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Review article

Laryngeal sarcoidosis: Presentation and management in the pediatric population

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ABSTRACT

Background: Sarcoidosis is a disease characterized by systemic non-necrotizing granulomas of unknown etiology. Laryngeal sarcoidosis is extremely uncommon, especially among pediatric patients. The clinical presentation and management of this entity in the pediatric population are poorly understood.
Methods: A comprehensive search in PubMed was conducted to identify all cases in the published literature. We also present a case of isolated pediatric laryngeal sarcoidosis and outline the multidisciplinary approach to evaluation and management.
Results: A previously healthy 13-year-old female presented with a five-month history of mild dysphonia, dyspnea on exertion, and diffuse supraglottic edema. Biopsy showed non-necrotizing granulomas. Treatment with methotrexate led to marked improvement. The literature search identified seven previously published cases of pediatric laryngeal sarcoidosis, four in which disease was isolated to the larynx. All patients presented with a symptomatic and diffusely edematous supraglottis. Diagnoses were based on supraglottic biopsies showing non-necrotizing granulomas; all other possible etiopathologies were excluded. Three patients responded to corticosteroid therapy alone, one patient to tumor necrosis factor (TNF) inhibitor and methotrexate, and the remainder to a combination of corticosteroid therapy and surgical debulking.
Conclusions: Laryngeal sarcoidosis in the pediatric population is challenging to diagnose and manage. When epithelioid granulomas are encountered histologically, other causes of granulomatous inflammation must be ruled out before a diagnosis of sarcoidosis can be made. Corticosteroid therapy alone may be ineffective. Medical therapy with methotrexate alone or in combination with TNF inhibitors versus surgical debulking alone or as part of multimodality treatment should be considered. A multidisciplinary approach with involvement of an otolaryngologist, pathologist, and rheumatologist is suggested.

Contents

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1. Introduction

Sarcoidosis is a multi-system disease that can affect most organ systems and is uncommon among pediatric patients [1]. The clinical presentation of this systemic granulomatous disease can vary greatly, and cases of laryngeal sarcoidosis are exceedingly rare. To our knowledge, only seven previous cases of have been reported in the literature. The purpose of this paper is to discuss the presentation, evaluation, and management of pediatric laryngeal sarcoidosis via a multidisciplinary team approach.

2. Materials and methods

A relevant case of a pediatric laryngeal sarcoidosis is presented. A literature search was conducted for peer-reviewed English-language publications using the online search database PubMed on January 26, 2015. Search terms included: laryngeal sarcoidosis, pediatric sarcoidosis, and pediatric laryngeal sarcoidosis. Reference lists were scanned for additional case reports.

3. Results

3.1. Patient presentation

A previously healthy and physically active 13-year-old Caucasian female presented with a five-month history of mild dysphonia and dyspnea on physical exertion. She reported nighttime coughing and difficulty sleeping in the supine position. She denied dysphagia, constitutional symptoms including fever and weight loss, epistaxis, hemoptysis, trauma or vocal abuse, recent respiratory tract infection, exposure to fumes or gases, or illicit drug use. Review of systems was otherwise negative. The patient had previously been treated with oral corticosteroids (multiple courses), anti-reflux medication, antibiotics, and albuterol without improvement.

Flexible fiberoptic examination of her larynx revealed marked edema of the epiglottis, arytenoids, and aryepiglottic folds. The laryngeal inlet could not be visualized. A computerized tomography (CT) scan showed thickening of the supraglottic tissues. The chest X-ray was within normal limits.

Laboratory studies including blood counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), anti-nuclear antibody (ANA), angiotensin-converting enzyme (ACE), antineutrophil cytoplasmic antibody (ANCA), lysozyme, thyroid function tests, immunoglobulins, and complement levels were within normal limits. Urinalysis and renal function were also normal. Purified protein derivative (PPD) test was negative.

The supraglottic tissues showed generalized edema (Fig. 1) upon direct microlaryngoscopy with rigid bronchoscopy under general anesthesia. Vocal folds and distal airway were normal. Biopsies were taken from the lingual surface of the epiglottis.

Histopathological examination showed non-necrotizing epithelioid granulomas bordered by reactive lymphoid tissue with germinal center formation (Fig. 2). Special stains (Gram, Grocott methenamine silver, and acid-fast bacillus) highlighted mucosal surface bacteria but were otherwise negative for organisms. Microbiologic tissue cultures were negative.

A chest CT suggested non-specific right upper lobe tree-in-bud opacities, corresponding to bronchiole inflammation. There was no evidence of mediastinal lymphadenopathy. Pulmonary function tests (PFTs) were within normal limits.

The presumed diagnosis of laryngeal sarcoidosis was based on supraglottic biopsies showing non-necrotizing granulomas. All other possible etiopathologies (infection, autoimmune, infiltrative, inhalant, benign and malignant tumors, and hypothyroidism) were excluded based on the aforementioned history and clinical presentation, laboratory and microbiology tests, and imaging studies.

The patient's symptoms worsened. Supraglottic injection of triamcinolone led to a modest week-long improvement, but symptoms recrudesced thereafter. Accordingly, oral methotrexate (20 mg weekly) was recommended by her rheumatologist. This led to symptomatic improvement, and fiberoptic laryngeal examination showed marked improvement after 12 weeks of therapy (Fig. 3). She continues on methotrexate maintenance therapy and has been followed for six months thus far.

3.2. Literature review

Seven reported pediatric patients with laryngeal sarcoidosis were identified [2–8] and are summarized along with the present case in Table 1. All patients presented in adolescence, similar to the patient reported herein. There was an equal gender distribution. Most patients presented with dyspnea on exertion, dysphonia, and symptoms of nocturnal airway obstruction. All patients presented with a diffusely edematous supraglottis. Three patients presented with extra-laryngeal manifestations.

Diagnoses were based on supraglottic biopsies showing non-necrotizing granulomas, and all other possible etiopathologies were considered and excluded. Elevated serum ACE, known to be an inaccurate marker for sarcoidosis [9], was only found to be elevated in one reported case of pediatric laryngeal sarcoidosis [4]. Three patients responded to corticosteroid therapy alone. Our patient improved with methotrexate, whereas another patient responded to a TNF inhibitor plus methotrexate. The remainder required a combination of corticosteroid therapy and surgical debulking.

4. Discussion

Sarcoidosis is a disease characterized by systemic non-necrotizing granulomas [1]. There are three criteria for diagnosis:

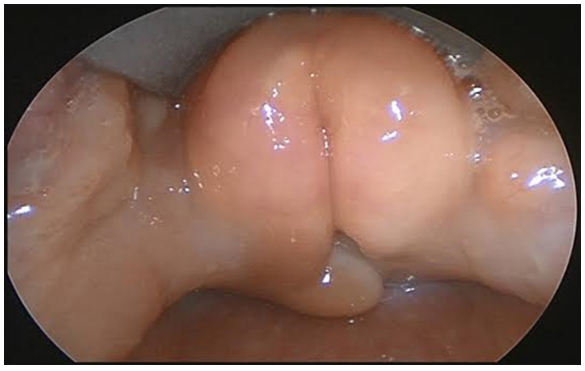

Fig. 1. Direct microlaryngoscopy with 4 mm Hopkins telescope at presentation. The laryngoscope is positioned in the vallecula and there is diffuse edema of the epiglottis, aryepiglottic folds, and arytenoids (the left arytenoid is scissoring over and obstructing the view of the right arytenoid). The glottic inlet is not visible.