Sarcoidosis Presenting as Bilateral Vocal Fold Immobility

*Justin M. Hintze, †Sharon H. Gnagi, and *,†David G. Lott, *†Phoenix, Arizona

Summary: Bilateral true vocal fold paralysis is rarely attributable to inflammatory diseases. Sarcoidosis is a rare but important etiology of bilateral true vocal fold paralysis by compressive lymphadenopathy, granulomatous infiltration, and neural involvement. We describe the first reported case of sarcoidosis presenting as bilateral vocal fold immobility caused by direct fixation by granulomatous infiltration severe enough to necessitate tracheostomy insertion. In addition, we discuss the presentation, the pathophysiology, and the treatment of this disease with a review of the literature of previously reported cases of sarcoidosis-related vocal fold immobility. Sarcoidosis should therefore be an important consideration for the otolaryngologist's differential diagnosis of true vocal fold immobility.

Key Words: Sarcoidosis–Bilateral vocal fold immobility–Laryngeal sarcoidosis–Respiratory sarcoidosis–Neurosarcoidosis.

INTRODUCTION

Sarcoidosis is a granulomatous disease that affects multiple organ systems. It is most commonly diagnosed in young adults ages 20–40 and is more prevalent in the African American population. The exact etiology is unknown and is considered multifactorial. Prevalence of sarcoidosis ranges from 10 to 35 out of 100,000, whereas laryngeal involvement occurs in 1%–5% of patients.[1] Sarcoidosis has been reported in a few cases in the literature as a rare etiology of true vocal fold paralysis, most commonly via compressive lymphadenopathy, granulomatous infiltration of the larynx, and neurosarcoidosis affecting one or multiple cranial nerves. We describe the first reported case of sarcoidosis presenting as bilateral vocal fold immobility caused by direct fixation by granulomatous infiltration severe enough to necessitate tracheostomy insertion.

CASE REPORT

A 49-year-old African American woman presented to the emergency department with a 2-day history of progressive dyspnea and inspiratory stridor. Over the previous 5 months, the patient had been evaluated at an outside facility for chronic cough. Over the course of her disease process, the patient developed episodes of aspiration pneumonia, gastroparesis, and esophageal dysmotility, requiring the temporary insertion of a gastrostomy tube; the patient's background history also included osteopenia. The workup included a computed tomography of the chest that revealed symmetric hilar and mediastinal lymph node enlargements, with some faint developing calcification. Subsequent biopsy via an endobronchial ultrasound (EBUS) revealed no evidence of malignancy or granulomatous disease. Angiotensin-converting enzyme levels were normal (48), although the patient's antinuclear antibody was elevated. At the time of our examination, the patient had bilateral true vocal fold immobility on flexible laryngoscopy (Figure 1) and moderate respiratory distress requiring a tracheostomy. An EBUS at our institution revealed similar results, necessitating a surgical mediastinal lymph node biopsy for diagnosis. Pathology showed a sclerosing non-necrotizing granulomatous inflammation consistent with sarcoidosis (Figure 2). Laryngeal electromyography (EMG) was performed 9 months after symptom onset and revealed normal resting activity and normal motor unit potentials in both vocalis muscles, suggesting direct laryngeal infiltration rather than neural involvement. The patient was treated initially with IV methylprednisolone (40 mg) and subsequently switched to oral prednisolone (40 mg) with a slow taper over the next 6 months, but did not regain vocal fold mobility over the next year.

The patient's job involves extensive voice use. Therefore, the patient ultimately chose to optimize her voice rather than work toward removing the tracheostomy tube. The patient subsequently underwent Radiesse injection into the paraglottic spaces bilaterally. The patient reported a symptomatic improvement of her voice and was able to maintain a complete oral diet. On a swallow study, the patient showed no evidence of aspiration and her gastroparesis and esophageal dysmotility showed improvement, allowing for the removal of her gastrostomy tube. The patient is currently 4 years from initial presentation and remains with a tracheostomy.

DISCUSSION

Sarcoidosis is a multisystem granulomatous disorder of unknown etiology that affects individuals worldwide and is characterized pathologically by the presence of noncaseating granulomas in involved organs. Sarcoidosis can affect any organ in the body to varying extents and degrees. Sarcoidosis most commonly affects the respiratory tract, with a predilection for the lower tract.[2] Sarcoidosis of the upper respiratory tract is considered uncommon, but is probably more frequent than realized.[1,3] Presentation of sarcoidosis varies from asymptomatic to symptomatic, including both constitutional and organ-specific findings. General complaints include fatigue, fever, and weight loss.[4] Laryngeal involvement in patients with sarcoidosis is estimated to occur between 1% and 5%.[1] Laryngeal manifestations may include globus sensation, dysphonia, dysphagia, dyspnea, and cough.[3,5,6]

