RECURRENT WEGENER’S GRANULOMATOSIS WITH SUBGLOTTIC GRANULATION

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(Received May 2, 2000, accepted July 13, 2000)

Abstract: While following the course of patients with Wegener’s granulomatosis (WG) in which it had been possible to achieve a remission, we encountered a patient in whom we observed granuloma formation in the subglottis. A tracheotomy was performed because of the risk of respiratory distress, and after that there was a recrudescence of the patient’s WG. During the course of the above, the patient remained cANCA (anti-neutrophil cytoplasmic antibody with cytoplasmic pattern)-negative. When these facts were considered, it appeared that when the lesions are localized and progressing gradually, cANCA positivity does not develop. While cANCA test has gradually become a powerful tool for the diagnosis of WG, a comprehensive physical examination to identify localized lesions, together with biopsy and histopathological examination, should allow the diagnosis of WG.

Key words: Wegener’s granulomatosis, subglottic granuloma, anti-neutrophil cytoplasm antibody (ANCA)

INTRODUCTION

Although Wegener’s granulomatosis (WG) is a systemic necrotising granulomatous vasculitis, the first symptoms usually arise from the head and neck region in most patients1,2). Therefore, the majority of patients with this disease usually consult an otolaryngologist. We encountered a patient who developed WG after surgery for sinusitis, but recurred with subglottic granulation during a follow-up after a complete remission. A relapse occurred after tracheotomy performed for upper airway narrowing. We describe the clinical course in this patient, from the
onset to recurrence, demonstrating changes in anti-neutrophil cytoplasmic antibody with cytoplasmic pattern (cANCA) that correlates with disease activity; i.e., rise during exacerbation of the condition and fall or disappear during remission\textsuperscript{3–7}.

CASE REPORT

A 21-year-old male, with a past history of hospitalisation for pneumonia in January 1989, underwent a Caldwell-Luc operation for right chronic sinusitis in May 1989. The family history was negative and preoperative physical examination was also negative. The patient developed otitis media on the 8th day and facial paralysis on the 14th day after surgery for sinusitis which was treated as postoperative infection with antibiotics, anti-inflammatory agents and prednisolone. The symptoms improved, including those related to sinusitis, and the patient was discharged from our hospital in June 1989. However, during the postoperative follow-up at the outpatient clinic, he developed pneumonia and nephritis refractory to antibiotics. Based on the development of repeated infections within a short period of time, a provisional diagnosis of an immunocompromised state was made and the patient was admitted to the Department of Internal Medicine for further investigation. Tracheal and renal biopsies (Figs. 1 and 2) were obtained soon after admission which confirmed the diagnosis of WG on July 6, 1989. A positive cANCA titer (1:180) was noted at that stage. Pulse therapy with prednisolone was initiated which resulted in a complete remission, and a decrease in the titer of cANCA to undetectable levels on October 16 and November 20. The patient was discharged on December 14 after an uneventful post-treatment period, and followed-up at the outpatient clinic of the Department of Otolaryngology.

In April 1990, granulation was noted in the subglottic area on clinical examination and magnetic resonance imaging (Figs. 3 and 4). Although cANCA titer was negative on May 25, 1990, the subglottic granulation tissue had gradually increased.

Fig. 1. Photomicrograph of the tracheal biopsy.
Note the many giant cells and inflammatory cells with necrotising granuloma formation (\textasteriskcentered).
Fig. 2. Photomicrograph of the renal biopsy. Note the glomerulonephritis (*).

Fig. 3. Examination of the laryngeal region. Note the presence of granulation lesion (arrow) in the subglottic region protruding into the space between the vocal cords, causing narrowing of the upper airway.

Fig. 4. MRI image of the larynx. Note the presence of granulation lesion in the subglottic space (arrows).
in size and the patient complained general fatigue and low fever. We speculated a recurrence of WG from clinical viewpoint. The patient was readmitted to the Department of Otolaryngology in order to relieve progressive dyspnoea caused by glottic narrowing and was tracheotomised on October 3, 1990. A thorough preoperative examination was again negative except for a mild renal dysfunction. Tracheotomy was performed under local anesthesia. For this purpose, a longitudinal skin incision was made and the thyroid gland was exposed, ligated and separated in the midline, and tracheostoma was created at the third tracheal ring. A careful examination of the upper trachea and subglottic area through the tracheal stoma showed granulomatous lesions restricted to the subglottic area without any other lesions in the respiratory tract (Fig. 5). A tracheal cannula was inserted through the stoma. Examination on the first few postoperative days showed no change in renal function and a negative titer of cANCA. The patient was discharged on October 15, 1990. During the follow-up at the outpatient clinic, pus (Staphylococcus aureus was detected on culture) and granulation tissue (histopathologically confirmed) were noted around the tracheostoma on October 26, 1990. Although no deviations of the trachea or abnormal shadows were detected on a chest X-ray film, the patient was diagnosed as having recurrent WG at the Department of Internal Medicine and was readmitted for further evaluation. Prednisolone pulse therapy resulted in a complete remission and the patient was discharged from the hospital on November 15, 1990. During the most recent follow-up visit almost six years after the last hospitalisation, the patient was well with no evidence of recurrence and the titer of cANCA was still negative. Although a small subglottic granulation tissue was evident, it had remained dormant throughout the period.
DISCUSSION

Several external stimuli participate in the development of WG\(^9\). WG initially developed in our patient one month after surgery for sinusitis and recurred 24 days after tracheotomy. Thus, surgery seemed to induce exacerbation of WG in our patient.

Early diagnosis of WG is difficult but important because untreated WG usually runs a rapidly fatal course with the mean survival of untreated WG being 5 months with 82% of patients dying within the first year\(^9\). The disease begins often as a localized process, and the initial lesions develop in the head and neck region in most patients\(^1,2\). Therefore, otolaryngologists should be aware of the early manifestations of this disease and are also responsible for early diagnosis. The diagnosis of WG was based on a combination of clinical and histopathological features in the past. However, recent studies have identified cANCA in the serum as a specific diagnostic marker of WG\(^5,10\). Two ANCA patterns may be seen; a cytoplasmic pattern (cANCA) and the artifactual perinuclear pattern pANCA\(^11,12\). Although some clinical overlap has been seen between these, the two patterns have different disease associations. However, cANCA has predominantly been associated with WG, and pANCA with microscopic polyarteritis, other vasculitides, idiopathic necrotizing and crescentic glomerulonephritis, and other diseases\(^4,11,13\). There also appears to be a good correlation between disease activity with cANCA titer increasing during exacerbation of the disease and decreasing or becoming undetectable during remission\(^3,7,14\). More laboratories are currently using cANCA test as the third criterion for establishing the diagnosis of WG.

In the present case, cANCA titer was high (1:180) at the onset of the disease and then decreased during remission. However, the titer remained negative although subglottic granulation and renal dysfunction developed subsequently in this patient. Recurrence of WG was considered to have developed after tracheotomy although the specific antibody was not detected in the serum. This finding suggests that localized, slow growing WG lesions are perhaps not associated with elevation of cANCA titer. Therefore, measurement of cANCA titer should be regarded as an auxiliary diagnostic test for WG and patients with localized WG lesions may be negative for cANCA. Similarly, some reports described negative cANCA test results with WG, even those with local active disease\(^5,10\). While cANCA test has gradually become a powerful tool for the diagnosis of WG, a comprehensive physical examination to identify localized lesions, together with biopsy and histopathological examination, should allow the diagnosis of WG.

REFERENCES


