

Vocal fold deposits in macrophagic myofasciitis

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Abstract

Macrophagic myofasciitis was first reported in 1998. This disease manifests as diffuse myalgia and chronic fatigue. Its pathophysiology has been traced to the presence of an aluminum adjuvant used in vaccines against hepatitis A and B virus and tetanus toxoid; the adjuvant aggregates at the site of injection. One-third of patients with macrophagic myofasciitis develop autoimmune disease. Vocal fold deposits have been described in autoimmune diseases such as sarcoidosis, systemic lupus erythematosus, multiple sclerosis, rheumatoid arthritis, Sjögren's syndrome, and Hashimoto's thyroiditis. We report what to the best of our knowledge is the first published case of vocal fold deposits in macrophagic myofasciitis.

Introduction

Macrophagic myofasciitis was first reported by Gherardi et al in 1998.¹ Since then, more than 200 definite cases have been identified in France, and a few isolated cases have been recorded in other countries.² The condition manifests as diffuse myalgia and chronic fatigue. In about half of affected patients, symptoms meet the Oxford criteria³ for chronic fatigue syndrome as well as the criteria established by the Centers for Disease Control and Prevention.⁴

In this article, we describe what to the best of our knowledge is the first reported case of vocal fold deposits in a patient with macrophagic myofasciitis.

Case report

A 46-year-old man was referred to our otolaryngology service in Ireland with a 3-month history of hoarseness and intermittent aphonia. Two years earlier, he had been diagnosed with macrophagic myofasciitis. He was a non-smoker, and he worked as a university lecturer.

Direct laryngoscopy revealed the presence of several whitish-yellow, bandlike lesions in the submucosal space, approximately at the middle of the membranous portion of

the vocal fold (figure 1). The lesions were bilateral but not exactly opposite each other. They were lying transversely, and they caused a slight convexity of the upper vocal fold surface. On stroboscopy, reduced mucosal wave and vibration amplitude were noted at the site of the lesions. Histologic examination of these submucosal nodules revealed the classic appearance of a rheumatoid lesion with central fibrinoid necrosis and peripheral histiocytic palisading (figure 2).

The patient declined surgical intervention. He was prescribed a course of oral steroids, and his voice quality improved significantly.

During follow-up, all autoimmune serologic tests—including tests for anti-smooth-muscle antibodies, anti-mitochondrial antibodies, gastric parietal cell antibodies, rheumatoid factor, anti-Rho, anti-La, SS-A, SS-B, RNP, and antinuclear antibodies—were negative.

Discussion

The histologic characteristics of the lesions in our patient appeared to be the same as those of subcutaneous rheumatoid nodules. Also, the lesions appeared to be the same as those described by Woo et al⁵ and the same as the autoimmune deposits described by Hosako-Naito et al.⁶ In our patient, all autoimmune antibodies and serology were negative. These vocal fold deposits have not been previously described in patients with macrophagic myofasciitis.

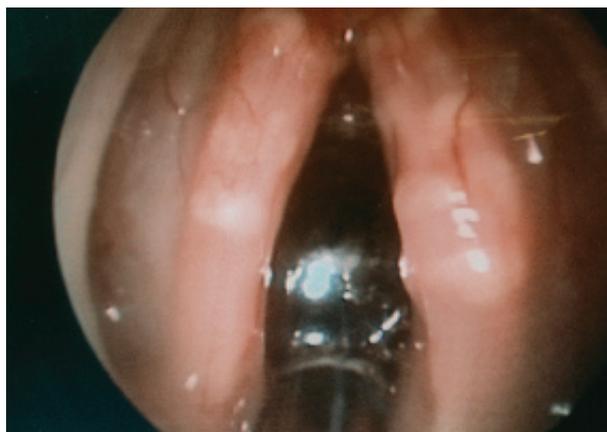


Figure 1. Direct laryngoscopy shows the multiple whitish-yellow, bandlike deposits in the submucosal space.

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One-third of patients with macrophagic myofasciitis develop an autoimmune disease.² Even in the absence of overt autoimmune disease, affected patients may show subtle signs of chronic immune stimulation. Many of these patients are in the HLA-DRB1*01 group, a phenotype at risk of developing polymyalgia rheumatica and rheumatoid arthritis. Macrophagic myofasciitis is characterized by a stereotyped and immunologically active lesion seen on deltoid muscle biopsy.

The etiology of macrophagic myofasciitis remained obscure until 2001.⁷ At that time, electron microscopy, microanalytical studies, experimental procedures, and an epidemiologic study demonstrated that the lesion is caused by the presence of an aluminum adjuvant used in vaccines against hepatitis A and B virus and tetanus toxoid; the aluminum remains accumulated at the site of injection.² Aluminum hydroxide is known to potently stimulate the immune system. It is plausible that persistent immune activation that fails to “switch off” can lead to vocal fold deposits.

