Figure 3. Anti-BPI autoantibody levels during 3-month follow-up. All sera were diluted 1:100 and results were expressed as a percentage of a reference sample. Squares represent IgG and triangles IgA anti-BPI levels. The dashed line indicates the upper normal limit for both isotypes, which is the mean + 3 SD of 46 normal blood donors. Arrows indicate the onset or relapses of pulmonary infection and rash.

tase,13 and it has been shown that both elastase and proteinase 3 can cleave BPI.14 It is possible that infection with P. aeruginosa in the presence of α1-AT deficiency results in an excess of free proteinases within the lung, which can further damage the lung and could exacerbate the effect of anti-BPI antibodies. The nonneutralized products of the LBP-LPS-monocyte interaction would be free to initiate endothelial damage and a vasculitis. These mechanisms may account for the rather unusual observations of progressive bronchiectasis and a leukocytoclastic vasculitis involving skin and probably kidneys at the times of P. aeruginosa infection.

This is the first demonstration of an association between a well-defined ANCA specificity BPI and bronchiectasis. We suggest that infection plays an etiologic role in the development of vasculitis and that anti-BPI autoimmunity, by interfering with the ability of BPI to neutralize Gram-negative bacteria, also may be important.

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Treatment of Diffuse Tracheomalacia Secondary to Relapsing Polychondritis With Continuous Positive Airway Pressure*

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Relapsing polychondritis (RP) is a rare disease characterized by recurrent inflammation and destruction of the cartilaginous structures. Tracheobronchial chondritis is a dreaded complication of RP. We wish to report a case of RP of the trachea and bronchi which was treated with nasal continuous positive airway pressure. (CHEST 1997; 112:1701-04)

Key words: CPAP; relapsing polychondritis; tracheomalacia

Abbreviations: CPAP=continuous positive airway pressure; RP=relapsing polychondritis

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Relapsing polychondritis (RP) is a rare disease of unknown cause characterized by inflammation of the cartilaginous structures. It typically manifests as auricular chondritis, polyarthritis, and nasal chondritis.\textsuperscript{1,2} Involvement of the respiratory tract is a dreaded complication and typically occurs later in the course of RP. Up to 50% of patients will die from respiratory tract complications. Treatment for RP-related tracheomalacia is limited and surgical repair is generally restricted to patients with localized disease. Herein is the report of a patient who had dramatic and extensive tracheomalacia as the sole feature of RP. Continuous positive airway pressure (CPAP) was used effectively during her illness.

**Case Report**

A 46-year-old woman was transferred to the Toronto Hospital for management of subglottic stenosis. She had been managed in the past for presumed asthma with bronchodilators and oral corticosteroids. She never smoked and had no occupational exposures. Six months prior to admission she developed increasing paroxysms of breathlessness and cough. Her activities of daily living were becoming increasingly limited owing to persistent dyspnea, and she eventually became completely bedridden. There was no history of fever or sputum production. She had no eye or otolaryngologic complaints. Examination revealed use of accessory muscles, and marked inspiratory and expiratory wheezing was heard throughout both lungs. There was no evidence of auricular or nasal abnormalities. Plain chest radiography was normal. A CT scan of the lung was performed and demonstrated diffuse narrowing of the tracheobronchial tree (Fig 1). There was also diffuse thickening of the bronchial walls. Small flecks of calcium in the bronchi were seen in some areas. Rigid bronchoscopy demonstrated extensive airway collapse during expiration. Repeated endobronchial biopsies taken at that time revealed only dense subepithelial fibrosis and patchy squamous dysplasia. The diagnosis of idiopathic tracheobronchomalacia was made. She was treated initially with prednisone, 30 mg/d. Because of the severity of her symptoms and extensive respiratory tract involvement, she began receiving nasal CPAP at 10 cm H\textsubscript{2}O. This was accompanied by a marked improvement in her breathlessness and reduction in bronchodilator use. Episodes of wheezing and stridor occurred less frequently and responded to nebulized racemic epinephrine.

