EUR. J. ONCOL.; Vol. 20, n. 2, pp. 109-113, 2015

A rare case of tracheal lymphoma presenting with severe tracheal stenosis

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Summary. Primary malignant lymphoma of the trachea is rare and its underlying mechanism remains unknown. Primary tracheal tumors are also very rare causes of airway obstructions. This case report features a 60 year-old woman who presented with the complaint of dyspnea. A mass narrowing the tracheal lumen posteriorly in the subglottic area and mediastinal lymphadenopathy was detected by computed tomography scan and a rijit bronchoscopy was performed. This showed polypoid, variable-sized, irregular nodules causing narrowing of the tracheal lumen over a 3 cm segment in the middle part of the trachea and a mass protruding into the tracheal lumen from the posterior part of the proximal trachea. Multiple biopsy was carried out from the nodules and the airway obstruction was treated with Argon Plasma Coagulation (APC). After removal of the debris, tracheal lumen patency was obtained. The histopathology examination revealed a small lymphocytic primary non-Hodgkin's lymphoma of the trachea. To our knowledge, this is the first case of small lymphocytic primary tracheal lymphoma in the literature.

Key words: tracheal lymphoma, tracheal stenosis, interventional bronchoscopy

«Un raro caso di linfoma della trachea con stenosi severa»

Riassunto. Il linfoma primitivo maligno della trachea è raro e il suo meccanismo sottostante ancora sconosciuto. I tumori primitivi della trachea, inoltre, raramente sono causa di ostruzioni delle vie aeree. Questo report presenta il caso di una donna di 60 anni con dispnea. Eseguendo una tomografia computerizzata e una broncoscopia, sono state rilevate una massa nella zona sub-glottica con restringimento del lume della trachea nella parte posteriore ed una linfoadenopatia mediastinica. Polipi di diverse dimensioni e noduli irregolari causavano il ristringimento del lume della trachea di circa 3 cm nella parte centrale mentre era presente anche una massa sporgente nel lume prossimale della trachea. E' stata effettuata una biopsia multipla sui noduli mentre l'ostruzione è stata trattata con APC (Argon Plasma Coagulation). Dopo la rimozione dell'essudato si è ottenuto la pervietà del lume della trachea. L'esame istopatologico, ha evidenziato nella trachea un piccolo linfocita primitivo del linfoma Non-Hodgkin's. Sulla base delle nostre conoscenze, questo è il primo caso di linfocita primitivo della trachea esistente in letteratura.

Parole chiave: linfoma della trachea, stenosi tracheale, broncoscopia interventistica

Introduction

Primary neoplasms of the trachea are uncommon, accounting for only 0.1% of all malignancies (1). The most frequent tumors of the trachea are squamous cell carcinoma and adenoid cystic carcinoma (2). Primary presentation of extranodal lymphoma affecting the trachea is quite unusual. Primary tracheal non-Hodgkin's lymphoma (NHL) accounts for only 0.2% to 3% of all tracheal tumors (2-4). Small lymphocytic primary tracheal lymphoma is likewise quite rare. Despite its rarity, tracheal lymphoma can cause life-threatening airway obstruction. We present the case of a patient with small lymphocytic primary tracheal lymphoma succesfully treated for airway obstruction with APC (Argon Plasma Coagulation). A review of the literature regarding primary tracheal small lymphocytic lymphoma is provided to better define the clinical characteristics and management of this uncommon disease.

Case report

A 60-year-old woman was referred to our hospital with the complaint of dyspnea for 4 years and increasing symptoms over the last 2 months. Her medical, smoking and family histories were all noncontributory. She was dyspneic and had stridor at presentation. Her other physical examination was unrevealing. Laboratory data revealed normal blood count (WBC 4900 and absolute lymphocyte count 1700), renal and liver functions. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) were higher than normal range. A computed tomography (CT) scan of the chest showed soft tissue masses adjacent to the trachea causing narrowing of the tracheal lumen and mediastinal lymphadenopathy (Figure 1). Rigid bronchoscopy showed polypoid, variable-sized, and irregular nodules causing narrowing of the tracheal lumen over a 3 cm segment in the middle part of the trachea and a mass protruding into the tracheal lumen from the posterior part of the proximal trachea (Figure 2). Multiple biopsy was carried out from the nodules and the airway obstruction was treated with APC. After removal of the debris, tracheal lumen patency was obtained. Pathological examination of the specimen revealed a small lymphocytic lymphoma (Figure 3). In the immunohistochemical study, CD20, CD5, BCL-2 receptors were positive and Cyclin-D1, CD10, CD3, CD23 and BCL6 receptors were negative. The patient was referred to the medical hematoncology department for further management. A chemotherapy regimen was planned to follow the procedure.

