Spontaneous improvement of laryngeal sarcoidosis resistant to systemic corticosteroid administration

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Abstract
We report herein a case of laryngeal sarcoidosis that was refractory to systemic corticosteroids, but that improved spontaneously. A 49-year-old woman complained of dysphagia and hoarseness with accompanying edematous swellings of both arytenoid regions. She was referred to our hospital after systemic corticosteroid therapy failed to achieve any improvement. Laryngoscopy showed marked edema of the epiglottis and both arytenoid regions. The flow–volume curve on spirometry showed flattening of the expiratory flows. Histopathological examination of the arytenoid region showed non-caseating epithelioid granulomas, and laryngeal sarcoidosis was diagnosed with the result of BAL study. She was observed without treatment as symptoms were mild. Although edema of the left arytenoid region seemed to be somewhat worsened after 6 months, she continued to be followed closely because of improvements in the flow–volume curve and increasing peak expiratory flow. By 1 year after onset, symptoms and epiglottal swelling had spontaneously improved.

Introduction
Sarcoidosis is a chronic granulomatous disease of undetermined etiology that can involve any organ system of the body. Sarcoidosis commonly involves the hilar and mediastinal lymph nodes, lungs, eyes, and skin lesions. Laryngeal involvement is rare, with an estimated incidence of 0.33–2.1% [1]. Various modalities have been used in the treatment of laryngeal sarcoidosis. Systemic corticosteroid therapy is effective in most cases [2]. We present herein a case of laryngeal sarcoidosis that proved resistant to systemic corticosteroid administration, but that improved spontaneously in 1 year.

Case Report
A 49-year-old woman had been suspected of having sarcoidosis because of cervical enlarged lymph nodes, which are characterized by non-caseating granulomatous inflammation without acid-fast bacterium, 10 years previously. Sarcoidosis had not been diagnosed for the absence of other organ involvement and her cervical lymph node enlargement had resolved spontaneously.

She was seen in an otolaryngology clinic for dysphagia and hoarseness over a few weeks. Laryngoscopy showed edematous swelling of both arytenoid regions with unknown etiology. Corticosteroids were administered intravenously (methylprednisolone at 125 mg/day for 6 days and prednisolone at 0.5 mg/kg/day for 2 weeks). Because no improvement of arytenoid swelling or symptoms was seen despite corticosteroid treatment for 3 weeks, treatment was discontinued. Two months after discontinuation of treatment, arytenoid swelling was still apparent, and biopsy specimens were obtained. Histological examination revealed non-caseating epithelioid granulomas. Relapse of sarcoidosis was suspected and the patient was referred to our hospital.
No obvious abnormalities were observed on systemic physical examination or laboratory testing, including serum levels of calcium, angiotensin-converting enzyme, and soluble interleukin-2 receptor and anti-neutrophil cytoplasmic antibody. Tuberculin skin testing yielded negative results. Interferon-gamma release assay was also negative. Laryngoscopy showed marked edema of the epiglottis and both arytenoid regions (Fig. 1A). Computed tomography (CT) revealed thickening of the epiglottis with paraglottic fat infiltration at the supraglottic level (Fig. 1B). Fluorodeoxyglucose (FDG)-positron emission tomography (PET) demonstrated increased uptake of 18F-FDG in the larynx (maximum standardized uptake value = 2.7). (D) Maximal expiratory flow-volume loop shows flattening of maximal expiratory flows. (E) Histopathological study of the arytenoid region shows non-caseating epithelioid granulomas in the submucosal space (hematoxylin and eosin, x200).

The patient was carefully observed without treatment because of the lack of hypoxia and abnormalities from stroboscopy and voice testing. Although edema of the left arytenoid region seemed to be slightly worsened on laryngoscopy after 6 months, follow-up pulmonary function testing showed an increase in peak expiratory flow and improvement of the flattening of expiratory flows (Fig. 2B). She continued to be followed closely because of these improvements in airway obstruction on spirometry. By 1 year after onset, symptoms such as dysphagia and hoarseness, and swelling of the laryngeal regions had resolved (Fig. 2A, C).

Figure 1. Appearance of the larynx. (A) Fiberscopic findings reveal pale, edematous swelling of the epiglottis (turban-like thickening) and arytenoid regions. (B) Computed tomography shows thickening of the epiglottis with paraglottic fat infiltration at the supraglottic level. (C) On 18 fluorodeoxyglucose (FDG)-positron emission tomography, FDG uptake is increased in the larynx (maximum standardized uptake value = 2.7). (D) Maximal expiratory flow-volume loop shows flattening of maximal expiratory flows. (E) Histopathological study of the arytenoid region shows non-caseating epithelioid granulomas in the submucosal space (hematoxylin and eosin, x200).
Discussion
Sarcoidosis of the larynx shows a predilection toward developing in the supraglottic area, most commonly involving the epiglottis followed by the arytenoids, aryepiglottic folds, and false vocal folds [1]. Laryngeal sarcoidosis may therefore progress to cause severe airway obstruction and is thus potentially life threatening. Bower et al. reported various treatment modalities for laryngeal sarcoidosis, including systemic corticosteroids, intralesional corticosteroid injection, surgical excision, and radiation. These treatment modalities were effective in most cases [2]. On the other hand, 10% of cases of laryngeal sarcoidosis showed spontaneous remission [2]. For cases refractory to systemic corticosteroid administration, immunosuppressive agents, intralesional steroid injection, and/or laser surgery appear to represent attractive alternatives [1, 3]. In our case, sarcoidosis of the larynx showed an interesting clinical course notable in the finding that laryngeal sarcoidosis can resolve spontaneously even when refractory to corticosteroid administration. Whether the risks associated with treatment are worth the modest benefit seen in patients with mild symptoms is thus unclear.

If untreated, laryngeal sarcoidosis would require close follow-up. For assessing the course of the disease, convenient and minimally invasive examinations might be preferable. In our case, pulmonary function testing, in particular the flow–volume curve, was more effective for evaluating upper airway obstruction than CT.

In our case, laryngeal sarcoidosis was diagnosed 10 years after our patient was suspected of cervical lymph node sarcoidosis. Rizzato and Montemurro reported 43 patients presenting with sarcoid granuloma in peripheral lymph nodes; 33 patients were eventually diagnosed with sarcoidosis months or years later [4]. We supposed cervical lymphadenopathy had been sarcoidosis because of the laryngeal granulomatous lesion. However, at the time of diagnosis of cervical lymphadenopathy, an asymptomatic laryngeal involvement might have been present. Bower et al. reported that it was asymptomatic in 18% of laryngeal sarcoidosis [2]. Recently, 18F-FDG-PET has been reported as useful in assessing the extent of organ involvement [5]. Possibly, if FDG-PET had been performed 10 years previously, laryngeal sarcoidosis might have been detected.

Laryngeal sarcoidosis may cause upper airway obstruction and thus prove life threatening. We should therefore pay close attention to laryngeal involvement in patients with sarcoidosis using various imaging and functional tests to devise appropriate treatment strategies, including careful follow-up.

Disclosure Statements
No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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