

# Subglottic stenosis in Wegener's granulomatosis: development during cyclophosphamide treatment with response to carbon dioxide laser therapy

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## Abstract

**A patient with Wegener's granulomatosis rapidly developed a circumferential subglottic stenosis while on a cyclophosphamide regimen that had caused resolution of systemic symptoms and pulmonary infiltrates. The stenosis developed in the area of previously noted tracheal ulceration and responded satisfactorily to carbon dioxide laser therapy.**

Disease of the upper airway is a common presenting manifestation of Wegener's granulomatosis.<sup>1</sup> Nasal or oral ulceration, epistaxis, sinusitis, or otitis is found in more than 90% of cases.<sup>2</sup> Although the larynx and trachea are frequently ulcerated,<sup>3</sup> subglottic and tracheal stenoses causing upper airway obstruction are rare. We describe a patient with Wegener's granulomatosis, apparently in remission while taking cyclophosphamide and prednisone, who developed upper airway obstruction that responded to carbon dioxide laser photoresection.

## Case report

A 21 year old college student developed cough, fever, hoarseness, sinusitis, and migratory arthralgia in January 1988. Haematuria and proteinuria were present. Chest radiography showed a right upper lobe infiltrate that cavitated after a course of erythromycin. Bronchoscopy showed circumferential ulcers in the subglottic area and smaller ulcers in the distal trachea. Tracheal and transbronchial biopsy specimens showed necrotising granulomas containing multinucleated giant cells. An open lung biopsy disclosed an active vasculitis in addition to necrotising granulomatous inflammation, consistent with Wegener's granulomatosis. In March 1988 treatment with oral cyclophosphamide 100 mg/day and prednisone 30 mg/day was started.

Over the next two months the right upper lobe pulmonary infiltrates disappeared completely and the patient became symptom free. In June 1988 increasing stridor developed over one week. Repeat bronchoscopy showed a circumferential subglottic stenosis 1 cm long with a 7 mm orifice. Biopsy of the granulation tissue showed fibrinoid necrosis of venous walls with a polymorphonuclear and histiocytic inflammatory infiltrate consistent with active Wegener's granulomatosis. The subglottic stenosis progressed despite increasing the cyclophosphamide dose to 150 mg daily. Severe dyspnoea during minimal exertion prompted surgical intervention. Suspension microlaryngoscopy with jet ventilation stabilised the airway. Carbon dioxide laser photoresection was performed without complications by microtrapdoor and radial excision techniques. Bronchoscopy six weeks after operation showed functionally normal airway without inflammation. At follow up at six months an asymptomatic narrowing in the subglottis responded to repeat laser treatment. The patient remains symptom free at one year.

## Discussion

Since the first cases of laryngeal lesions in Wegener's granulomatosis were reported in 1954<sup>4</sup> more than 30 cases of symptomatic subglottic stenosis have been described. Although laryngeal ulceration is found in 25% of untreated cases of Wegener's granulomatosis at necropsy,<sup>3</sup> subglottic stenosis causing upper airway obstruction remains a rare complication with heterogeneous modes of presentation.

Why Wegener's granulomatosis preferentially affects the subglottic area has not been explained. Although stenosis of the trachea and major bronchi has been recorded, most cases of airway obstruction affect the subglottis. In our case and others<sup>4</sup> ulcers at the site of subsequent areas of stenosis have been recorded. Endotracheal tubes and biopsies have been mentioned as possible causes of exacerbation,<sup>5</sup> but the biopsy specimens showing active vasculitis virtually exclude this possibility in our patient. Although multisystem disease is the most common presentation in younger patients,<sup>6</sup> isolated upper airway obstruction may be the presenting complaint<sup>7,8</sup> or may develop when the disease in other organs has been in complete remission for up to two years.<sup>5</sup>

Development of subglottic stenosis may occur during cyclophosphamide treatment, as our case and others show.<sup>2,9</sup> A less active vasculitis may predispose to the formation of granulation tissue as opposed to ulceration, for pathological specimens from tracheal stenoses in Wegener's granulomatosis show more fibrosis than active vasculitis.<sup>10</sup> We attempted a trial of more intensive medical treatment in view of the biopsy proved vasculitis, but the lesion was refractory to drug treatment.

Failure of medical treatment is not unique, and the course of subglottic stenosis in Wegener's granulomatosis remains variable. Spontaneous regression<sup>10</sup> and response to corticosteroids,<sup>8</sup> azathioprine,<sup>11</sup> and cyclophosphamide<sup>12</sup> have been reported. Radiotherapy of

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the area of stenosis in a dose of 1250 rads (12.5 Gy) over three weeks was of symptomatic benefit to one patient.<sup>7</sup> Mechanical relief of tracheal obstruction has been obtained with bronchoscopic dilation,<sup>10</sup> often at repeated intervals. Tracheotomy for progressive upper airway obstruction has remained the mainstay of treatment and is necessary in about one third of cases.

