LARYNGEAL PRESENTATION OF CHURG-STRAUSS SYNDROME IN CHILDHOOD,

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By
Ahmed Y. Al-Ammar, MD, FKSU*

Subhan. S. Yasin. MD, M.S*

Saleh Zaid Al-Muhsen, MD, FRCPC, AmBP**

Muslim Mohammed Al-Saadi MBBS, ABP**

Mohammad O Alsohaibani, FCAP, FRCPATH***

*From the department of Otolaryngology Head and Neck Surgery.
** From the department of pediatrics.
*** From the department of pathology
King Abdulaziz university hospital.
Riyadh, Saudi Arabia

Abstract:

Objective: to report what could be the first case of Churg-Strauss syndrome (CSS) presenting as laryngeal mass.

Case report: A 10 years-old female who is known to have a bronchial asthma, had unusual presentation with laryngeal lesion, eventually diagnosed as CSS. She was referred to our hospital with history of recurrent stridor. The larynx on endoscopy showed signs similar to Recurrent Respiratory Papillomatosis (RRP).

Conclusion: CSS is a systemic disorder and is now defined as one of the ANCA-associated vasculitis. So a case of a bronchial asthma presenting with RRP may not be as straight forward as it seems.

Key words; Churg-Strauss syndrome, laryngeal mass, papilloma, stridor.

INTRODUCTION:

Churg-Strauss syndrome (CSS) is a systemic disease characterized by asthma, blood and tissue eosinophilia, and necrotizing vasculitis with extravascular eosinophilic granulomas.[1] It is defined as one of the ANCA-associated (antineutrophil cytoplasmic autoantibody) vasculitis.[2] Despite recent interests, it is still a rare disease with a poorly understood pathogenesis. In France, the prevalence of CSS was recently estimated at 10.7 per million adults.[3] Ear, Nose and Throat involvement is a common finding, usually manifesting as allergic rhinitis and chronic rhinosinusitis with or without nasal polyposis.[4] Other rare symptoms like otitis media, facial palsy and vocal cord paralysis are also seen. This paper describes a unique case of CSS which presented with laryngeal mass, stridor and findings resembling Recurrent Respiratory Papillomatosis (RRP).

Case Report:

A 10 year old girl was referred to our institution, King Abdulaziz University Hospital, Riyadh, Saudi Arabia for the management of stridor. According to the referral history, the patient was a known case of bronchial asthma and presented initially with difficulty in breathing at the age of 9 years. She apparently had no other medical history and was healthy prior to the first presentation. On endoscopy they had seen growth in the larynx similar to polyposis of the larynx, and was diagnosed as a case of Recurrent Respiratory Papillomatosis (RRP), that mass was excised. She again developed the same symptoms and was operated for that. She was referred for further management because of the recurrence of her symptoms.

At the time of presentation to our institute she had biphasic stridor, with minimal signs of respiratory distress and so was admitted for work-up. Her general and systemic examination was unremarkable. ENT examination was also unremarkable. On fiberoptic endoscopy, the larynx showed papillomatous growth involving both the true vocal cords and interarytenoid area. She had a narrow airway. Her vocal cords were mobile. Her blood work showed WBC count of $12.9x10^3$/ul, with eosinophil count of 60%. PPD was negative and Serology for HPV 6 and 11 was negative**.** Her c-ANCA was elevated. Direct laryngoscopy was done which confirmed the involvement of the glottic region with papillomatus lesion bilaterally with extension into the subglottic region mainly in the left side (figure 1). Excision of the lesion was done using CO_2 laser and the growth was sent for histopathology (figure 2). The diagnosis of CSS was made based on both histopathological and serological finding along with suggestive clinical presentation.