Over the next 2 months, her level of activity increased and she felt well. Attempts to discontinue the nasal CPAP were accompanied by a marked increase in respiratory distress. A subsequent CT scan performed with and without CPAP was done, but it could not be reliably determined if CPAP increased the bronchial caliber. A portable battery-operated CPAP unit (Respirronics; Murrysville, Pa) was provided to improve ambulation and allowed her to venture outdoors. The unit was attached to a rechargeable 12-V marine battery linked to an AC/DC power converter. The battery lasted approximately 9 h and required 12 h to recharge. The entire system was mounted to a patient walker with the battery bolted into the basket and covered. The CPAP unit was fastened to the seat of the walker to facilitate the unit’s movement from the walker to the bedside. To facilitate further independence, she also used a Down’s mask with an expiratory positive airway pressure of 10 cm H\textsubscript{2}O. The Down’s mask is a full-face mask with two one-way valves—an inspiratory valve at the level of the mouth and an expiratory valve above it. A spring-loaded positive end-expiratory pressure valve was attached to the expiratory port to provide an expiratory positive pressure.

The patient found this to be less comfortable than nasal CPAP. The Down’s mask was used as a backup system in case of equipment failure and for activities such as bathing.

Unfortunately, 3 months following the initiation of nasal CPAP, her breathlessness recurred and was refractory to an increase in CPAP to 12.5 cm H\textsubscript{2}O. She also noted difficulty with clearing secretions due to pain from recent lumbar fractures related to steroid therapy.

She was readmitted to our hospital and a T-Y stent was placed through the third tracheal cartilage, and its position was confirmed bronchoscopically. This stent is made of a soft pliable plastic (Silastic; Benson Hood Laboratories; Pembroke, Mass) and was positioned cephalad 1 cm below the vocal cords and extended midway down the left mainstem bronchus and down the right stem bronchus to the upper lobe takeoff of the right lung. Her symptoms were significantly improved with the T-Y stent.

**Figure 1.** Noncontrast CT scan which was representative of the diffuse airway narrowing seen in this patient. There is marked narrowing of the right bronchus intermedius (arrow) and left mainstem bronchus (5-mm collimation).

**Figure 2.** Photomicrograph of tracheal cartilage showing numerous empty lacunae and significant erosion by a mixed population of inflammatory cells composed of neutrophils, eosinophils, lymphocytes, plasma cells, and occasional giant cells, consistent with polychondritis (hematoxylin-eosin, original ×100).
stent; however, she experienced difficulty in clearing secretions. The stent was later replaced with a Montgomery T-tube to allow for easier clearance of secretions. After surgery, the patient continued to require nasal CPAP intermittently (with the T-tube cuffed) for episodes of stridor and respiratory distress. Eventually, a tracheobronchoplasty was performed with the use of Marlex surgical mesh (Davol, Inc; Cranston, RI) in an attempt to create permanent airway stenting. Via a right thoracotomy, the entire airway from the apex of the chest to the bronchial bifurcations bilaterally was exposed. A double sheet of Marlex (Trelec; Meadox Medical, Inc; Oakland, NJ) was sutured to the tracheobronchial tree with multiple interrupted 4-0 Ticon (Ethicon; Somerville, NJ) sutures in order to "mattress" the Marlex to the membranous trachea and bronchi.

After a 2-week period of improvement, she developed episodes of hypoxia, pneumonia, and mucus plugging which required mechanical ventilation. Unfortunately, her course was further complicated by the development of the suture line in the posterior membranous trachea. Attempts to ventilate the patient using high-frequency jet ventilation were unsuccessful, and the patient died. An autopsy was performed and revealed erosion of the tracheal and bronchial cartilage by a mixed population of inflammatory cells consistent with the diagnosis of RP (Fig 2). The inflammatory process was diffuse and extended well beyond the region of the airway that was stented. Consequently, the histologic findings were not secondary to trauma or from manipulation of the airway.