Vaporisation of tissue with minimal surrounding thermal damage has been the carbon dioxide laser's main contribution to the endoscopic management of subglottic stenosis. The techniques of microtrapdoor<sup>13</sup> and radial excision<sup>14</sup> are well suited to this wavelength and allow a considerable amount of tissue to be removed without circumferential denuding of the subglottis and the subsequent risk of a circumferential cicatrix. Suspension micro-laryngoscopy with jet ventilation afforded control over an airway that could not easily accommodate a 5.5 mm endotracheal tube. Although the techniques would not be suitable for a lesion obstructing the entire trachea, our 1 cm lesion was easily managed. The potential for restenosis after carbon dioxide laser excision of Wegener's induced subglottic stenosis is unknown. The recurrence of mild stenosis in our patient has necessitated the continuance of cyclophosphamide and prednisone despite the absence of clinical pulmonary or renal lesions.

An upper airway obstruction from subglottic

stenosis in Wegener's granulomatosis remains a challenging clinical problem. The addition of carbon dioxide laser photoresection to the therapeutic armamentarium appears to be useful in this rare disorder.

- 1 Wegener F. Uber generalisierte, septische Gefasserkrankungen. *Verhandl Deutsch Pathol Gesellsch* 1936;29:202-9.
- 2 Fauci AS, Haynes BF, Katz P, Wolff SM. Wegener's granulomatosis: prospective clinical and therapeutic experience with 85 patients for 21 years. *Ann Intern Med* 1983;98:76-85.
- 3 Walton EW. Giant cell granuloma of the respiratory tract. *Br Med J* 1958;ii:265-70.
- 4 Fahey JL, Leonard E, Churg J, Godman G. Wegener's granulomatosis. *Am J Med* 1954;17:168-79.
- 5 Lampman JH, Querubin R, Kondapalli P. Subglottic stenosis in Wegener's granulomatosis. *Chest* 1981;79:230-2.
- 6 Halstead LA, Larmody CS, Wolff SM. Presentation of Wegener's granulomatosis in young patients. *Otolaryngol Head Neck Surg* 1986;94:368-71.
- 7 Talerman A, Wright D. Laryngeal obstruction due to Wegener's granulomatosis. *Arch Otolaryngol* 1972;96:376-9.
- 8 Thomas K. Laryngeal manifestations of Wegener's granuloma. *J Laryngol Otol* 1970;84:101-6.
- 9 Rosenberg DM, Weinberger SE, Fulmer JD, et al. Functional correlates of lung involvement in Wegener's granulomatosis. *Am J Med* 1980;69:387-94.
- 10 Djalilian M, McDonald TJ, Devine KD, Weiland LH. Nontraumatic non-neoplastic subglottic stenosis. *Ann Otol* 1975;84:757-63.
- 11 Martin PD. Wegener's granulomatosis. *N Z Med J* 1974;79:965-9.
- 12 Flye MW, Mundinger GH, Fauci AS. Diagnostic and therapeutic aspects of the surgical approach to Wegener's granulomatosis. *J Thorac Cardiovasc Surg* 1979;77:331-7.
- 13 Dedo HH, Sooy CD. Endoscopic laser repair of posterior glottic, subglottic and tracheal stenosis by division or microtrapdoor flap. *Laryngoscope* 1984;94:445-50.
- 14 Shapshay SM, Beamis JF, Hybels RL, Bohegian RK. Endoscopic treatment of subglottic and tracheal stenosis by radial incision and dilation. *Ann Otol Rhinol Laryngol* 1987;96:661-4.

## BOOK NOTICE

**Adverse Reactions to Drug Formulation Agents: A Handbook of Excipients.** Murray Weiner, I L Bernstein. (Pp 463; \$150.) New York: Dekker, 1989. ISBN 0-8247-7944-4.

After I had decided to read this book over the Christmas holiday the thought weighed somewhat heavily after reading the subtitle *A Handbook of Excipients* (meaning that it dealt with adverse reactions to all non-pharmacological aspects of drug treatment, from delivery systems to drug containers). After reading two pages or so I was pleasantly surprised to find that the style was simple and readable. The volume is clearly divided into three parts, one of which is to be read, the second browsed through, and the third used as a work of reference. In part 1 the authors give an excellent introduction to the intricacies of the immunological system and its role in allergic reactions. The text is factual and heavily referenced but suffers from a lack of diagrams. These would have helped to explain some of the more complex mechanisms of immunological

defence and in particular cell mediated immunity. I was initially surprised to find such a comprehensive introduction to what was basically a pharmacological text; but the second author, I L Bernstein, is co-director of the allergy research laboratory at Cincinnati Medical School and the book reflects his knowledge in a commonsense (if American biased) review. The second part of the book deals in detail with the adverse reactions to excipients and divides them according to the type of material used—that is, bulk materials, coatings, flavouring agents, colourings, etc. Once again the text is heavily referenced, though some of the more modern methods of drug delivery, such as microencapsulation of materials, is dealt with rather scantily. Some of the more interesting clinical syndromes, such as the "ginger jake paralysis" associated with drinking sesame oil, are glossed over; more details of such curiosities would have made a more interesting book. Of particular interest to respiratory physicians is the section on propellents, including discussion of the increased mortality rate in young people with asthma in the UK in the 1060s. The final part of the book deals with allergic reactions to excipients and covers possible allergies in medical practice, including those from hearing aids and rubber gloves, in great detail. This section contains much useful information in addition to some of a more trivial nature. This is a useful addition to the allergy clinic library.—AHM