

Respiratory Failure Secondary to Relapsing Polychondritis

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Introduction

Diffuse airway narrowing of the trachea or main bronchus may result from various autoimmune connective tissue diseases. A careful clinical and pathological evaluation is warranted given the broad differential diagnosis. Relapsing polychondritis (RP) is a rare multisystem disorder that primarily targets cartilaginous structures; however, non-cartilaginous tissue invasion is also seen. Airway involvement by RP is not uncommon, and extra pulmonary manifestations are almost always the key to the diagnosis. Airway chondritis, diffuse tracheobronchial disease with tracheomalacia, and recurrent inflammation and infections as seen with RP are associated with poor prognosis. Hence, making an early diagnosis and providing prompt treatment in the early stages of the disease can change patient outcome. We report a case of a patient presenting with fever, cough, and RP who was diagnosed based on characteristic clinical and pathological findings.

Case Summary

A 65-y-old African American male presented with a 3-week history of fever, dry cough, ear and nose pain, and new onset hoarseness of voice. He had received 1 week of oral antibiotics for the treatment of community-acquired pneumonia and otitis externa. He denied nasal or ear discharge, skin rash, joint pain, nausea, vomiting, diarrhea, abdominal pain, hematuria, night sweats, chills, rigors, and appetite or weight

loss. On presentation, he was febrile at 38.2°C and tachypneic at 30 breaths/min, and he had a blood pressure of 105/70 mm Hg. Prominent physical findings included a flattened nasal bridge and swollen erythematous auricles that were tender to palpation (Fig. 1). A chest examination revealed diminished breath sounds in the left base with no adventitious sounds. A complete blood profile was significant for anemia, with hemoglobin of 8 g/dL and leukocytosis of 27,000 white blood cells/ μ L. Arterial blood gas results revealed respiratory acidosis with pH 7.29, P_{aCO_2} 58 mm Hg, and P_{aO_2} 84 mm Hg on 2 L/min oxygen. He was initiated on

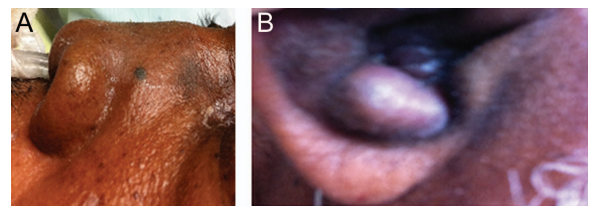


Fig. 1. A: Flattened nasal bridge (saddle nose deformity). B: Swollen and erythematous pinna and tragus of the left ear.

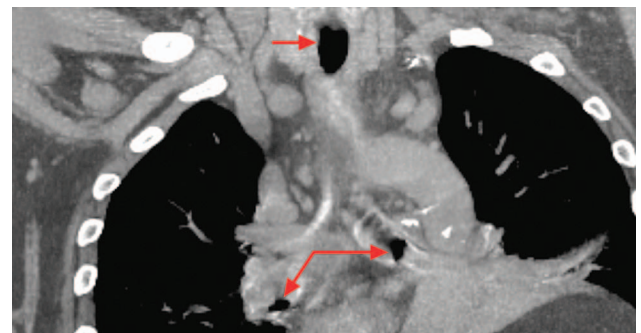


Fig. 2. Diffuse narrowing of the trachea and right and left main bronchus (arrows).

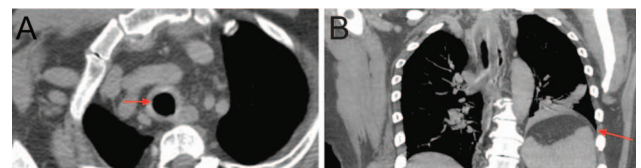


Fig. 3. Computed tomograms showing tracheobronchial wall thickening and hemidiaphragm elevation (arrows).

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The authors have disclosed no conflicts of interest.

