Laryngeal Manifestation of Autoimmune Disease: Rheumatoid Arthritis Mimicking a Cartilaginous Neoplasm

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Case Report

A 56-year-old male presented with acute airway obstruction. He reported rapid progression of dyspnea over the last few days since developing an upper respiratory infection. The patient had been followed by an otolaryngologist for slowly progressive dyspnea over a 1?-year period following an upper respiratory tract infection. Recently, while under treatment for “atypical” asthma, he had undergone a flexible bronchoscopy. A subglottic lesion was noted and biopsied. He reported dysphagia of solids and a recent 10-pound weight loss. He quit tobacco use 25 years earlier and had been treated 5 years previously with nonsteroidal anti-inflammatory drugs (NSAIDs) for arthritis.

On examination, the patient demonstrated biphasic stridor, with suprasternal retractions. Flexible fiberoptic laryngoscopy revealed bilateral vocal fold immobility, with edematous vocal cords fixed in the midline. The glottic aperture was estimated to be 3 to 4 mm. The respiratory rate was 16 to 18 breaths per minute, and oxygen saturations remained above 95% on room air. The patient was administered a helium-oxygen mixture by mask and intravenous dexamethasone (10 mg every 8 hours) and was placed in a monitored setting.

Within 24 hours, his symptoms improved. Laboratory investigations, including a complete blood cell count, differential white blood cell count, electrolyte levels, liver function tests, thyroid function test, blood cultures, and urine analysis, were unremarkable. Anti-neutrophilic cytoplasmic antibody and syphilis (Veneral Disease Research Laboratories) serologies were also negative. The erythrocyte sedimentation rate was elevated to 80 mm/h (normal < 20 mm/h). A computed tomographic (CT) scan of the neck (Figure 1) exhibited a soft tissue lesion involving the posterior region of the subglottis and contiguous circumferential thickening of the cricopharyngeus. The lesion appeared to be distinct from the thyroid gland. Barium swallow revealed no mucosal abnormalities.

The patient was brought to the operating room for tracheostomy, panendoscopy, and biopsy. On laryngoscopy, a white, friable soft tissue lesion situated in the left posterior subglottis was biopsied. An interarytenoid band was noted and lysed. Both cricoarytenoid joints were immobile to palpation. A firm circumferential submucosal thickening of the cricopharyngeus made passage of a 10 mm esophagoscope difficult. The remainder of the esophagoscopy and bronchoscopy was normal. Multiple biopsies were taken of the subglottis and proximal esophageal mucosa.

Pathologic examination of the subglottic lesion was reported as squamous mucosa with focal acute and severe chronic nonspecific inflammation of the stroma with significant eosinophilia. There was no evidence of malignancy, vasculitis, necrosis, or granuloma. Special stains were negative for microorganisms. Esophageal

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biopsies revealed only normal esophageal mucosa. The initial bronchoscopic biopsies (unavailable until this time) were similarly reported as focal acute and severe chronic nonspecific inflammation. Independent review of the slides was in agreement.

Further investigations were performed, including magnetic resonance imaging of the larynx (Figure 2), which showed an irregular thickening with enhancement of the subglottic mucosa, as well as the undersurface of both vocal cords and posterior tracheal wall. Chest CT and abdominal ultrasonography were unremarkable.

The clinical history, location of the lesion, and radiologic imaging could have been consistent with chondrosarcoma, which often requires multiple deep biopsies to establish a pathologic diagnosis. The patient was again taken to the operating room for biopsy. Multiple endolaryngeal deep biopsies of the subglottis and open biopsies of the tracheal-esophageal parting wall were obtained. Intraoperatively, the proximal 1 cm of the tracheal-esophageal parting wall was exceptionally firm and difficult to biopsy. Frozen sections demonstrated acute on chronic nonspecific inflammation. Final pathology reports were identical to the previous ones and remained nondiagnostic. Additionally, Congo red stains, as well as immunohistochemical staining for S-100 protein, keratin, and cytokeratin, were all negative.

The patient was ultimately discharged home tracheostomy dependent and was closely followed. It was believed that the pathologic process would eventually declare itself.

After 3 months of uneventful otolaryngology follow-up, the patient presented with new-onset, severe large-joint arthralgias. Rheumatologic consultation revealed olecranon bursitis, with persistent elevation of the sedimentation rate and positive titres for rheumatoid antibodies consistent with active disease. The patient was begun on methotrexate, prednisone, and NSAIDS. His large-joint complaints improved with treatment. Otolaryngology follow-up, with repeat radiologic imaging at 9 months following completion of medical therapy, failed to show clinical or radiologic improvement of the laryngeal lesion. To date, the patient is tracheostomy dependent.

**Discussion**

Retrospective review of all biopsy specimens did not reveal a central area of fibrinoid necrosis surrounded by pallisading epithelioid macrophages and other mononuclear cells, which is the classic histopathologic pattern of a rheumatoid nodule. The eosinophilia supported the presence of an autoimmune state but was not pathognomonic. These results are consistent with, but not specific for, rheumatoid involvement of the larynx. In light of the systemic manifestations of active rheumatoid arthritis, a diagnosis of acute on chronic cricoarytenoiditis with ankylosis was established.