DISCUSSION

Patients with RP typically present with auricular chondritis, inflammatory arthritis, and nasal chondritis. Respiratory tract involvement in RP is an uncommon presenting feature, but its incidence increases as the disease progresses. Females develop airway complications more frequently.\textsuperscript{5-7} Patients who present with respiratory tract involvement have a worse prognosis than those with other organ involvement and have a poorer response to oral corticosteroids.\textsuperscript{2,3,5} The patient reported herein was unusual in that she had no other organ involvement from RP apart from extensive and severe airway disease.

The mainstay of therapy for RP consists of nonsteroidal anti-inflammatory drugs, high-dose corticosteroids, and immunosuppressants.\textsuperscript{2,3,6} There are few therapeutic options available for patients who develop airway complications. During acute exacerbations of respiratory RP, racemic ephedrine may be beneficial in relieving symptoms.\textsuperscript{7} Surgical interventions may not be beneficial in patients with extensive airway involvement but may be useful for localized diseased areas.\textsuperscript{8} The few surgical options available for RP include tracheotomies and Montgomery T-tube stents. Most case reports of surgical resection or tracheoplasties have shown poor outcomes and are thus rarely considered palliative.\textsuperscript{9,10} In fact, if the diagnosis of RP had been made earlier, surgery would not have been performed.

There is no mention in the medical literature of the use of nasal CPAP for the treatment of RP. Nasal CPAP is noninvasive, is relatively simple to use, and has few side effects. It effectively acts as a "pneumatic" splint for the affected airway and prevents tracheobronchial collapse.\textsuperscript{10} CPAP has been reported in the treatment of patients with variable intrathoracic obstruction.\textsuperscript{11} As best as can be determined, only one previous report has described the use of CPAP in adults with tracheomalacia. Ferguson and Benoist\textsuperscript{10} described three patients with tracheobronchomalacia in whom CPAP therapy improved airflow limitation. This was demonstrated by comparing spirometry values with and without the use of CPAP and by using bronchoscopically recorded pictures to demonstrate an improvement in the patency of the lower airway during exhalation while the patient was receiving CPAP. There have been several case reports describing the use of CPAP in tracheobronchomalacia in children.\textsuperscript{8,12} In one report in infants, the level of CPAP required was determined fluoroscopically by monitoring airway collapse during the breathing. The level of inspiratory pressure was then titrated to the level that abolished the segmental collapse.\textsuperscript{8} In the patient reported herein, an attempt was made to use CT to demonstrate the degree of airway collapse and document the effect of CPAP. Improvement in airway caliber could not reliably be detected using this imaging modality. Spiral CT scans may have more reliably demonstrated collapse of the airway during breathing. Unfortunately, this technology was not available at the Toronto Hospital at the time.

Due to the patient's dependence on CPAP, a backup system was required in case of equipment failure. Unfortunately, the expiratory positive airway pressure system or Down's mask was tolerated for only short periods of time. This system required a significant increase in inspiratory effort since large subatmospheric pressures had to be generated to open the mask's valves.

Our patient improved with relatively low levels of expiratory pressure via CPAP. With few surgical options available for patients with diffuse respiratory tract disease from RP, nasal CPAP represents a potentially effective, albeit temporary therapeutic modality.

REFERENCES

Necrotizing Tracheobronchitis With Progressive Airflow Obstruction Associated With Paraneoplastic Pemphigus*

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Paraneoplastic pemphigus (PNP) is an autoimmune disease associated with leukemia and non-Hodgkin’s lymphoma. A patient with stage IVB poorly differentiated lymphocytic lymphoma developed characteristic upper and lower airway involvement with profound mucocutaneous erosion and tracheobronchial epithelial desquamation. Immunofluorescence testing confirmed autoantibody deposition along the basement membrane of bronchial epithelium. Disruption of the cellular adhesion mechanisms, including desmosomes, hemidesmosomes, and possibly the integrim subunits, is presumed to have led to disruption and desquamation of the tracheobronchial epithelial barrier, severe obstruction of the airways and hypoxia, and possibly bacterial superinfection. As far as can be determined, the feature of airflow obstruction occurring in association with PNP has not been described. Physicians should be aware that these complications of PNP may rapidly lead to hypoxic respiratory failure and death. (CHEST 1997; 112:1704-07)

