

Case Report

Wegener's Granulomatosis Presenting With Stridor

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Wegener's Granulomatosis is a necrotising granulomatous disease affecting the upper and or lower respiratory tracts and associated with focal glomerulonephritis. Although multi-system disease, a localized form is well recognized as a distinct sub-type, with a better prognosis. We describe a case of localised tracheal Wegener's granulomatosis presenting with stridor. Otolaryngology perspectives of localized Wegener's granulomatosis have been discussed.

Key words: Tracheal stenosis, Wegener's granulomatosis, Stridor,

Wegener's granulomatosis (WG) is a granulomatous disease described by Wegener in 1936 and then in 1939 in the German-language literature¹⁻². He described a group of patients presented with upper respiratory tract disease and subsequently died of renal failure. In the English literature, Howells³ gave the first description of this disease in 1950 when he presented a case of a granulomatous lesion of the nose with necrotising vasculitis resembling polyarteritis nodosa. It fell to Godman and Churg⁴ in 1954 to highlight the three classic features of WG: necrotising granulomatous lesions of the upper and or lower respiratory tract, vasculitis and glomerulonephritis. These lesions can involve vessels of any size but predominantly small arteries, arterioles, veins, venules, and capillaries.

The aetiology of the disease remains unknown but it is believed to be an exaggerated or aberrant hypersensitivity reaction to an unknown antigen. The disease can present at any age with the mean age of onset of 45 years.

WG manifests in two forms: the disseminated disease, which involves mainly the respiratory tracts and kidneys, and the localized form (LWG) in which the kidneys are spared but any other system or site can be affected. In both forms, WG may present initially with head and neck signs and symptoms.

Case history

A 45-year-old lady presented in causality with intermittent breathing difficulty for last 7-8 months, which had gone worse for few days. In the past she had been under physicians for this symptom and was treated with various forms of inhalers. There was no previous admission or any medical illness. On examination she was afebrile, pale, looked exhausted with marked supraclavicular recession and alar flaring. She was unable to lie flat. She had biphasic stridor with initial Oxygen saturation of 85%. Systemic examination was unremarkable. A chest and lateral soft tissue neck X-rays were unremarkable.

Initial clinical impression was of an upper airway obstruction. She was immediately given 100 mg

Hydrocortisone and continuous Oxygen inhalation. ENT opinion was requested.

In ENT history she denied any hoarseness of voice, dysphagia or loss of weight. She was non-smoker with no previous surgery to upper aerodigestive tract or trauma. Examination with flexible nasendoscope revealed normal and mobile vocal cords. Rest of the head and neck examination was normal. Initial clinical diagnosis of subglottic obstruction with possibility of tumour.

A coronal laryngo-tracheo-tomogram showed significant narrowing of upper tracheal lumen (Fig. 1).



Fig. 1. A coronal laryngo-tracheal tomogram showing narrowing (arrows) of the upper tracheal lumen.

Blood tests showed white cell count 11/dl, Hb 10 g/dl, ESR 60 and CRP 45. Urinalysis and renal and liver function tests were normal. For further assessment she underwent laryngo-bronchoscopy under general anesthetic. This revealed granular mass extending from just below the subglottic area of larynx cords to upper 2-3 cm of trachea. Biopsy of this tissue showed chronic inflammatory cells with granuloma formation and blood vessels with necrotizing fibrinoid vasculitis (Fig 2), features consistent with WG. She was referred to clinical immunologist. At this stage anti-neutrophil cytoplasm antibody assay (ANCA) was positive cytoplasmic pattern i.e. c-ANCA.

Treatment was started as cyclophosphamide 50 mg TDS and prednisolone 30 mg a day. She showed significant improvement in her breathing. Repeat CRP and ANCA titres also followed the clinical improvement. Prednisolone was stopped after 2 months and cyclophosphamide after 18 months. She is currently on remission and on

trimethoprim-sulphonamide 600 mg once a day. There is no renal or pulmonary involvement at follow up after 24 months of initial presentation.

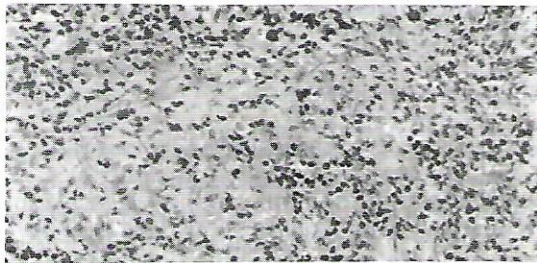


Fig. 2. Subglottic biopsy showing necrotizing fibrinoid vasculitis and mixed inflammatory cells destroying the surrounding tissue. (Hematoxylin-eosin, x 20)

Discussion

The concept of a localized form of WG was first given by Fienberg⁵. He described a case of localized pulmonary lesion under the name of "idiopneumonitic angiitis and granulomatosis". Carrington and Liebow⁶ further expanded this idea by presenting a series of 16 patients with similar pulmonary lesions. These lesions showed pathological features typical of WG and some of these patients showed longer periods of remission. This was followed by a series of four cases with localized pulmonary diseases⁷. The concept of LWG remained confined to lungs for a long time, based on the idea that "WG almost always involve pulmonary vessels"⁶. Gradually the awareness of involvements of head and neck areas further strengthens the existence of LWG as sub-type of the disease. One of the authors have also published a series of 6 cases of LWG with no renal or pulmonary involvement detected at the presentation or during follow-up of 3-7 years⁸.