Rheumatoid nodules are most likely to appear in areas subject to repeated microtrauma (e.g., the elbows).⁸ In the larynx, contact forces are greatest during vibration at the midpoint of the membranous vocal folds, which might explain why the rheumatic deposits in our patient developed at this specific site and not elsewhere. We also postulate that patients who use their voice professionally—such as our patient, who was a lecturer—may be more prone to developing these lesions.⁹

Two other diseases of interest as differential diagnoses of vocal fold deposits are amyloidosis and lipid proteinosis (Urbach-Wiethe’s disease):

- Amyloidosis is an uncommon disease characterized by extracellular fibrillar proteins that stain with Congo red.⁹ The most common sites in the larynx are the ventricle, false vocal folds, true vocal folds, epiglottis, aryepiglottic folds, subglottis, and trachea, in that order.¹⁰

- Lipoid proteinosis is a rare genetic defect associated with deposition of hyaline material in various tissues, including the skin, mucous membranes (especially in the upper respiratory tract), and internal organs. The deposits are always periodic acid-Schiff–positive and often sudanophil-positive.¹¹ Laryngoscopic findings include (1) thickened vocal folds, often with irregular borders, and (2) when deposits are abundant, decreased abduction, adduction, or even immobilization of the vocal folds. In the larynx, the deposits may also affect the epiglottis, aryepiglottic folds, and false vocal folds. Minor lesions on the vocal fold margins may look like submucosal autoimmune deposits.

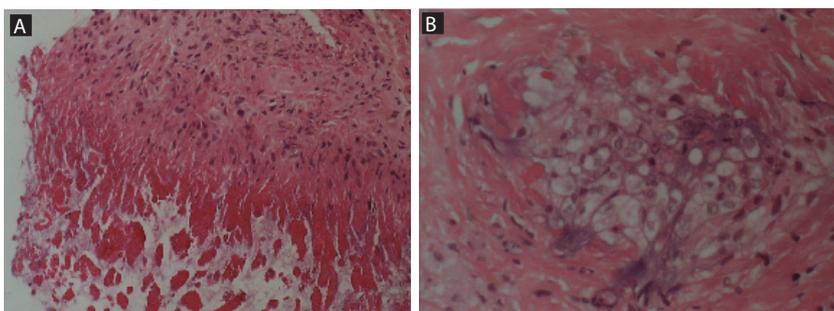


Figure 2. **A:** Histology shows the characteristic picket-fence pattern of a rheumatoid lesion with fibrinoid-degenerated collagen and peripheral histiocytic palisading (H&E, original magnification $\times 20$). **B:** The fibrinoid-degenerated collagen is seen under higher power, along with pale-blue histiocytes (H&E, original magnification $\times 40$).

The first symptom of autoimmune disease has been reported to be hoarseness or other changes in the quality of voice.^{12,13} Otolaryngologists play an important role in the care and investigation of such patients because immune-mediated vocal fold deposits may, in fact, be the first presentation of these systemic diseases. To our knowledge, our case represents the first reported instance of immune-mediated vocal fold deposits in a patient with macrophagic myofasciitis.

References

1. Gherardi RK, Coquet M, Cherin P, et al. Macrophagic myofasciitis: An emerging entity. Groupe d'Etudes et Recherche sur les Maladies Musculaires Acquisées et Dysimmunitaires (GERMMAD) de l'Association Française contre les Myopathies (AFM). *Lancet* 1998;352:347-52.
2. Gherardi RK. [Lessons from macrophagic myofasciitis: Towards definition of a vaccine adjuvant-related syndrome]. *Rev Neurol (Paris)* 2003;159:162-4.
3. Sharpe MC, Archard LC, Bantavala JE, et al. A report—chronic fatigue syndrome: Guidelines for research. *J R Soc Med* 1991;84:118-21.
4. Centers for Disease Control and Prevention. Diagnostic criteria for chronic fatigue syndrome. Available at <http://www.immunesupport.com/chronic-fatigue-syndrome-diagnostic.htm> (access verified Feb. 19, 2007).
5. Woo P, Mendelsohn J, Humphrey D. Rheumatoid nodules of the larynx. *Otolaryngol Head Neck Surg* 1995;113:147-50.
6. Hosako-Naito Y, Tayama N, Niimi S, et al. Diagnosis and pathophysiology of laryngeal deposits in autoimmune disease. *ORL J Otorhinolaryngol Relat Spec* 1999;61:151-7.
7. Gherardi RK, Coquet M, Cherin P, et al. Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminium hydroxide in muscle. *Brain* 2001;124:1821-31.
8. Brooker DS. Rheumatoid arthritis: Otorhinolaryngological manifestations. *Clin Otolaryngol Allied Sci* 1988;13:239-46.
9. Elghetany MT, Saleem A. Methods for staining amyloid in tissues: A review. *Stain Technol* 1988;63:201-12.
10. Mitrani M, Biller HF. Laryngeal amyloidosis. *Laryngoscope* 1985;95:1346-7.
11. Newton FH, Rosenberg RN, Lampert PW, O'Brien JS. Neurologic involvement in Urbach-Wiethe's disease (lipoid proteinosis). A clinical, ultrastructural, and chemical study. *Neurology* 1971;21:1205-13.
12. Prytz S. Vocal nodules in Sjogren's syndrome. *J Laryngol Otol* 1980;94:197-203.
13. Tsunoda K, Soda Y. Hoarseness as the initial manifestation of systemic lupus erythematosus. *J Laryngol Otol* 1996;110:478-9.