Key words: airway obstruction; autoantibody; desmosome; hemidesmosome; necrotizing tracheobronchitis; non-Hodgkin’s lymphoma; paraneoplastic pemphigus

Abbreviations: IIF=indirect immunofluorescence; PNP=paraneoplastic pemphigus

Paraneoplastic pemphigus (PNP) is an autoimmune disease which occurs in association with leukemia, malignant lymphomas, and other neoplasms.1-4 Wide-spread inflammatory vesiculobullous lesions involving the skin and the oral and conjunctival mucosae are characteristic.1,3,5 Polyclonal IgG autoantibodies that bind to epithelial proteins of desmosome and hemidesmosome origin have been identified by immunoprecipitation techniques.1,5-7 These proteins have been implicated as a cause of the blistering and erosive mucocutaneous lesions found in PNP.1,5,7,8

Although pulmonary involvement leading to respiratory compromise in patients with PNP has been previously reported, the information about this association is limited. A man with non-Hodgkin’s lymphoma developed PNP and a necrotizing tracheobronchitis associated with severe airflow obstruction and hypoxia. This case report will help further define the pulmonary manifestations of this increasingly recognized but uncommon paraneoplastic process.

REPORT OF A CASE

A 57-year-old man who had never smoked had stage IVB nodular poorly differentiated lymphocytic lymphoma and was treated with cyclophosphamide, doxorubicin, vincristine, and prednisone combination therapy in 1990. From 1991 through 1992, several chemotherapeutic regimens were administered because of persistent lymphomatous infiltration of the bone marrow, eventually with successful control of the disease.

In October 1993, vesiculobullous lesions developed over his trunk, upper extremities, lips, oral mucosa, and conjunctivae. A skin biopsy specimen failed to reveal evidence of acantholysis or deposition of IgG, IgM, IgA, and complement. A presumptive diagnosis of bullous pemphigoid was made, and treatment with dapsone and prednisone was instituted. Four months later, he presented with progressive dyspnea, wheeze, and cough. He described two-pillow orthopnea and rare episodes of paroxysmal nocturnal dyspnea and denied fever, diaphoresis, or chest pain. Initial examination revealed a respiratory rate of 18 breaths per minute, a clear chest examination, and normal heart sounds. A maculopapular rash was present over the trunk and extremities and pustular vesiculobullous lesions were found to cover the buccal mucosa, the gums, the soft palate, the lips, and the nasal and conjunctival mucosa.

Laboratory examination revealed a WBC count of 5.100/mm^3. The chest radiograph showed a diffuse, faint reticular pattern.

With the patient breathing room air, arterial blood gas values were as follow: pH, 7.46; PCO2, 44 mm Hg; and PaO2, 55 mm Hg.

A high resolution chest CT scan revealed normal pulmonary parenchyma and pleura and nonpathologic mediastinal lymphadenopathy. Pulmonary function testing revealed moderate obstruction with air-trapping and a significant reduction in the diffusing capacity (Table 1, examination 1).

Another skin biopsy was done, and it demonstrated suprabasal acantholysis and focal erosion. Indirect immunofluorescence (IIF) studies confirmed linear deposition of IgG along the basement membrane zone and on the surface of keratinocytes in the lower portion of the dermis. These findings supported a diagnosis of PNP. A bronchoscopy performed to exclude the possibility of an opportunistic infection disclosed pustular, vesiculobullous lesions which covered the nasal, nasopharyngeal, and laryngeal mucosa. Copious mucopurulent secretions filled the tracheobronchial lumina. The airways were edematous and erythematous and exhibited white, plaqueike lesions which were adherent to the bronchial mucosa throughout the tracheobronchial tree.

Cytopathologic examination was negative for lymphomatous