Discussion

Tracheal neoplasms account for less than 0.1% of all malignancies (1). Tracheal tumors may be primary or, more commonly, secondary to the invasion of tumors arising from neighboring structures. Primary tra-

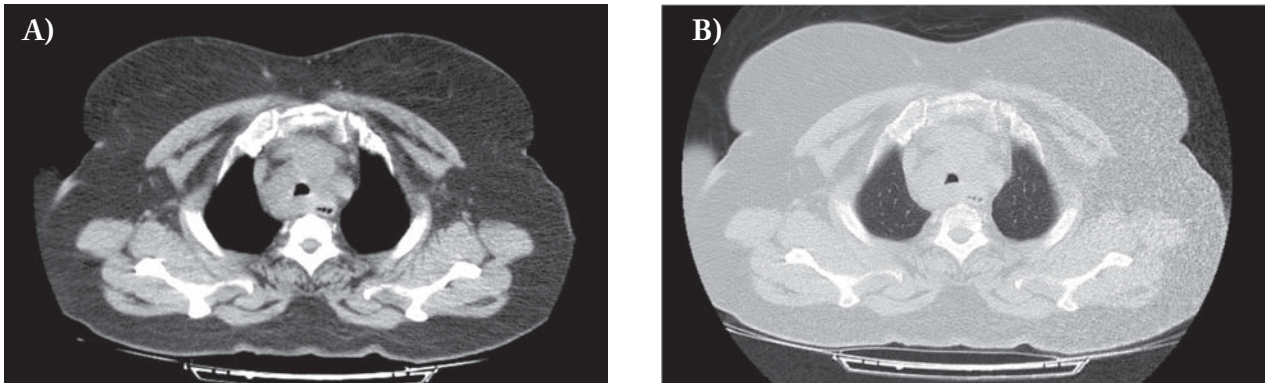

Figure 1. Computed tomography (CT) scan of the chest showed multiple soft tissue masses adjacent to the trachea, causing diffuse narrowing of the tracheal lumen. A) Mediastinal window. B) Pulmonary window.

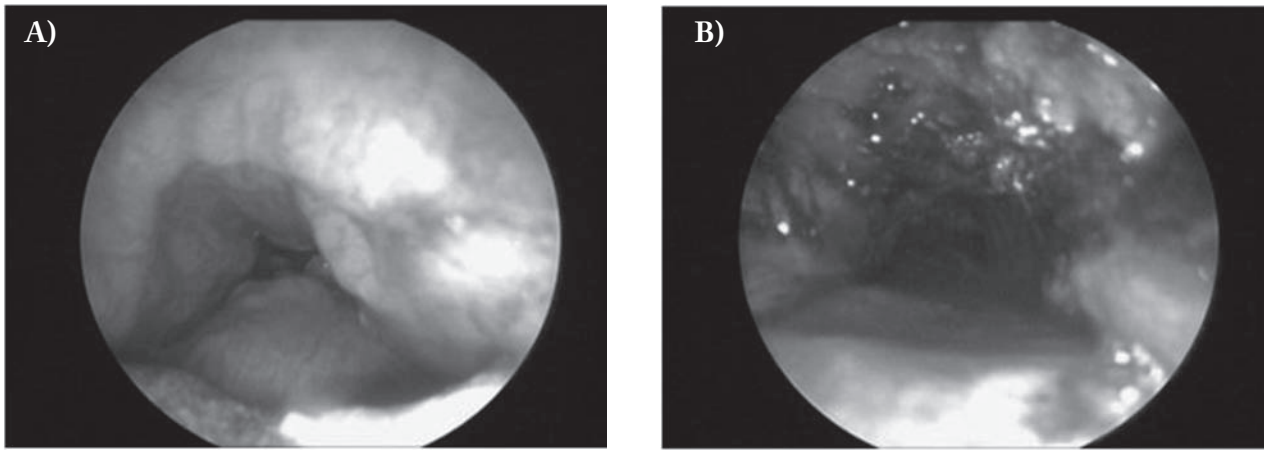

Figure 2. The presentation of fibrobronchoscopy showed polypoid, variable-sized, irregular nodules. A) Narrowing of the tracheal lumen in the middle of the trachea. B) The patency of the lumen after APC.

