

## case report

# Primary anaplastic large cell lymphoma of trachea with subcutaneous emphysema and progressive dyspnea

Kian Khodadad,<sup>a</sup> Shirin Karimi,<sup>b</sup> Mehrdad Arab,<sup>c</sup> Zahra Esfahani-Monfared<sup>a</sup>

From the <sup>a</sup>Thoracic Oncology Department, Chronic Respiratory Disease Research Center, <sup>b</sup>Pathology Department, Mycobacteriology Research Center, and <sup>c</sup>Thoracic Surgery Department, Tracheal Disease Research Center, Masih Daneshvari Hospital, National Research Institute of Tuberculosis and Lung Disease, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Correspondence: Kian Khodadad, MD · Thoracic Oncology Department, Chronic Respiratory Disease Research Center, Masih Daneshvari Hospital, National Research Institute of Tuberculosis and Lung Disease, Shahid Beheshti University of Medical Sciences, Shahid Bahonar Ave., Darabad, Tehran 1955841452, Iran · T: +982126109946, F: +982126109946 · [kiankhodadad@yahoo.com](mailto:kiankhodadad@yahoo.com) · Accepted: May 2011

Hematol Oncol Stem Cell Ther 2011; 4(4): 188-191

DOI: 10.5144/1658-3876.2011.188

Primary anaplastic large cell lymphoma of the trachea is a rare tumor. Common complaints are dyspnea and cough that could mimic a partially refractory asthma in some cases. We report a 16-year-old female with an anaplastic large cell lymphoma (null cell type) in which tracheal involvement was presented with life-threatening airway obstruction and subcutaneous emphysema. After debulking the tumor by endobronchial curettage, the patient was treated with chemotherapy followed by local radiotherapy. She had no evidence of local or distant recurrence after 25 months. Primary anaplastic large cell lymphoma of the trachea is a rare life-threatening disease. Nevertheless, this condition has a good prognosis if diagnosed immediately and treated with chemotherapy and radiotherapy.

Primary tumors of the trachea can be benign or malignant. Benign tumors compose 10% of primary tumors and are usually misdiagnosed as asthma or chronic lung disease.<sup>1</sup> Primary malignant tumors of the trachea are uncommon,<sup>2,3</sup> accounting for 0.1% to 0.4% of all malignancies.<sup>1</sup> Squamous cell carcinoma and adenoid cystic carcinoma are the most prevalent pathology.<sup>2</sup> Primary presentation of extranodal lymphoma in trachea is rare.<sup>4</sup> Previous studies in combined data from 7 series of 425 cases of tracheal tumors (between 1930 and 1989), reported only 1 (0.23%) case with primary tracheal lymphoma (PTL).<sup>5-9</sup> In a case series of primary tracheal tumors from Taiwan, lymphomas comprised 3% of the cohort<sup>10</sup> and histologic subtype of anaplastic large cell lymphoma (ALCL) of the trachea was a rare finding.<sup>4</sup> We describe a patient with PTL with an unusual presentation of subcutaneous emphysema that was treated with combined modality of debulking curettage, chemotherapy and local radiotherapy.

## CASE

A 16-year-old nonsmoking female with a 3-week his-

tory of dry cough and progressive dyspnea, treated as asthma, abruptly developed subcutaneous emphysema in the neck and upper chest. The patient was subsequently transferred to our center for further management. At the time of admission she had subcutaneous emphysema in the neck and upper chest and bilateral coarse crackles without peripheral lymphadenopathy or organomegaly.

In a primary work-up, chest computed tomography (CT) showed a tracheal wall mass in the mid-trachea (40 mm) that protruded into the lumen and led to severe stenosis. In the distal portion of the trachea the tumor invaded the lumen and air leakage was seen. Paratracheal lymphadenopathy was noted without adjacent vessels invasion. No lymphadenopathy was evident in other parts of mediastinum and pulmonary parenchyma was also clear on the CT scan. It also demonstrated pneumomediastinum and bilateral axillary soft tissue emphysema (Figures 1a, 1b). Abdominal and pelvic CT scans were normal. Results of all blood tests including CBC and biochemistry, including LDH were within normal limits.