Within the next two months the patient had recurrence of symptoms and was again admitted with stridor. Along with stridor, she had developed a mass in the right vestibule of the nose. Flexible fibreoptic examination showed papillomatous growth involving the true vocal cord on the left side, the anterior commissure, inter-aryetnoid region, subglottic region and the dorsum of posterior third of tongue. Her vocal cords were mobile. Another surgical intervention was made to clear the airway. Excisional biopsies of nasal mass and tongue base mass were done during the same intervention. CT scan of the chest was done post operatively, showed chronic inflammatory airway disease with small rounded lesion seen in the right lung. A lung biopsy (figure 3) was performed among a repeat of other investigations. The result of nasal, tongue and lung biopsy were consistent with the same pathology (CSS).

At the time the child was started on prednisone with a dose of 1 mg/kg/day for 6 months and this dose was tapered down over four month. The child was under regular follow up both by the pediatrician and our team with no further airway compromise. Her last follow-up was 4 years after the last intervention, when flexible fiberoptic examination of her larynx showed a clear airway. She has however been to the emergency department from time to time for acute exacerbation of bronchial asthma.

During the course of follow up there was no sign suggesting neurological or cardiac involvement.

Discussion:

CSS is a systemic disease also referred to as *Allergic granulomatosis,* was first described in 1951 by Jacob Churg and Lotte Strauss as a syndrome consisting of “asthma, eosinophilia, fever, and accompanying vasculitis of various organ systems”.[1] CSS shares

many of the clinical and pathological features of polyarteritis nodosa ("PAN", another type of vasculitis). Churg and Strauss discovered that the presence of granulomas as well as the abundance of eosinophils distinguished this disease from PAN. The American College of Rheumatology (ACR) has established criteria that must be fulfilled in order to classify a patient as having CSS.[5] These criteria were intended to distinguish CSS from other forms of vasculitis. In order to be classified as a CSS, a patient should have at least 4 of the 6 following ACR criteria; 1) asthma, 2) eosinophilia [>10% on differential WBC count], 3) mononeuropathy, 4) transient pulmonary infiltrates on chest X-rays, 5) para-nasal sinus abnormalities and 6) biopsy containing a blood vessel with extravascular eosinophils. The presence of 4 or more of these 6 criteria yielded a sensitivity of 85% and a specificity of 99.7%. [5]

Our patient clearly fulfilled five out of six criteria outlined by the ACR. Interestingly, she is one of the few known cases of CSS primarily presenting with laryngeal symptoms and with laryngeal pathology. In a previous case report by Mazzantini et.al[6], they had a patient whose first clinical manifestation was a persistent dysphonia. Video-laryngostroboscopic examination had revealed paresis of the right vocal fold with a reduction in adduction together with incomplete glottal closure and laryngeal electromyography revealed neurogenic damage of the right thyroarytenoid and crycoarytenoid muscles. In the reported case there was only neurological involvement of the larynx, however in our case the larynx was involved by a mass lesion, which is why our case is unique in presentation. To our knowledge, this is the first case reported in the literature with such laryngeal findings. There are numerous other studies of CSS presenting with Gastro-Intestinal symptoms or with nasal symptoms particularly allergic

rhinitis and nasal polyposis[4], and occurrence in children has seen to be infrequent.[7] Other symptoms like otitis media, facial palsy and vocal cord palsy are also seen but rarely. Subglottic involvement of the larynx with vasculitis lesions in cases of Wegener's granulomatosis is reported, however, a rare finding.[8,9] Grans et.al,[10] suggested that the presence of autoantibodies along with subglottic stenosis places such patients within the spectrum of necrotizing (granulomatous) vasculitis.

Other clinical studies[11] found that the clinical characteristics of patients with CCS varied according to their ANCA status: cardiomyopathy is predominant in ANCA negative patients while necrotizing glomerulonephritis is more often observed in ANCA positive patients. These histologically documented findings suggest the existence of different CCS subtypes, characterized by the predominance of distinct pathogenetic mechanisms.

