Case Report

A Rare Case of Mucosa-associated Lymphoid Tissue (MALT) Lymphoma in a Child with Sjögren's Syndrome Presenting with Parotid Mass and Subglottic Stenosis

TWY Cheung, CH Li, TL Ku, SY Lam, SN Wong

Abstract

Sjögren's syndrome is a chronic inflammatory autoimmune disorder characterised by lymphocytic infiltration and destruction of the salivary and lacrimal glands by auto-antibodies. Although considered a benign disease, it is associated with a range of complications manifested in multiple organ systems and even higher risk for developing lymphoma, one of which is mucosa-associated lymphoid tissue (MALT) lymphoma. It is a rare complication and predominantly occurs in adults, with limited reports in the paediatric population. We report a case of MALT lymphoma presenting with a left parotid mass and subglottic stenosis in a 13-year-old girl with known history of Sjögren's syndrome. Although cases of children with Sjögren's syndrome have been reported, the development of MALT lymphoma in children presenting with subglottic stenosis is rarely reported. Clinicians should be alerted for the possibility of malignant infiltration.

Key words

Children; MALT; Mucosa-associated lymphoid tissue lymphoma; Sjögren's syndrome; Subglottic

Introduction

Marginal zone lymphomas (MZL) are mature B-cell lymphomas. They account for a small percentage of non-Hodgkin lymphomas. There are 3 main types of marginal zone lymphomas, namely nodal MZL, splenic MZL and mucosa-associated lymphoid tissue type (MALT) lymphoma. The MALT lymphoma comprises 7-8% of all B-cell lymphomas.1

Most cases of MALT lymphoma occur in adults with a median age of 60 and in mucosa-associated lymphoid tissue, including the orbit, conjunctiva, salivary glands, skin, thyroid gland, lungs, stomach, and intestine.2 Patients with certain autoimmune diseases, such as Sjögren's syndrome or Hashimoto thyroiditis and Helicobacter pylori associated chronic gastritis, are at increased risk of developing MALT lymphoma.

Subglottic stenosis is a narrowing of the subglottic airway and is clinically manifested as dyspnoea and stridor. Although an uncommon condition in children, there is a wide range of underlying aetiology accounting for subglottic stenosis; it can be attributed to in-utero congenital malformations or acquired conditions such as post traumatic due to prolonged intubation and ventilation, post infective, and some cases with cause undetermined.3

We report a paediatric patient with a known history of Sjögren's syndrome, presenting with upper airway obstruction symptoms, subsequently found to show subglottic stenosis due to MALT lymphoma involving the airway.
Case Report

A 13-year-old Chinese girl presented to the paediatric clinic for two-year history of a left parotid mass and xerophthalmia. Examination revealed a 2-cm firm mass in the left parotid region. Lymphadenopathy, hepatosplenomegaly, and other joint abnormalities were absent on physical examination. Further investigations including ultrasound scan of the parotid revealed chronic parotitis changes. Serological tests showed a positive ANA serology titre of 2560 (normal <40), positive rheumatoid factor IgM, anti-La and anti-Ro antibodies. The diagnosis of Sjögren’s syndrome was confirmed with salivary gland biopsy and positive Schirmer’s test.

Subsequently the girl complained of shortness of breath and decreased exercise tolerance for a few weeks. She had neither stridor nor hoarseness. Fiber-optic laryngoscopy revealed subglottic stenosis occupying approximately 50% narrowing of the lumen with an indistinct lower border. Contrast computed tomography scans demonstrated circumferential mural thickening of trachea involving the inferior aryepiglottic folds, glottic and subglottic regions, extending approximately 3 cm in length leading to airway narrowing (Figure 1). A 3.4 cm x 2.2 cm x 3.2 cm solid enhancing area was suspicious of a mass in superficial left parotid gland. Baseline spirometry revealed fixed upper airway obstruction pattern. Bronchoscopy performed several weeks after the first airway assessment showed subglottic stenosis with suspected increase in severity of obstruction (Figure 2). With the severity of the obstruction, the bronchoscope was not passed further beyond the site of stenosis. The differential diagnosis of Wegener’s granulomatosis was unlikely due to negative results for serum anti-neutrophil cytoplasm antibody assay.

Sjögren’s syndrome with subglottic involvement was an unusual presentation. A biopsy of the parotid mass and subglottic mass was performed. Histopathologic examination of the parotid tissue showed dense infiltration of lymphoid cells with almost complete acinar destruction and few remaining ductal structures. In most areas, the

Figure 1  Computed tomography scan showing subglottic stenosis in different views.
lymphoid infiltrate comprised of small sized lymphocyte with pale cytoplasm and twisted irregular nuclei consistent with cells with marginal zone differentiation. These cells grew in thick pale bands around residual ductal structures, which were also infiltrated by those lymphoid cells forming lymphoepithelial lesions. Immunohistochemical stains confirmed that the thick bands of small lymphoid cells are CD20+B cells, which were BCL2+, CD10-, and BCL6-. They did not co-express CD5, CD23 or CD43. The findings were in keeping with an extranodal marginal zone B cell lymphoma (MALT lymphoma). No large cell transformation was seen. The sections of fragments obtained from subglottic region showed submucosa infiltrated by a dense lymphoid infiltrate. Immunostain showed prominently B cells (CD 20+) with features similar to the biopsy specimen of left parotid gland. No lymphoepithelial lesion was seen. The dense B cell infiltrate were characteristic of marginal zone B cell lymphoma.