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From the *Head and Neck Regeneration Program, Center for Regenerative Medicine, Mayo Clinic, Phoenix, Arizona; and the †Department of Otorhinolaryngology, Mayo Clinic Arizona, Phoenix, Arizona.
Address correspondence and reprint requests to David G. Lott, Department of Otorhinolaryngology, Mayo Clinic Arizona, 5777 E Mayo Blvd, Phoenix, AZ 85050. E-mail: lott.david@mayo.edu
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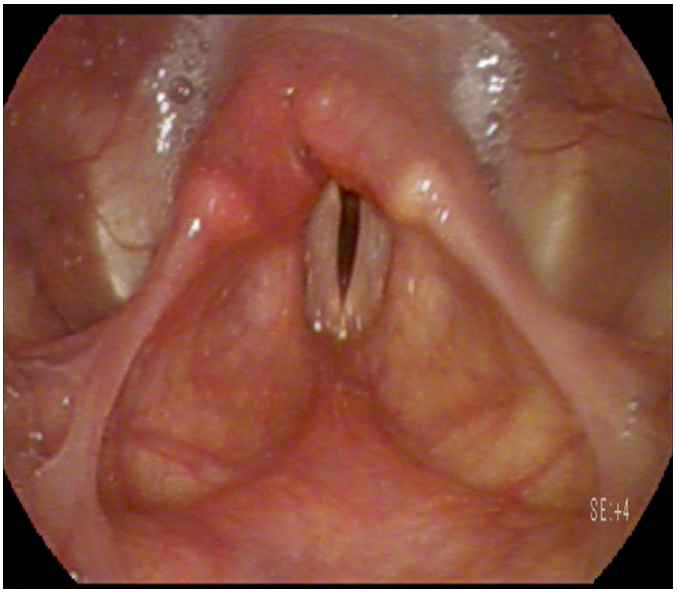

FIGURE 1. Laryngoscopy showing fixed vocal folds in the paramedian position with pooling of secretions and edematous arytenoid mucosa.

Severe cases, such as the case reported here, may present as respiratory distress and stridor necessitating a tracheostomy; however, this case is the first reported to require a tracheostomy. Other organ-specific findings may also be present.

The diagnosis of sarcoidosis is made by clinical, radiological, and histopathologic detection of noncaseating granulomas. However, it remains a diagnosis of exclusion. In laryngeal sarcoidosis, laryngoscopy classically reveals edematous, elevated, and pale mucosa found in the following sites in decreasing order: epiglottis, arytenoids, aryepiglottic folds, vestibular folds, and subglottis.[1] Immobility of the vocal folds may occur by three separate mechanisms: compression of the recurrent laryngeal nerve by lymphadenopathy,[5,7–16] direct invasion of the larynx by granulomas (this case), or neurosarcoidosis.[5,17] The most commonly reported cause is compressive lymphadenopathy (Table 1). Direct invasion of the larynx is rare. This may be due to the fact that sarcoidosis affects the reticuloendothelial system, and there are relatively few lymphatics in the larynx.[1,18] Laryngeal EMG may be beneficial in elucidating the cause of immobility. If laryngeal EMG is suggestive of neural injury, neural biopsy may further help to differentiate between direct neural invasion and neurosarcoidosis. As in our case, a normal EMG suggested direct infiltration of the larynx rather than neural involvement. Neural involvement can occur in 5% of cases of sarcoidosis[19] and can affect the facial, optic, vagus, and trigeminal nerves.[5] Chest imaging often reveals mediastinal lymphadenopathy (in 60%–90% of cases[8,16]), which may also cause vocal fold immobility via compression of the vagus nerve. Although laboratory evaluation is typically unrevealing, hypercalcemia or angiotensin-converting enzyme levels may be elevated. Biopsy of affected lymph nodes via EBUS or video-assisted thoracic surgery reveals noncaseating granulomas on histology. Other granulomatous diseases and malignancy should be excluded.

Table 1 describes the previously reported cases of vocal fold immobility caused by sarcoidosis. The average age of presentation was 49 years. Women were involved in 8 out of the 14 cases (57%), and the left vocal fold was most frequently affected (57%). Ethnicity was reported in only 43% of the cases, with four cases occurring in African Americans and two in Caucasians. Only one case of right-sided vocal fold paralysis has been reported.[7] Left recurrent laryngeal nerve compression by lymph nodes as it hooks around the aorta likely explains this predilection, along with its long intrathoracic course. Bilateral vocal fold immobility has been reported only five times (including our case). One case was caused by vagal neurosarcoidosis,[17] three by compressive lymphadenopathy,[5,9,13] and one by direct invasion (this case).

Our case is the only reported case of bilateral true vocal fold immobility caused by sarcoidosis, severe enough to require tracheostomy placement. It is also the only reported case utilizing EMG to help determine the true pathophysiology of the paralysis.

Treatment typically consists of systemic corticosteroids, although other systemic therapies including cytotoxic agents may be offered.[20] Intralesional steroid injections, as well as surgical resection of problematic lesions of the larynx or mediastinal lymph nodes, have also been described. Complete recovery of vocal fold immobility associated with sarcoidosis was reported in 57% of the cases, with one patient requiring a lymphadenectomy for nerve decompression[7] and one patient requiring maintenance steroid treatment.[9]

CONCLUSION

Sarcoidosis with laryngeal involvement is infrequent, with vocal fold immobility being a rarely associated clinical finding. This report is the only documentation of bilateral vocal fold immobility

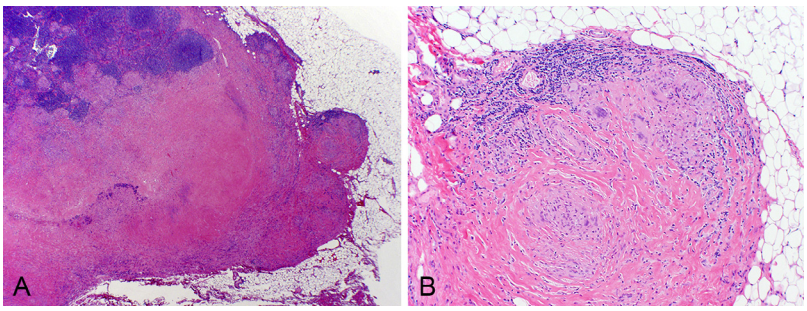

FIGURE 2. Pathology of the mediastinal lymph nodes reveals sclerosing non-necrotizing granulomatous inflammation consistent with the diagnosis of sarcoidosis in low-power (**A**) and high-power (**B**) magnification.