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Case report

Wegener's granulomatosis: isolated involvement of the trachea and larynx

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SUMMARY A 26 year old man with subacute hoarseness and stridor was shown to have Wegener's granulomatosis isolated to the trachea and larynx. Although isolated laryngeal Wegener's is unusual, a review of the literature suggests that early treatment with cyclophosphamide is warranted.

Key words: vasculitis, cyclophosphamide, stridor.

Wegener's granulomatosis typically presents as sinusitis, pulmonary infiltrates, and glomerulonephritis.[1–3] Occasionally, Wegener's granulomatosis appears, at least initially, to involve only one organ or one region, most commonly the lung.[2–4] Wegener's granulomatosis isolated to the tracheolarynx is rare and especially difficult to recognise since biopsies of this region rarely demonstrate vasculitis.[5–11] In an effort to promote early diagnosis of this now treatable disorder we report a case of isolated tracheolaryngeal Wegener's granulomatosis and review the pertinent literature.

Case report

A previously healthy 26 year old man was referred in July 1985 for evaluation of hoarseness, stridor, and dyspnoea. He had lost 3·5 kg but denied other symptoms. A detailed general physical examination was normal. Indirect laryngoscopy showed the subglottic larynx to be greatly narrowed circumferentially by boggy, erythematous folds of redundant tissue. The vocal cords were mobile.

The blood counts, chemistries, and urine analysis were normal. Skin tests for tuberculosis and coccidioidomycosis were negative. Chest and sinus *x* rays were normal. A computed axial tomographic

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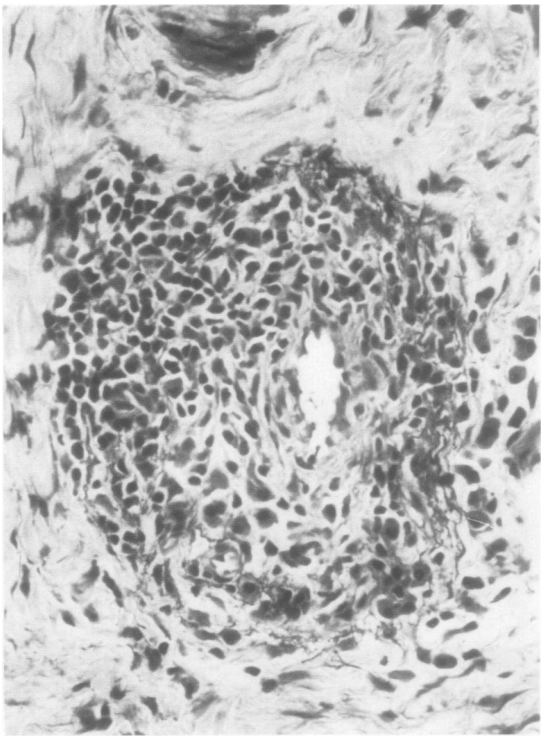

Fig. 1 *Laryngeal biopsy specimen showing small vessel vasculitis.*

Table 1 *Literature review of primary tracheolaryngeal Wegener's granulomatosis*

Reference No	*Sex*	*Age*	*Initial symptoms*	*Disease location*	*Laryngeal biopsy findings*	*Late manifestations*	*Therapy*	*Outcome (follow up)*
8	M	18	Hoarseness, dyspnoea	Upper trachea subglottis	Granuloma	Saddle nose, sinusitis, haematuria, proteinuria	Corticosteroids	*Death*
9	F	17	Hoarseness, sore throat, stridor	Subglottis, vocal cords	Not available	Skin vasculitis, glomerulonephritis	None stated	Tracheostomy, dialysis (14 mo)
7	M	55	Hoarseness	Subglottic mass	Granuloma	Glomerulonephritis	Cyclophosphamide, corticosteroids, azathioprine	Tracheostomy, transient renal, failure, remission (9 mo)
6	F	39	Hoarseness, stridor	Subglottis	Granuloma inflammation	Glomerulonephritis, lung vasculitis	Radiation, corticosteroids	Tracheostomy, *death* from renal failure
5	F	14	Hoarseness	Subglottis	Granuloma inflammation	Haematuria skin ulcers	Corticosteroids	Tracheostomy, skin ulcers, alive (10 mo)
11	M	51	Dyspnoea	Subglottis	Non-specific inflammation	Glomerulonephritis, skin purpura	Corticosteroids, cyclophosphamide	Tracheostomy, renal insufficiency, alive (1 mo)
10	M	52	Hoarseness	Vocal cords, subglottis	Necrosis, granuloma	None	Corticosteroids	*Death* from tracheal obstruction (54 mo)
This report	M	26	Hoarseness, stridor	Subglottis to carina	Granuloma, necrosis, vasculitis	None	Corticosteroids, cyclophosphamide	Tracheostomy, improved (12 mo)

(CT) scan of the trachea showed concentric soft tissue, narrowing from the subglottic region to the left mainstem bronchus. A description of the CT findings has been reported previously.[12]

Because of the severity of the laryngeal obstruction a tracheostomy was performed and biopsy specimens were obtained. Cultures of the biopsy specimens were negative. One biopsy specimen from the anterior tracheal wall contained a zone of granulation tissue infiltrated by inflammatory cells. A small vessel located in a non-inflamed area showed a destructive granulomatous vasculitis (Fig. 1).