A variety of non-invasive imaging techniques is now becoming available to investigate patients with vasculitis.[12] These include Ultrasonography, MRI coupled to angiographic sequences, PET, single photon emission computed tomography (SPECT). Their role is being evaluated and their characteristics exploited to address issues specific to each vasculitis.

Prior to the advent of prednisone, CSS was often a fatal disease. The majority of patients died from rampant, uncontrolled disease. With the present therapy, constitutional symptoms begin to resolve quite quickly, with gradual improvement in cardiac and renal function, as well as improvement in the pain that results from peripheral nerve involvement. To date, with appropriate therapeutic intervention (i.e. corticosteroids and, when required, immunosuppressants), the overall outcome is very good, with 5-year

survival exceeding 90%.[11] Corticosteroids are the cornerstone of treatment for CSS. Because these drugs are usually sufficient for treatment of most patients who do not have severe organ involvement, they should be viewed as first-line therapy.[13] Prednisone (1 mg/kg/day) or its equivalent methylprednisolone tapered over 6 months may be tried first**.** In patients with severe or multi-organ involvement, the administration of methylprednisolone 1 g for 3 days is recommended, followed by prednisone 40-60 mg daily continued until no evidence of disease is present and then gradually tapered.[14] When corticosteroid therapy does not induce remission, or when patients have poor prognostic factors, immunosuppressive cytotoxic therapy is indicated with drugs such as azathioprine, cellcept, methotrexate, or cyclophosphamide used in addition to prednisone.[15,16] The combination of pulse corticosteroids, pulse cyclophosphamide and high dose intravenous immunoglobulins seem effective for the acute phase of severe CSS.[15] Intra-Venous Immunoglobulin therapy is a hopeful candidate for second-line treatment, particularly in the case of neuropathy and/or cardiomyopathy, which are resistant to conventional therapy.[16] The new biological therapies under development are anti-interleukin-5 or anti-immunoglobulin E monoclonal antibodies as Omilizumab.[7]

The patient's response to treatment and the continuation of disease control during lowering of the prednisone dose are the primary determinants of how long therapy is continued. Laboratory monitoring of blood tests is very helpful in gauging the activity of disease. Some of the most useful laboratory tests for follow up are the ESR and the eosinophil count.[13]

Conclusion:

CSS is a systemic disorder and is now defined as one of the ANCA-associated vasculitis. Despite recent interests it is still a rare disease with a poorly understood pathogenesis. This paper describes a unique case of CSS which presented with laryngeal mass, stridor and findings resembling RRP. So a case of a bronchial asthma presenting with RRP may not be as straight forward as it seems.

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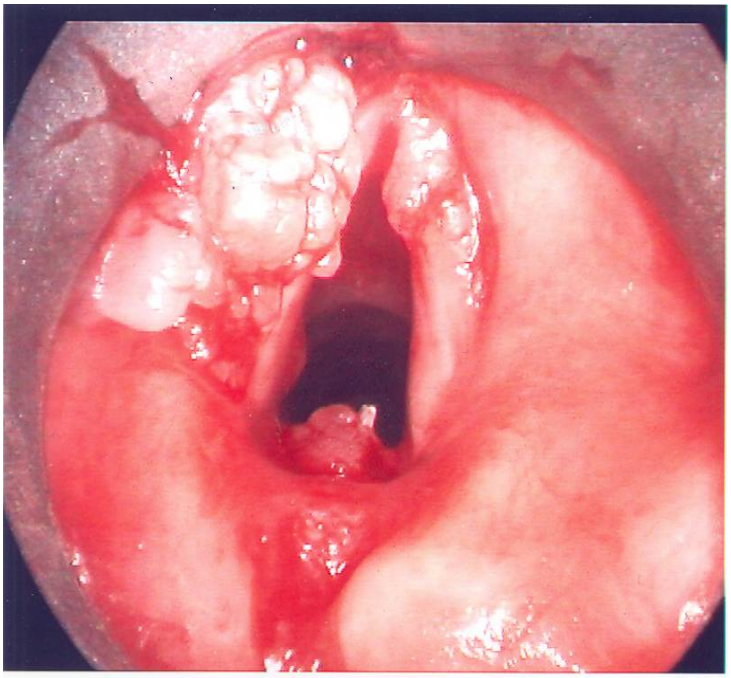

Figure 1: The lesion involving both vocal cords and interarytenoid area.