Positron emission tomography (PET) scans revealed an abnormal mass measuring 3.6 cm x 2 cm at the left parotid gland with elevated FDG uptake ($SUV_{max}$=6.3). Thicken with FDG uptake is noted over the vocal cord. A bone marrow biopsy revealed no evidence of lymphoma infiltration.

The chemotherapy regimen (R-CHOP) containing rituximab, cyclophosphamide, doxorubicin and prednisolone was commenced. Prompt clinical response noted with examination showing shrinkage in size of the left parotid mass and relief of respiratory symptoms after the initial course of chemotherapy. After the second course of chemotherapy, the spirometry showed the peak inspiratory flow improved from 1.92 L/sec to 5.41 L/sec and the FEV1 (% predicted) improved from 54.5% before treatment to 95%. CT thorax demonstrated significant interval shrinkage of the enhancing lesion of the left parotid gland. 3D virtual reconstruction of the airway and lungs showed that the airway was no longer narrowed with resolution of the previously seen wall thickening along glottic and subglottic region. Lung function testing revealed a normal spirometry, lung volume and DLCO. There was no longer evidence of upper airway obstruction as previously seen on flow volume loops.

A total of 6 courses of chemotherapy were given. The end-of-treatment whole body PET scan showed resolution of previously detected FDG-avid mucosal thickening at the nasopharynx. No sizable mass lesion of abnormal FDG uptake was noted. There was also an interval reduction in size and metabolic activity of the hypoenhancing lesion at the left parotid region, measuring 2.35 cm x 1.79 cm ($SUV_{max}$ =1.5). This lesion further regressed and was not visible in the follow up PET scan performed 6 months later. Reassessment bronchoscopy was performed at 1 month after completion of treatment. The subglottis was of normal caliber and the rest of the airway was unremarkable. Lung function studies performed 4 months after completion of chemotherapy were also unremarkable. The patient remained disease free at 4 years post-treatment follow up.

Discussion

Sjögren's syndrome is a chronic inflammatory autoimmune disorder characterised by lymphocytic infiltration and destruction of the salivary and lacrimal glands by autoantibodies, resulting in xerostomia and keratoconjunctivitis sicca. Up to 4 to 10% of the patients suffering from Sjögren's syndrome are at risk for developing lymphoma, the majority being MALT lymphoma. The risk is believed to be approximately 44 times that seen in the general population. Nevertheless, the incidence of MALT lymphoma in the paediatric population is uncommon. Despite observation that MALT lymphomas are commonly derived from a background of chronic inflammatory disorders, including autoimmune diseases, in a large review of MALT lymphoma in children in 2004, of

![Figure 2](image-url) Subglottic stenosis demonstrated on bronchoscopy.
the 15 report cases with salivary gland MALT lymphoma, none had an associated history of Sjögren's syndrome, or other autoimmune disorders. One recent article reported on two cases of MALT lymphomas arising in the parotid glands of two teenagers with Sjögren's syndrome.

Likewise, subglottic stenosis is a rare condition in children. There is a wide range of underlying aetiology accounting for subglottic stenosis; it can be attributed to in-utero congenital malformations or acquired conditions such as post traumatic due to prolonged intubation, post infective, some cases the cause remains undetermined. Few case reports have described MALT lymphoma presenting with subglottic stenosis but all beyond the paediatric population.

Sjögren's syndrome complicated with MALT lymphoma presenting with subglottic stenosis have not been well documented previously in paediatric population according to a Pubmed search in the English language prior to 2018. Pubmed search using keywords including "Sjögren's syndrome", "upper airway OR subglottic OR trachea", "subglottic stenosis" yielded 21 citations (only 4 relevant and 1 in Japanese) but all of which mentioned case reports of the elder population. Until recently, Pubmed search yielded two similar cases reported in July 2019 of MALT lymphoma in a 15 year old child with Sjögren's syndrome. This case report describes one of the first few cases of patients with history of Sjögren's syndrome presenting with subglottic stenosis in our locality, subsequently proven to be MALT lymphoma of the subglottis.

Most MALT lymphomas in adult patients are treated conservatively, by surgery or local radiotherapy for early stage cases. Chemotherapy is reserved for disseminated diseases. In the paediatric age group regardless of an association with Sjögren's syndrome, the consensus of treatment is lacking. Most clinicians follow the experience from adult series. Majority of MALT lymphoma in adults have an indolent clinical course and prognosis is usually favourable, with 5-year overall survival reported between 86% and 95%.

Paediatric marginal zone lymphoma (be it nodal or extranodal) also shows very good prognosis. In our case, prompt treatment with chemotherapy showed rapid response and good outcome and remain disease free since treatment.

Conclusion

Although rare, it is important to recognise MALT lymphoma as a developing complication in paediatric population with Sjögren's syndrome and it may present insidiously with subglottic stenosis causing significant symptoms. This was previously not reported in children. Early recognition is important for initiating prompt treatment, as the condition tends to show good and rapid clinical response to chemotherapy with favourable and lasting outcomes.

Conflict of Interest

The authors have no conflicts of interest to disclose.

References