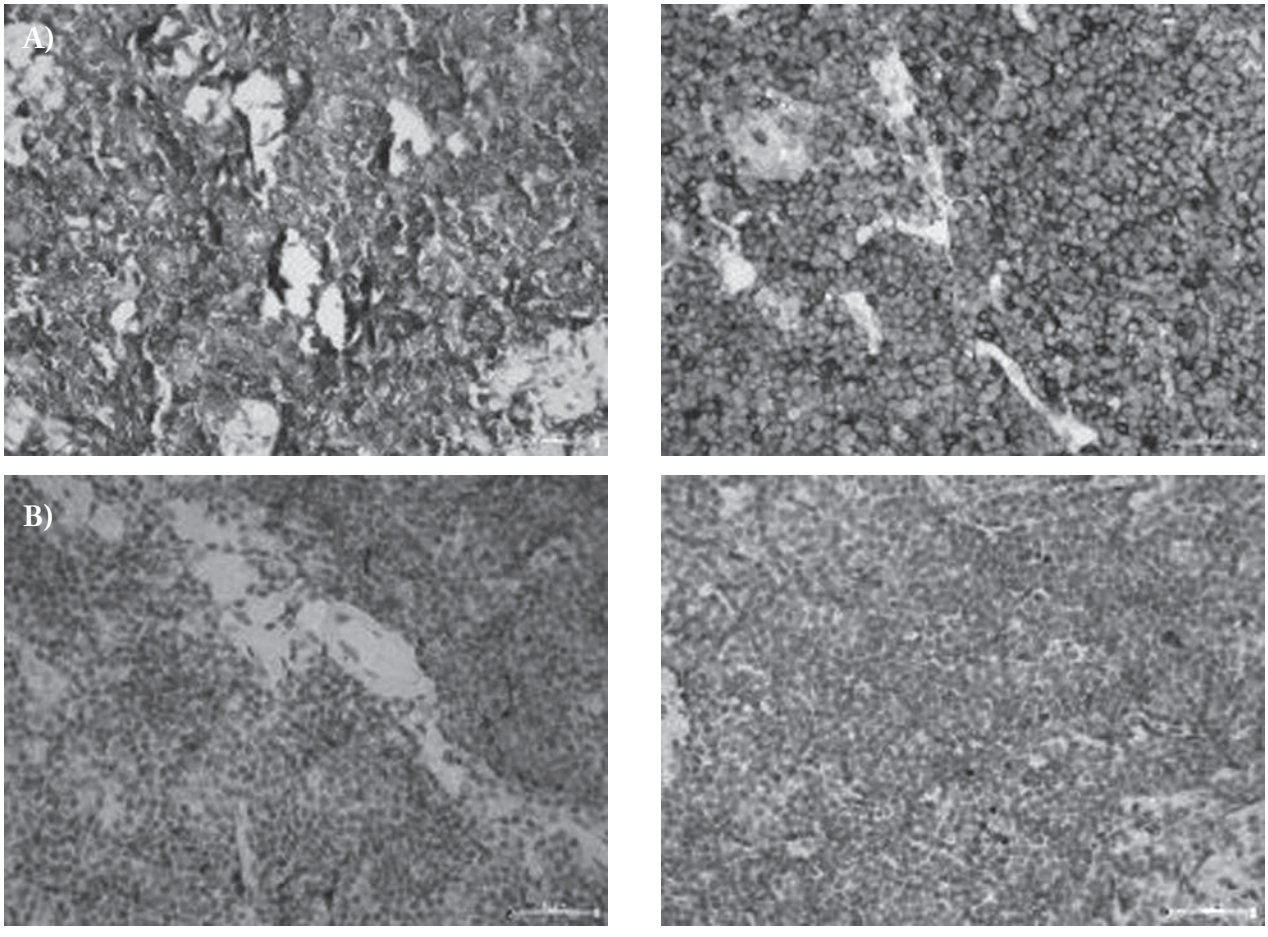

Figure 3. A) Microscopic appearance of tracheal tissue (hematoxylin and eosin stain, 400x) showing proliferation of small lymphoid cells beneath the intact tracheal mucosa. B) The immunohistochemical results (DAB, 400x) showed the presence of markers. CD20 (1), CD20 (2), CD23 (3) and BCL 6 (4).

cheal tumors develop very rarely, with an incidence of about 0.1 per 100,000 persons and over 90% of these are malignant. Primary non-Hodgkin's lymphoma of the trachea is even more rarely encountered, representing 0.23% of all tracheal tumors (5, 6). Non-Hodgkin's lymphomas (NHLs) are closely related yet heterogeneous diseases distinguished by specific morphologic, immunophenotypic, genetic, and clinical features (7). There is increasing evidence to support some etiologic heterogeneity among NHL subtypes as well, varying considerably in risk for infectious agents, autoimmune diseases, and genetic susceptibility (8-12).