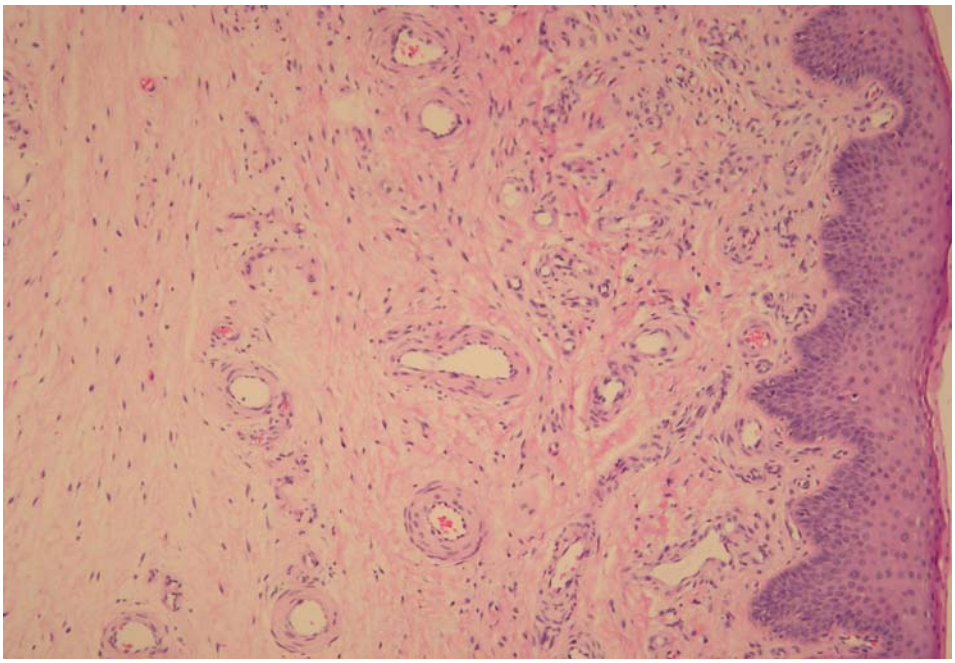

Figure 2; (hematoxylin and eosin stain original magnification x 128) section shows multiple vessels with evidence of vasculitis. The vessel walls show fibrin deposits. Perivascular area shows number of eosinophils, plasma cells and macrophages.

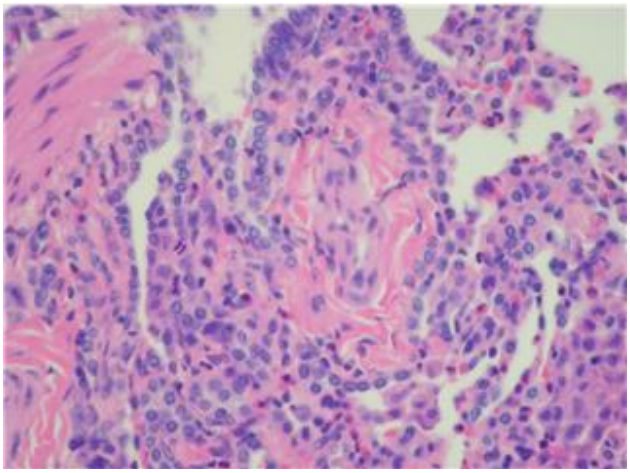

Figure 3; (hematoxylin and eosin stain original magnification x 320) section shows lung tissue with parenchymal fibrosis, lymphocytic, plasma cells and eosinophils infiltration along with fibrinoid thickening of medium sized blood vessels.