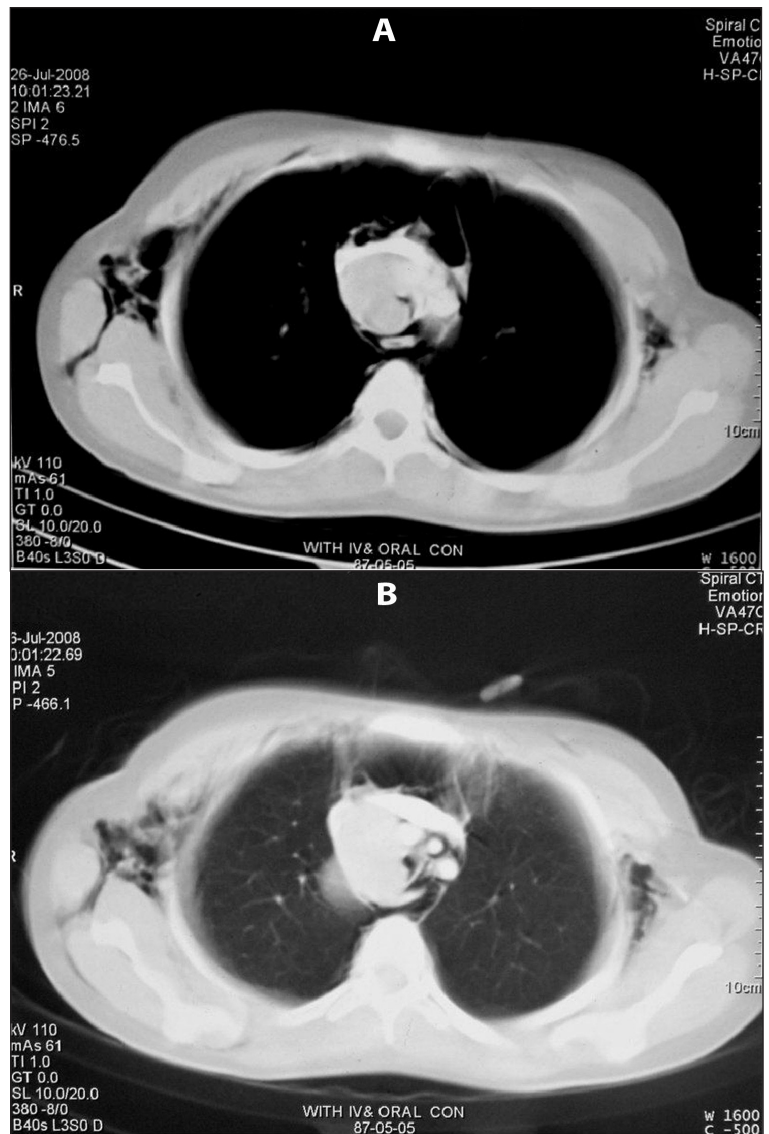
By rigid bronchoscopy, a mass lesion protruding

from the posterior wall of the trachea 5-6 cm distal to the vocal cord was seen. The mass had occluded 5/6 of the luminal space, which was partially resected through a curettage procedure. Immediately after this procedure the dyspnea was resolved and she was admitted to ICU. Histopathological analysis of tumoral sections showed disintegrated fragments of neoplastic tissue, fibrinoleukocytic exudates, necrosis and an ulcerated metaplastic bronchial epithelium. The neoplastic tissue was composed of a proliferation of discohesive large anaplastic malignant cells associated with foci of delicate sclerosis. The sclerosis resulted in pseudocompartmentalization of the tumoral cells. The tumoral cells had large pleomorphic vesicular nucleolated nuclei. Numerous mitotic figures, as well as foci of necrosis, were also noted (Figure 2). Immunohistochemical study revealed that tumoral cells were diffusely and strongly positive for LCA and CD30 (membranous and cytoplasmic). Most of the tumoral cells showed both nuclei and cytoplasm positive for ALK staining. They were totally negative for pancytokeratin,  $\alpha$ -fetoprotein, CD 20, CD79 and CD3. The Ki67 staining showed a high proliferation index. This finding confirmed the diagnosis of anaplastic large cell lymphoma, null cell type.