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DOI: 10.4187/respcare.02381

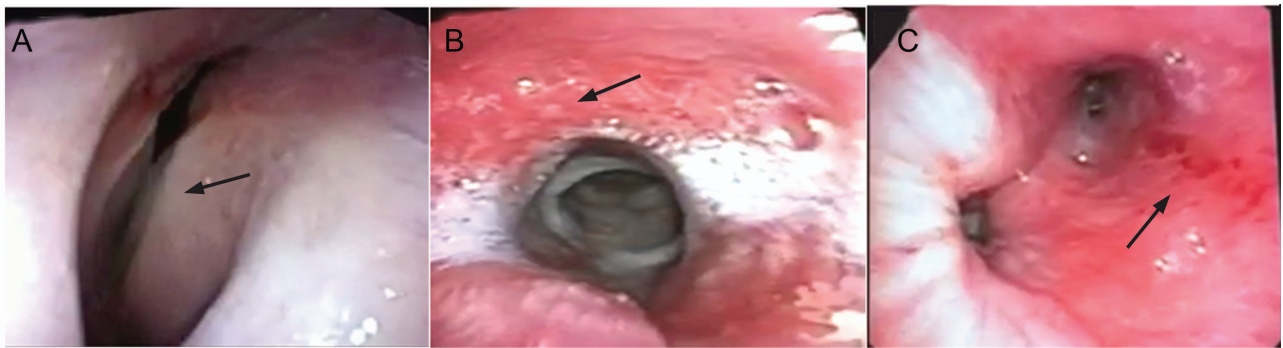


Fig. 4. A: Apposition of vocal cords during inspiration: paroxysmal vocal cord motion. B: Mucosal edema and erythema of the lower trachea and left main bronchus. C: Mucosal edema and erythema of the left lower lobe bronchus.

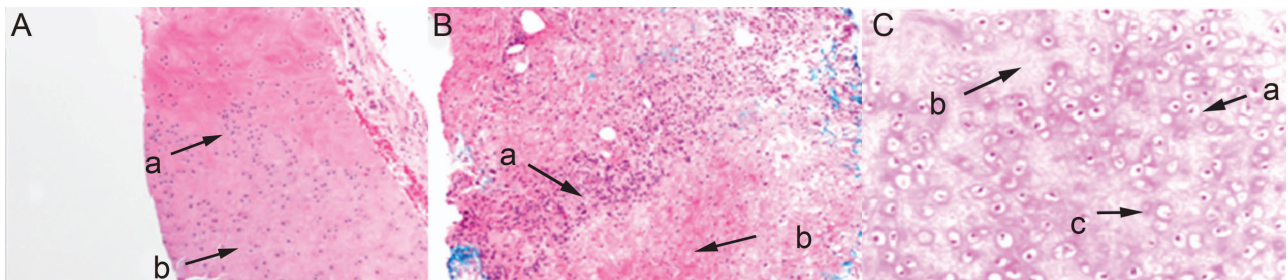


Fig. 5. A: Degenerated matrix (a) and normal matrix (b). B: Granulation tissue with fibroblasts (a) and degeneration of the matrix at the junction of granulation tissue and normal cartilage (b). C: Normal chondrocyte (a), degeneration of the matrix (b), and chondrocyte with area of necrosis (c).

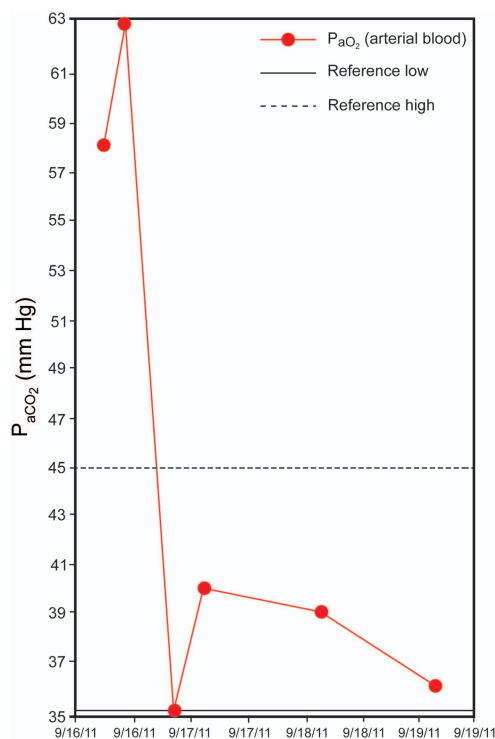


Fig. 6. Downtrend of P_{aCO_2} after initiation of noninvasive ventilation. The dashed line represents the normal P_{aCO_2} of 45 mm Hg.

noninvasive ventilation at an inspiratory pressure of 10 cm H₂O and an expiratory pressure of 5 cm H₂O along with 2 L/min oxygen. A computed tomography scan of the chest showed circumferential thickening of the trachea and an elevated left hemidiaphragm (Figs. 2 and 3).