The absence of renal involvement, which has been the most important prognostic factor in this disease, reduces the morbidity significantly in these cases. However, the destructive lesions may invade the surrounding tissues like orbit or intra-cranium. Therefore, it is essential to diagnose and treat these cases early in order to reduce the morbidity.

The three characteristic histological features are necrosis, granulomatous inflammation and vasculitis⁹. The necrosis is of aseptic type with a patchy distribution throughout the affected tissue and with irregular margins. Granulomatous inflammatory response is the aggregates of macrophages with multinucleated giant cells and varying degree of chronic or acute inflammatory cells. The vasculitis is typically in the form of a fibrinoid necrosis affecting the walls of small arteries or veins. The later is accompanied by varying degree of transmural infiltration of chronic inflammatory cells or in some instances by granuloma formation. The head and neck biopsies from patients that subsequently have been proven to have WG, lack one, two or even all of these "classic" features¹⁰.

The nose is the commonest site of involvement of WG¹¹. This was even known when this disease was not clearly defined and it was initially described as rhinogenic granuloma. The incidence of LWG in nose has been described 29-36%¹², in contrast to 64-80% in generalized disease¹³. Frequent crust formation is a common symptom and, nasal obstruction, serosanguineous discharge, bleeding, facial pain, vague nasal pain and loss of smell are the other features. Examination of the nose may be normal but may show granulations or thick crust, which upon removal reveal friable mucosa or a septal perforation. Examination of the nasopharynx may show an eroded and ulcerated vomer. Saddling of nose, due to destruction of septal cartilage has also been described¹¹. Progressive destructive lesions may extend into the orbit or intracranium.

Laryngeal involvement is in the form of a circumferential subglottic narrowing, usually without involvement of the vocal cords or distal trachea¹⁴. Once the stenosis is severe, it can result in intermittent stridor or acute upper airway obstruction and death. In majority of cases the laryngeal disease manifest late in the course of WG and rarely reported as an initial presentation¹⁵, unlike in our case. The differential diagnosis is considerable and includes tuberculosis, sarcoidosis, histoplasmosis and malignant tumours.

The incidence of ear involvement varies from 19-61%¹⁶. Serous otitis media is the commonest manifestation, which can either be unilateral or bilateral. The underlying pathology is a granulomatous obstruction of eustachian tube. Facial nerve palsy of lower motor neuron type can occur as a complication of otitis media. Acute mastoiditis can also complicate acute otitis media. Sensorineural hearing loss may occur due to granulomatous involvement of cochlear nerve¹⁷, immune complex deposition in the cochlea or vasculitis of the cochlear vessels.

The diagnosis is based on clinical features, Anti-neutrophil cytoplasm antibodies (ANCA) and biopsy of affected site. Non-specific abnormalities such as high ESR, normochromic normocytic anaemia, elevated immunoglobulins and positive rheumatoid factor are commonly seen in these patients. ANCA test was initially reported positive in 25 of 27 patients with active disease and 4 out of 32 with inactive disease¹⁸. Subsequently more specific form evolved i.e. cytoplasmic pattern of immunofluorescence (C-ANCA), which reflected the presence of antibodies to proteinase 3 (PR 3). Another pattern is P-ANCA, which shows antibodies to myeloperoxidase and is relatively non-specific.

The positive predictive value of ANCA increases with a C-ANCA pattern. The sensitivity of the C-ANCA is 60% in active loco-regional disease and 93% in generalized active disease¹⁹. The titres can be monitored to correlate the disease activity, treatment response and relapse after a period of remission.

The nasal biopsy can miss the patchy lesions of WG and some time a small biopsy with insufficient tissue shows a non-specific picture. Even in appropriate biopsy, the histological appearance may show granulomatous changes with or without necrotising vasculitis, but these features may be due to other forms of granulomatous conditions. Therefore, although multiple and repeated biopsies are essential, however the definite diagnosis relies on a combination of histological features with other findings, particularly a positive C-ANCA test.

The MRI scans of involved area can show granulomas as low signal intensity lesions²⁰. However in nasal involvement in early lesions, it is not possible to differentiate between mucosal inflammation and granulomatous tissue. Computerised Tomography (CT) scan may be helpful in the cases of bony destruction and intracranial extension of nasal lesions.

Cytotoxic drugs (such as cyclophosphamide, azathioprine, methotrexate) and corticosteroids are the mainstay of treatment²¹. Cyclophosphamide is the most efficacious drug treatment. In fulminant disease it can be given intravenously and then can be changed orally for continuation. The patient should be treated one year after remission has been achieved and then re-evaluated periodically for disease relapse. More recently antibiotics such as trimethoprim-sulfamethoxazole have been employed with some success²², especially in patients who are in remission to prevent further relapse.

Treatment with immunosuppressive agents combined with steroids will result in remission in over 90% of patients and a 75% five-year survival is expected²⁰. There is no difference in the treatment policy for LWG, although the treatment is more likely to be successful if the kidneys are not involved. Our case highlights the fact that this responds well to chemotherapy.

Conclusions

In otolaryngology patients can present as rhino-sinusitis, otitis media, hearing loss, facial palsy or laryngeal obstruction. Nasal biopsies and ANCA test should be performed in cases of abnormal appearance of nasal mucosa or septal perforation. Serial serological tests may be necessary to clinch a diagnosis. Our case highlights that not only the otolaryngologists but the physicians as well surgeons should aware of the potential for Wegener's granulomatosis to present with upper airway symptoms. A high index of suspicion will help to prevent diagnostic delay and the treatment may prevent the progression of destructive lesions.

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