Case Report

A case report of narrowing primary tracheal mucosa-associated lymphoid tissue lymphoma: A multidisciplinary approach

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ABSTRACT

Extranodal marginal zone lymphomas of mucosa-associated lymphoid tissue (MALT) are low-grade B-cell neoplasms, which arise in mucosal sites with prolonged lymphoid proliferation. Primary tracheal MALT lymphoma is an exceedingly rare entity for which the optimal treatment approach has not been determined. Here, we report a case of MALT lymphoma involving the trachea in a 64-year-old smoking woman who received desobstructive endoscopy and was thereafter successfully treated with (anti-CD20) immunotherapy and radiotherapy.

Key words: Immunotherapy, mucosa-associated lymphoid tissue lymphoma, radiotherapy, trachea, treatment modality

INTRODUCTION

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) is classified among low-grade B-cell neoplasms. Referring to most frequently involved anatomical sites, three main categories are defined: Gastric, cutaneous and nongastric/noncutaneous.[1,2] Among nongastric/noncutaneous MALT lymphomas, primary involvement of tracheal mucosa is extremely rare likely because of the low lymphoid tissue representation along the tracheo-bronchial tree. Based on a few series, it may represent the 0.5% of all tracheal cancers.[3,4]

Here, we describe a case of primary tracheal MALT lymphoma in a 64-year-old woman treated with a multi-modal approach including disobstructive surgery (S), anti-CD20 immunotherapy (IT) and radiotherapy (RT).

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CASE REPORT

In March 2013 a 64-year-old smoking woman presented to our hospital with a 18 months-history of persistent cough and worsening dyspnea. The work-up included a chest X-ray, which was normal; spirometry could not be performed because of severe dyspnea; the general physical examination showed normal findings; full blood count (FBC), renal and liver function tests, coagulation parameters, velocity of erythrocyte sedimentation rate and beta 2-microglobulin were unremarkable; ferritin level was 202 ng/mL and serum protein electrophoresis showed a tiny peak in the α1- and α2-globulin regions. A chest computed tomography (CT) revealed a vegetant endotracheal lesion of approximately 17 mm located at the lower third of trachea. The mass caused a luminal narrowing of about 50% and was in continuity with a definite right paratracheal tissue 35 mm in width [Figure 1]. Due to the worsening of her clinical symptoms, the patient subsequently underwent desobstructive endoscopy. The histological examination revealed the presence of dense infiltrates of small mature lymphocytes with a CD20+/CD21+/CD10 − phenotype

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on immunohistochemistry, suggesting the diagnosis of MALT [Figure 2a-c]. Molecular characterization of the IgVH gene showed a monoclonal pattern. Disease staging was completed with a fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/CT scan (PET/CT), which showed mild ^{18}F-FDG uptake in the mediastinum (i.e. peritracheal) [Figure 3]. Bone marrow biopsy and aspirate resulted negative for involvement by lymphoproliferative disease.

Finally, the diagnosis was of B-cell MALT, stage IE on Ann-Arbor classification. In May 2013 the multidisciplinary team decided to treat the patient with a combined approach consisting of IT followed by RT, because, in absence of clear reference guidelines, this combined therapy could achieve the best response with minimal adverse events.

In June 2013, the patient was administered anti-CD20 monoclonal antibody Rituximab (Mabthera®) at a dose of 375 mg/m^2 BSA by i.v. infusion for a total of 4 cycles (on day 1, 8, 15, and 22); the treatment was well tolerated and no adverse events were registered. Three weeks after the end of IT, the patient underwent involved-field intensity modulated radiation therapy (IMRT). Planning CT images were co-registered with mutual information modality with diagnostic CT images. Gross tumor volume (GTV) was defined using radiological findings as the tract of trachea originally involved plus the paratracheal contiguous soft tissue. Clinical target volume (CTV) was considered as the volume at risk for subclinical disease and generated adding a margin of 1 cm to the GTV. The planning target volume (PTV) was obtained with a further isotropic expansion of 1 cm of the CTV. IMRT planning was performed with 8 coplanar fields and a 6 MV photon beam, using a step-and-shoot technique. Recommended dosimetric constraints for lung, esophagus, spinal cord, heart, larynx and lungs were satisfied according to Quantitative Analysis of Normal Tissue Effects in the Clinic.[5] From July 16 to August 8 2013, a total RT dose of 30.6 Gy was administered in 17 fractions with conventional fractionation schedule of 1.8 Gy, using a × 6 MeV photon beam produced by a linear accelerator (Synergy Platform; Elekta). According to Radiation Therapy Oncology Group scale, G1 esophageal toxicity (dysphagia) was recorded during the RT treatment.