Other relevant laboratory data included an elevated erythrocyte sedimentation rate of 120 mm/h and C-reactive protein of 23.7 mg/dL. The anti-neutrophil cytoplasmic antibody panel, anti-nuclear antibody, and rheumatoid factor were unremarkable. A flexible bronchoscopy performed with noninvasive ventilation revealed a paroxysmal vocal cord motion during inspiration (Fig. 4A), erythematous tracheal mucosa, and airway wall thickening of the left main bronchus (Fig. 4, B and C). An auricular biopsy showed areas of degenerated matrix and chondrocyte necrosis, with areas of granulation (Fig. 5). Based on the clinical presentation and histological findings, a diagnosis of RP was made. Treatment was initiated with prednisone at 60 mg/d. The patient's symptoms, including fever, dyspnea, hoarseness of voice, and ear and nose pain, markedly improved within 1 week. There was also improvement in ventilation, with a gradual downtrend of P_{aCO_2} (Fig. 6). Subsequently, the prednisone dose was gradually tapered over a period of 4 months. A repeat computed tomography scan of the chest at 4 months revealed resolution of tracheal wall thickness (Fig. 7). Five months after discontinuation of steroids, the patient had a relapse with an in-

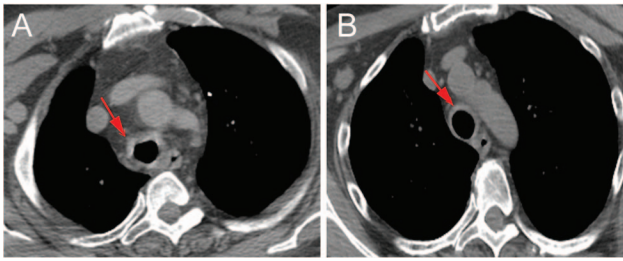


Fig. 7. A: Before prednisone therapy. B: Four months after prednisone therapy. Note the resolution of the circumferential thickening of the trachea after prednisone treatment (arrows).

creased erythrocyte sedimentation rate and C-reactive protein (Fig. 8). He was initiated on prednisone at 60 mg/d along with azathioprine at 100 mg/d. He continued to have persistent respiratory symptoms with elevated inflammatory markers; hydroxychloroquine at 200 mg twice daily was subsequently added to the regimen. The three-drug regimen was continued, with the patient demonstrating significant clinical improvement and reduced inflammatory marker levels.

Discussion

RP is a multisystem disease involving the ears and respiratory, musculoskeletal, skin, cardiovascular, renal, and

neurological systems. McAdam et al¹ initially proposed a diagnostic criterion that has since been modified. Currently, the diagnosis is made if there are at least three of the following features: ocular inflammation; audiovestibular damage; non-erosive seronegative polyarthritis; and bilateral auricular, nasal, and laryngotracheal chondritis, along with histological confirmation and response to steroids/dapsone.^{2,3}

Although commonly seen, airway involvement indicates poor prognosis if not diagnosed early.⁴ Involvement of larger airways such as the larynx and tracheobronchial tree is seen in almost half of patients with RP. Early bronchoscopy has a high diagnostic yield for diagnosing and preventing complications.⁵ The presenting symptoms can include hoarseness of voice, dysphonia, and respiratory distress.⁶ Cartilage inflammation leads to laryngeal and tracheal collapse with secondary infection.⁷ Apart from infection, a delay in diagnosing and treatment leads to tracheobronchomalacia and dynamic airway collapse.

Differential diagnosis of patients presenting with laryngotracheobronchial inflammation and narrowing should include granulomatosis with polyangiitis or Wegener's granulomatosis, amyloidosis, sarcoidosis, tracheopathia osteochondroplastica, and RP.⁸ In granulomatosis with polyangiitis, tracheal strictures, focal laryngeal stenosis, or cal-