The diagnosis of Wegener's granulomatosis was made, and treatment was started with prednisone 60 mg/day and cyclophosphamide 150 mg/day.

The stridor improved gradually. A CT scan in October 1985 showed a marked decrease in the soft tissue swelling throughout the larynx. When re-evaluated in May 1986, the patient was asymptomatic. Indirect laryngoscopy confirmed improvement in glottic and subglottic airway size.

Discussion

Our patient's presentation was unusual in two regards: firstly, his Wegener's granulomatosis appeared to be limited to one region, and secondly, the region of involvement was the larynx and trachea. Wegener's granulomatosis typically presents as a multisystem illness.[1–3] In some patients, however, the disease may appear to be limited to a single organ or region, most commonly the lung.[2 4] Many of these patients have subclinical evidence of other organ involvement or subsequently develop a life-threatening multisystem illness, thus emphasising the rarity of truly 'limited' disease.[2]

Wegener's granulomatosis presenting with isolated involvement of the trachea is rare.[13] Only seven previous cases of documented isolated laryngeal Wegener's granulomatosis have been described. Laryngeal disease more commonly occurs as a late complication of fully developed or previously treated Wegener's granulomatosis.[2 5–11 13–27]

Our patient's clinical picture resembles that of other patients with isolated laryngeal Wegener's granulomatosis (Table 1).[5–11] That our patient is male is consistent with the slight male predominance found both in isolated laryngeal Wegener's granulomatosis (male/female = 2·3) and in generalised Wegener's granulomatosis (male/female = 1·6). His relatively young age (26 years) is not surprising since patients with isolated laryngeal Wegener's are on average younger (36 years) than patients with typical Wegener's granulomatosis (44 years).[2] Indeed, three of the seven previously reported patients with laryngeal Wegener's granulomatosis were adolescents.[5 8 9] As with our patient, most other patients presented with subacute stridor or hoarseness, or both.

Additional similarities between our patient and those listed in Table 1 became evident when the larynx and upper airways were evaluated. In most patients, as in our case, direct laryngoscopy showed involvement of the subglottic region. Vocal cord involvement was less common. The disease can be localised, often to the posterior wall of the subglottic region, or diffuse, with circumferential narrowing. The mucosa may be erythematous, boggy, or ulcerated. Proliferation of granulation tissue produces mass lesions in some patients. Extension of the disease below the carina is quite rare. Tracheostomy was often required, as in our patient, to ensure adequate ventilation during the acute inflammatory phase of the disease.

The recognition of isolated laryngeal Wegener's granulomatosis is made especially difficult by the fact that the histopathology is often not considered diagnostic.[28] Typically, biopsy specimens from the upper respiratory tract of patients with Wegener's granulomatosis show acute and chronic inflammation with necrosis. Granuloma are often present, but vasculitis is rarely found.[25] Multiple laryngeal biopsies were performed in most of the seven previous cases, and vasculitis was found in none. In our patient, multiple biopsies at two different times were performed, one of which showed vasculitis, making this only the second time that vasculitis has been described on laryngeal tissue biopsy.[25]

The tendency to dismiss the diagnosis of Wegener's granulomatosis until and unless vasculitis is demonstrated is incorrect and results from a misconception of the clinicopathological features of Wegener's granulomatosis.[2 28 29] Although Wegener's granulomatosis is usually classified as a form of vasculitis, Wegener himself emphasised the importance of the necrosis with granuloma formation.[29] Of all the organs, the lung is the site where both the vasculitis and the granulomatosis necrosis are most frequently seen.[2] Biopsy specimens from other sites, especially the upper respiratory tract, rarely show all the 'classic' pathological findings.[2 28 29]

Thus the diagnosis of laryngeal Wegener's granulomatosis depends on the presence of a consistent clinicopathological picture as well as the exclusion of the other causes of laryngeal obstruction, which have recently been reviewed in detail.[25 30]

The outcome of primary laryngeal Wegener's granulomatosis appears to depend on the timing and

the type of treatment.[5–11] None of the seven previous cases received immunosuppressive therapy while the Wegener's granulomatosis was limited to the larynx. Subsequently, all seven developed either progressive laryngeal obstruction or disseminated disease (Table 1). Three patients, including our patient, were eventually treated with cyclophosphamide, and all improved. No patient remitted without cyclophosphamide therapy. This experience strongly suggests, but does not prove, the need for cyclophosphamide therapy in primary laryngeal Wegener's granulomatosis. Given the very poor outcome experienced by most patients with isolated laryngeal Wegener's granulomatosis who are untreated or treated after dissemination of their disease, early treatment with cyclophosphamide appears to be warranted.

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