Five days after first curettage she was transferred to the oncology ward in an ECOG performance status of 2, but at the time of admission her dyspnea was aggravated, which led to an urgent second bronchoscopy and curettage. Considering the patient's critical situation, in the presence of normal CBC and plaletes and a localized disease, a bone marrow study was not performed. Finally, at stage IAE and low risk on the International Prognostic Index,<sup>11</sup> tracheal curettage was immediately followed by systemic chemotherapy with a CHOP regimen (cyclophosphamide, doxorubicin, vincristine, and prednisolone) in ICU. She had a dramatic response to the first cycle of chemotherapy and in the following weeks, in observation, she did not develop any local progression. Her chemotherapy was continued for 6 cycles. Although, there was no evidence of residual tumor in the bronchoscopy and chest CT scan, radiation over the bed of the tumor was performed. After 25 months on follow-up she was in complete remission without any evidence of tumor recurrence in imaging and bronchoscopy.

## DISCUSSION

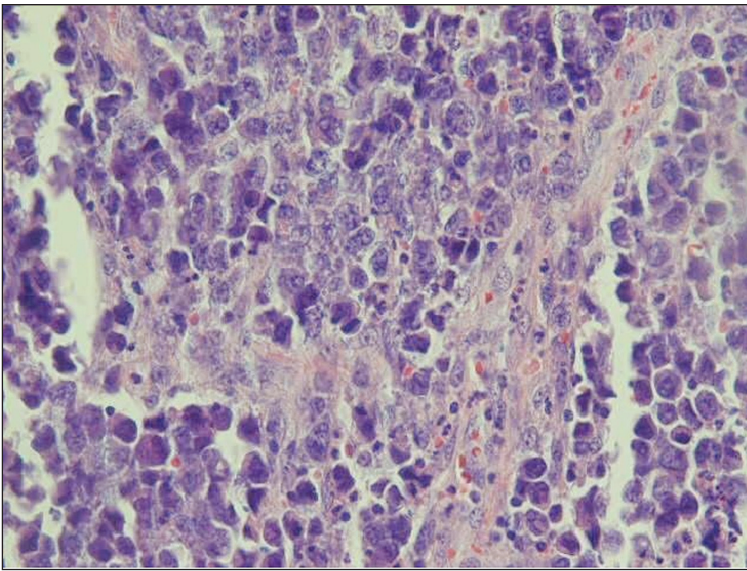
PTL originates from mesenchymal B and T cells probably involved in immunosurveillance of the upper airways.<sup>1</sup> In a large historical series of extranodal non-Hodgkin lymphoma (NHL), only 3.6% presented with involvement of the pulmonary parenchyma or tracheo-bronchial tree as the primary site of disease.<sup>12</sup> Indeed



**Figure 1a,b.** A right paratracheal mass infiltrating the tracheal lumen with subcutaneous emphysema.

even in a review of primary tracheal tumors from Taiwan, the prevalence of lymphoma was 3%.<sup>10</sup>

Various histological subtypes of PTL exist. In a review of 28 cases of PTL, the most frequent subtype was mucosa-associated lymphoid tissue (MALT) lymphoma comprising 5 (18%) of all cases. Except for 4 patients with unspecified T-cell lymphoma, the second most common subtypes were Hodgkin disease and anaplastic large cell lymphoma (ALCL). Each of these subtypes was reported in 3 (11%) of the 28 patients.<sup>4</sup> ALCL is a rare high-grade and aggressive type of NHL including 2% to 3% of lymphomas.<sup>4,13-16</sup> ALCL consists a distinctive anaplastic and polymorphous cell cytol-



**Figure 2.** On hematoxyline and eosin stain (×40), there are rather diffuse infiltration of highly anaplastic large lymphocytes with vesicular nucleolated nuclei, some with multilobulated nuclei and basophilic cytoplasm. There are also mixed population of PMNs and small lymphocytes as well as fine sclerosis (pseudocompartmentalization).

ogy<sup>13,14</sup> characteristically expressed by one or more T-cell-related antigens. Furthermore, in some of ALCL cases the loss of T-cell antigens may result in apparent null cell phenotype as showing T-cell lineage at the molecular level.<sup>17</sup> ALCL cells frequently spread into extranodal regions such as skin, lung, pleura, pericardium, liver and ovary, especially in the T and null-cell phenotype.<sup>18</sup> However T/null-cell type ALCL shows a favorable outcome, with 5-year survival reaching 81%<sup>19</sup> as in our patient and the other reported cases of ALCL.<sup>4,20</sup>