At the end of IT-RT treatment (September 2013) the physical examination was negative and the patient did not refer any therapy-related complain; FBC and biochemistry were unremarkable and a CT scan showed total regression of the paratracheal tumor tissue. At 5 months follow-up a restaging ^{18}F-FDG PET/CT was performed with no evidence of pathological FDG uptake [Figure 4]. After a follow-up of 10 months, the patient is alive with no evidence of disease and without clinical signs of therapy side effects.

DISCUSSION

Primary tracheal tumors are rare cancers, accounting for only 0.1% of all neoplasms. Epidemiological and clinical data are limited but it appears that squamous cell carcinoma is the most common histological type, followed by adenoid cystic carcinoma and adenocarcinoma. Tracheal involvement by non-Hodgkin lymphoma is sporadic, representing approximately 0.5% of all tracheal neoplasms;[4] among these tumors, primary MALT B-cell lymphomas of the trachea represent a distinct sub-category. Reviewing Pubmed literature we could identify only 13 previously published case reports of primary tracheal MALT.[2,3,6-15]

Clinical features of MALT include tendency to remain localized for a prolonged period of time,[6] with a low potential for transformation into more aggressive diseases. Takami *et al.*, observed that MALT occur most frequently in patients with median age of 44 years; 75% in stage IA at

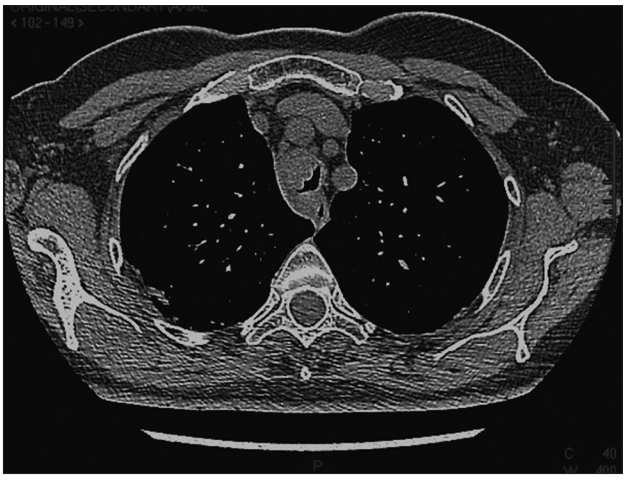

Figure 1: Mucosa-associated lymphoid tissue tracheal lesion on computed tomography scan on March 2013

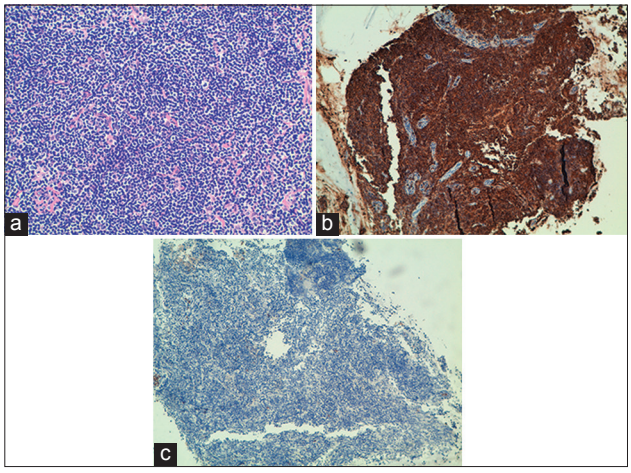

Figure 2: (a) Histopatological image – H and E, detail. (b) Immunohistochemical staining (CD20+/×10). (c) Immunohistochemical staining (CD10−/×10)