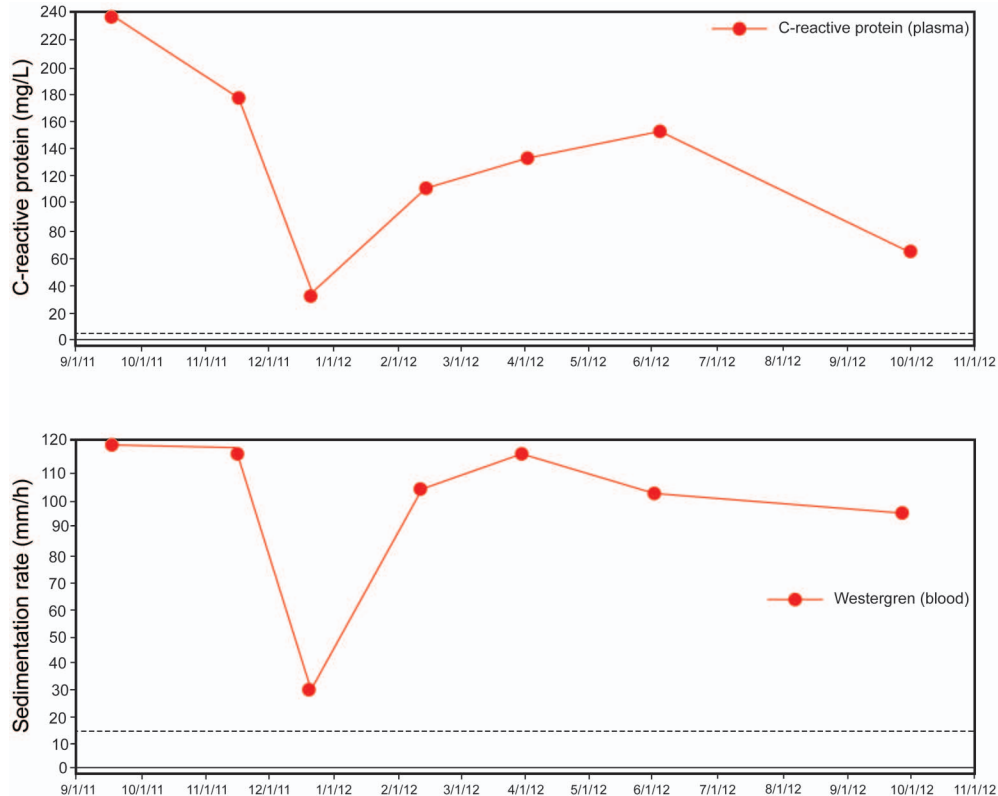


Fig. 8. Trends of erythrocyte sedimentation rate and C-reactive protein. The solid horizontal lines indicate reference low, and the dashed horizontal lines indicate reference high.

cified tracheal rings are commonly seen. Tracheobronchial amyloidosis commonly manifests as diffuse mural thickening and luminal narrowing. Mural calcification may be evident on computed tomography scan. Endobronchial granulomata in patients with sarcoidosis may rarely result in significant airway narrowing. Tracheopathia osteochondroplastica is a rare, idiopathic, asymptomatic disorder of older men, characterized by multiple osteocartilaginous masses adjacent to the tracheal rings. This entity is distinguished from tracheobronchial amyloidosis and RP because it does not involve the posterior membranous portion of the trachea.

Diagnosis of RP is based mainly on clinical criteria, and a tissue biopsy may not be required. Some of the distinctive histological features of RP are loss of basophilic stippling of the cartilage matrix and perichondrial inflammation at the soft tissue-cartilage interface. Chondrocytes become vacuolated and necrotic and are eventually replaced by fibrous tissue.

Management of RP is largely empiric and based on case series and reports. No clinical trials have been performed due to the rarity of the disease. Airway management along with early pharmacotherapy can lead to relief of symptoms.^{2,7,9} Glucocorticoids, other immunosuppressive agents (such as methotrexate, cyclophosphamide, colchicine, and azathioprine), and anti-tumor necrosis factor agents have been used with varying outcomes¹⁰⁻¹⁶ Relapse of the disease is common when therapy is tapered off.

Teaching Points

- Cartilaginous structures are often involved in RP, and auricular involvement is a common feature.
- Airway inflammation is also commonly reported and portends poor prognosis if undiagnosed for a prolonged period of time.
- The pathogenesis of RP is unclear, and involvement of non-cartilaginous structures such as proteoglycan-rich organs like eyes and cranial nerves has been reported.
- Pharmacologic therapy is largely empiric and based on experience. Systemic steroids are the treatment of choice.

- Surgical interventions such as stent placement, localized tracheal resection, and tracheotomy are warranted in life-threatening airway complications.

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