All patients should be informed of this potential risk. An unexpected reduction in oxygen saturation or blood pressure should prompt immediate auscultation and observation for asymmetric chest expansion. Endoscopic evaluation of the tracheobronchial tree and the lungs is essential to exclude blood or mucus plugs causing desaturation. A chest radiograph should be obtained in the operating room if pneumothorax is suspected.

Lasers may produce extensive thermal necrosis and damage subglottic mucosa, leading to an extensive fibro-

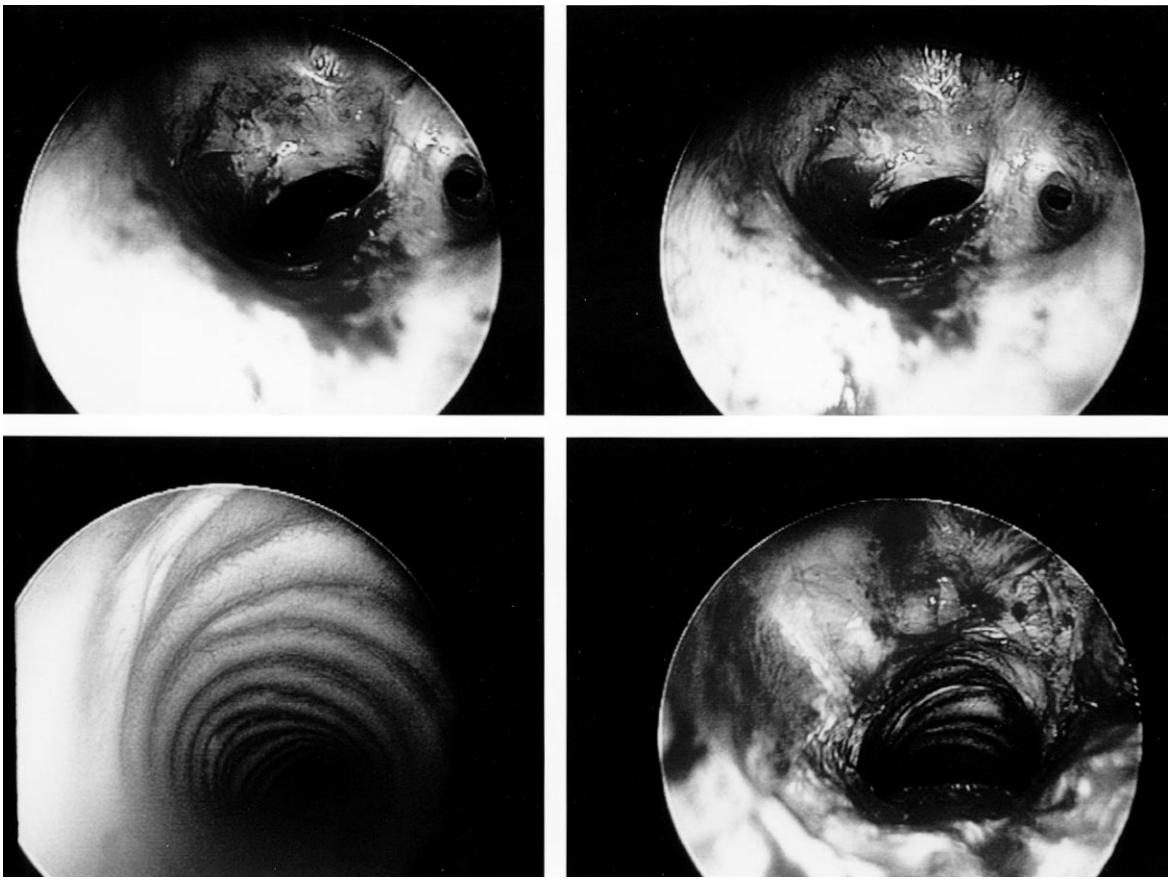

Figure 1. Endoscopic visualization of subglottic stenosis after laser resection and restenosis. Note the web of scar tissue (3 o'clock position) in the tracheal wall that was created by laser. Beyond the stenotic region, normal cartilaginous tracheal rings and mucosa can be seen (lower left panel).

blastic response[2]. In our series, all patients who presented with previous laser therapy had extensive secondary scarring.

Finally, it should be stressed that successful airway maintenance in WG goes beyond providing luminal patency of tubular structures. Clearance of secretions and meticulous care of the sinonasal tract are crucial. Humidification of the home environment, aerosol respiratory treatments, local nasal and sinus hygiene, liquid irrigation for removal of crusts, and lubricating creams and gels may all be helpful.

We conclude intralesional corticosteroid injection combined with dilation is an effective strategy to treat subglottic stenosis in WG. Best results were obtained in the absence of extensive scar caused by previous surgical procedures. We propose that ILCD be considered as an early first-line therapy for WG-SGS. The procedure can be safely repeated and does not cause tracheomalacia. The efficacy of this procedure eliminates the need for new tracheotomies in almost all patients. This observation stands in striking contrast to prior studies in which roughly half of all patients with WG-SGS required tracheotomy.

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