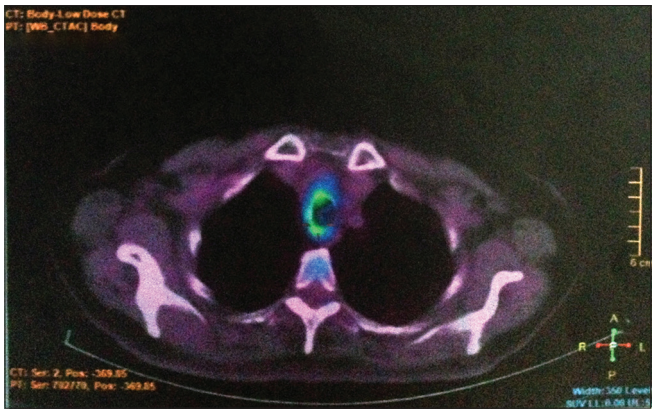

Figure 3: Staging positron emission tomography/computed tomography after endotracheal resection on April 2013

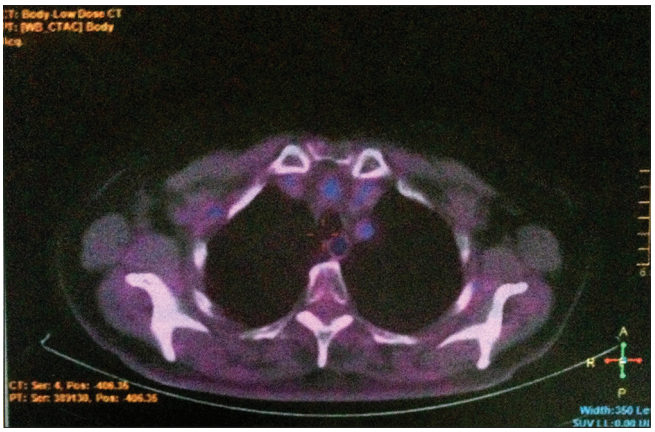

Figure 4: Positron emission tomography/computed tomography after combined treatment on January 2014

diagnosis.[7] Presenting symptoms, often delayed in adult patients because of large tracheal lumen, are similar to those of chronic obstructive pulmonary disease and include dyspnea, cough, stridor, and/or wheezing. Hemoptysis was described in two-thirds of patients, even though this is less frequently reported in tracheal lymphoma due to its submucosal location.[8] Useful staging procedures include a CT scan of the chest and bronchoscopy with direct biopsy of the lesion; gastrointestinal tract should be investigated through endoscopy. PET/CT scan should be performed in order to obtain information about diverse sites of involvement.

No guidelines for the optimal management of tracheobronchial MALT have been established.[9] S, RT, chemotherapy, IT, including anti-CD20 monoclonal antibodies, local ethanol injection, and temporary tracheal stenting have been used alone or in combination.[6,8,13] In the review of the literature by Takami *et al.*, on 28 cases of primary tracheal lymphomas, 5 of them were classified as stage I MALT and treated with RT or S, combined S and RT or chemo-RT, and laser photoresection therapy alone.[7] Mira-Avendano *et al.*, reported all the same combined treatment approaches on seven cases of proved MALT of the trachea.[2]

Our patient received IMRT after S and four cycles of IT with anti-CD20 monoclonal antibody (Mabthera) with a complete response documented at the end of treatment. In the case of MALT, the recommended RT dose is 24–30 Gy.[1] To the best of our knowledge, no previous report of a combined approach including S, anti-CD20 IT and IMRT has been published. Although prognosis is generally favorable, little is known about overall outcomes.

Our multi-modal treatment was well tolerated and to date-despite a short follow-up-the patient is alive with no radiological and clinical signs of disease. Although the optimal treatment remains debatable, and it probably should be tailored on patient presenting symptoms, a multi-disciplinary team management is mandatory.

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