Rheumatoid arthritis is the most common autoimmune disease, affecting up to 3% of the adult population, with a reported prevalence of 15 to 35 per 100,000 in the pediatric population. The natural history is variable, with periods of active disease and remission. The otorhinolaryngologic manifestations of rheumatoid arthritis are protean. Although joint manifestations remain the most active and symptomatic feature of the disease, including infrequent involvement of the temporomandibular joint, cricoarytenoid arthritis is usually most pertinent to otolaryngologists. It has been well documented that laryngeal involvement may be the sole manifestation of active disease, as occurred with this patient. Twenty-five to 50% of patients with long-standing disease have some level of laryngeal involvement. The clinical features of laryngeal pathology range from mild to severe and do not seem to be related to systemic disease activity. Laryngeal involvement may be in the form of cricoarytenoiditis or cricothyroid arthritis, which may result in the formation of rheumatoid nodules or nonspecific inflammation (acute on chronic). Damage may be severe enough to cause cricoarytenoid obliteration and ankylosis, with resultant airway obstruction and tracheostomy dependence. Other changes in the larynx include myositis of the intrinsic musculature, formation of rheumatoid nodules in the vocal folds, and idiopathic atrophy of the recurrent laryngeal nerve. Patients may present with vocal complaints, stridor, or dysphagia. Likewise, in the pediatric population, cricoarytenoiditis may be seen as an early sign of juvenile rheumatoid arthritis.
acute upper airway obstruction being the initial presentation. The classic pathologic rheumatoid sequence of cricoarytenoiditis, from the earliest synovitis to the obliteration and ankylosis of the joint, was well described by Bridger and colleagues in 1980.

Early identification and treatment are essential because it appears that certain sequelae of the disease are refractory to medical management. The use of steroids (systemic and/or locally) or NSAIDS may prevent the formation of nodules or fibrosis. Treatment usually results in the disappearance of subcutaneous nodules. The laryngeal nodules, by contrast, do not seem to respond to medical therapy. This may be due to a subclinical course of laryngeal rheumatoid nodule formation, which may be refractory to medical therapy by the time they are discovered. The use of methotrexate, one of the mainstays of the rheumatologic armamentarium for the treatment of active arthritis, has been implicated as the precipitating factor in the formation of rheumatic nodules in 5 to 10% of patients. Accelerated nodulosis, rapidly forming rheumatoid nodules, is also a potential complication of methotrexate treatment. With the increasing use of methotrexate, one can expect that the frequency of nodules involving the upper airway will increase. In the patient presented here, the extent of laryngeal involvement at presentation with airway obstruction would likely have been refractory to medical management even if a prompt diagnosis and initiation of treatment had been possible.

There is evidence in the literature that endotracheal intubation may cause quiescent laryngeal rheumatoid lesions to flare up. There is at least one reported fatality attributed to such an event. This is especially important if the patient has known laryngeal involvement. Cervical vertebral involvement may further complicate intubation and laryngoscopy by limiting head extension. The laryngeal (and cervical) status of patients with long-standing rheumatoid arthritis should be evaluated and transmitted to the anesthesiologist prior to endotracheal intubation.

Two aspects of this case warrant special discussion. The similarity in the presentation of this patient to one having a cartilaginous tumour should be noted. For example, both may present with a slowly progressive dyspnea, with “atypical” asthma diagnosis. Stridor from cartilaginous tumours is usually from narrowing of the airway lumen, although fixation of the joints and vocal fold immobility can occur. Additionally, the most common site of origin of chondrosarcomas is the internal aspect of the posterior cricoid lamina. This is near the cricoarytenoid joints, the region known to be affected by many arthropathies, including rheumatoid. Second, these tumours tend to be hard, smooth, broad-based, and covered with intact mucosa. This was precisely the impression of the postcricoid region during endoscopy. Chondrosarcomas are not infrequently difficult to biopsy owing to the composition of the tumour. Furthermore, the pathologic report was not consistent with that of a rheumatoid nodule and could have represented an inflammatory response to a neighbouring malignancy. In retrospect, however, this case did lack the classic features of a cartilaginous tumour. Calcifications were not noted on imaging (present in 75% of cartilaginous tumours radiographically), and although the “epicentre” of the lesion was the internal surface of the cricoid lamina, the circumferential esophageal submucosal involvement is not typical of these tumours. There is evidence in the literature regarding the use of positron emission tomography to differentiate inflammation from cancer of the larynx, which might have been useful in this patient.

In summary, the head and neck manifestations of rheumatoid arthritis may be more common than aggressive early intervention in selected cases eluding diagnosis. A high index of suspicion and a broad differential should be maintained at all times when treatment is predicated upon a “working” diagnosis.

References