Tracheobronchial involvement of NHL, whether primary or secondary, is likewise a rare event among patients with NHL. Both autopsy and radiographic series suggest that the most common mechanism of tracheal involvement by NHL is displacement of the (??) adjacent lymph nodes, with narrowing of the lumen or erosion through the tracheal wall (2). In a previous study, it was suggested that NHL also may arise de novo from lymphoid tissue present in the trachea (2). In non-Hodgkin's lymphoma, diffuse large B-cell lymphoma is the most common subtype which accounts for approximately 25% of cases (13). About 5% to 10% of all lymphomas are small lymphocytic lymphomas (14). Small lymphocytic lymphoma (SLL) is a slow-growing disease and usually not curable with standard treatments, but depending on the stage and growth rate of the disease, most patients live longer than 10 years. Sometimes, these slow-growing lymphomas turn into a more aggressive type. In SLL, the cancer cells are mainly in the lymph nodes and spleen (14). To our knowledge, this is the first small lymphocytic primary tracheal lymphoma case in the literature.

The incidence of NHL increases with age. The median age of patients with primary tracheal lymphoma is 44 years, with a range of 4 to 81 years. Most patients with NHL present with peripheral lymph node enlargement, with or without systemic symptoms. NHL may also involve mediastinal, intra-abdominal and pelvic lymph nodes with resulting symptoms. Primary endotracheobronchial involvement in NHL is a rare presentation. Laryngotracheal involvement of lymphoma is an uncommon cause of upper airway obstruction. Since they are often misdiagnosed as asthma or chronic lung disease, the diagnosis can be delayed for years. According to a review by Takami *et al.* (4) the most common presenting symptoms of tracheal lymphoma cases are dyspnea, cough, stridor, and wheezing. Airway obstruction is reported in 87% of the patients, half of whom require emergency intervention. Hemoptysis is an uncommon symptom, due to the submucosal localization of the tracheal lymphoma. The median duration of symptoms before diagnosis is 1 month. Diagnosis may also be delayed in adults because of the large functional reserve of the tracheal lumen, which often requires 50% to 75% occlusion before symptoms present (4, 15).

Symptomatic progression leads to diagnosis with bronchoscopy or CT scan. Conventional chest x-rays are not commonly diagnostic for tracheal diseases, and tumors can easily be overlooked. CT is the most useful method to assess tracheal tumors radiologically because itallows assessment of the tumor extent and its relationship to adjacent structures (16). In all cases, although CT and positron emission tomography scans are useful for staging, it is the biopsy and resulting pathology that determine treatment and prognosis.

Given the rarity of the diagnosis, there is no standard treatment regimen. Surgical intervention, chemotherapy, and radiotherapy have been used alone or in combination. Some NHLs are potentially curable with chemotherapy and, less often, radiotherapy; however, treatment protocols vary by NHL subtype and continue to evolve. Surgery is often undertaken for early stage disease, either alone or in combination with chemotherapy. Patients with indolent NHL, particularly chronic lymphocytic leukemia CLL/SLL, have well-characterized long-term immune dysfunction because of prediagnostic immune alterations, a relapsing-remitting disease course, and repeated exposure to immunosuppressive therapies over time (17, 18). The monoclonal antibodies used to treat SLL can be divided into groups according to which protein they target. A number of monoclonal antibody drugs used to treat SLL target the CD20 antigen and the CD52 antigen, which is found on the surface of SLL cells and many T lymphocytes (17, 18).

For patients with symptomatic stenosis, interventional bronchoscopy provides rapid relief that can be lifesaving and improve quality of life. In general, temporary tracheal dilatation as a palliative treatment can

be a favorable choice for a patient with tracheal stenosis by primary tracheal lymphoma. It is an integral part of multi-therapy methods.

Interventional bronchoscopy followed by chemotherapy, radiotherapy, or both, has been suggested as an approach in patients with symptomatic stenosis (19). Similarly, in our case a chemotherapy regimen was planned to follow the procedure.

The case presented here is the first reported case of small lymphocytic lymphoma in the literature. It is crucial to obtain an anatomopathological diagnosis from a specialized pathologist. Medical professionals should recognize that indolent NHL could rarely be confined to the trachea or bronchi when patients present with unexplained airway obstruction and interventional bronchoscopy is beneficial in the management of tracheal lymphoma with symptomatic airway stenosis, as in this case.

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Received: 27.3.2015
Accepted: 11.6.2015
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