In a review by Takami, 3 cases with a diagnosis of ALCL were aged between 20 to 60 years.<sup>4</sup> Our case was a 16-year-old and another ALCL case was a 24-year-old.<sup>20</sup> Common presenting symptoms include dyspnea, cough, wheezing and at later stages, stridor.<sup>5</sup> Hemoptysis is not a common complaint. These complaints could mimic a partially refractory asthma in some cases. Failure to respond to a bronchodilator should arise suspicion of a tracheal tumor.<sup>20</sup> To the best of our knowledge this is the sole reported tracheal lymphoma presenting with subcutaneous emphysema beside progressive dyspnea. Although the history of complaints,

and a precise physical examination could raise the suspicion of a tracheal tumor, a CT scan can also demonstrate a tracheal/paratracheal mass that may accompany local lymphadenopathies. However, for a definite diagnosis, bronchoscopy and biopsy is mandatory. Notably, early diagnosis could be life saving and mandate urgent diagnostic bronchoscopy and biopsy. Palliation of dyspnea could be achieved by curettage or stenting of the trachea. In PTL a high proliferation rate that is identified by high Ki-67 expression, can be a predictive value for a favorable response to chemotherapy and outcome. Treatment strategies for patients with primary tracheal lymphoma are controversial and may depend on pathology subtype. Surgery, chemotherapy, and radiation therapy usually are used either alone or in combination. In our case the high proliferative rate indicated a very rapid progression following the first curettage procedure and also a rapid dramatic response to the first chemotherapy cycle. Although our patient received local radiation after complete response to chemotherapy, its role in this scenario is questionable. Commonly, radiotherapy has been used in the postoperative setting or for palliative treatment of unresectable disease.<sup>3</sup> PTL are usually sensitive to both chemotherapy and radiotherapy and may be rapidly controlled by such modalities.<sup>7</sup> It was recently suggested that temporary tracheal stenting followed by chemotherapy and/or radiotherapy is beneficial in the management of tracheal lymphoma with symptomatic airways stenosis.<sup>7</sup> Additionally, debulking surgery is likely to remain the mainstay of initial urgent treatment in cases of severe upper airway obstruction by an unknown tracheal tumor,<sup>4</sup> as in our case, because this technique allows prompt diagnosis and reduce the risk of asphyxia, as well.

In conclusion, subcutaneous emphysema besides progressive dyspnea could be an alarming sign and symptom of PTL. Lymphomatous involvement of the airway is a rare but frightening presentation of an eminently treatable condition and should be considered with a high index of suspicion in patients with dyspnea and wheeze unresponsive to bronchodilators. Meanwhile, in our case, an anaplastic large cell lymphoma-null cell type demonstrated a dramatic response to combination treatment modalities of debulking, chemotherapy and radiotherapy with a very good prognosis.

## REFERENCES

1. Macchiarini P. Primary tracheal tumors. *Lancet*. 2006;7:83-91.
2. Allen MS. Malignant tracheal tumors. *Mayo Clin Proc*. 1993; 68:680-684.
3. Thotathil ZS, Agarwal JP, Shrivastava SK, Dinshaw KA. Primary malignant tumors of the trachea. The Tata Memorial Hospital Experience. *Med Princ Pract*. 2004;13:69-73.
4. Takami A, Okumura H, Maeda Y, Kumano Y, Asakura H, Oda M, Omura K, Nakao S. Primary tracheal lymphoma: case report and literature review. *Int J Hematol*. 2005;82:338-342.
5. Fidias P, Wright C, Harris NL, Urba W, Grossbard ML. Primary tracheal non-Hodgkin's lymphoma: a case report and review of the literature. *Cancer*. 1996;77:2332-2338.
6. Chaouat A, Fraisse P, Kessler R, Lang JM, Weitzenblum E. A life-threatening tracheal localization of lymphoma in a patient with AIDS. *Chest*. 1993;103:1297-1299.
7. Schmidt B, Massenkeil G, John M, Arnold R, Witt C. Temporary tracheobronchial stenting in malignant lymphoma. *Ann Thorac Surg*. 1999;67:1448-1450.
8. Gómez-Roman JJ, Pérez-Montes R, Pérez-Exposito MA, Richard C, Richard C, Baro J, Val-Bernal JF. Primary lymphoplasmacytoid lymphoma of the trachea with immunoglobulin G paraprotein. *Pathol Int*. 1999;49:1100-1104.
9. Danneberg C, Haupt R, Mantovani L, Skuballa A, Köhrholz D. Primary high-grade non-Hodgkin's lymphoma of the trachea in an adolescent. *Pediatr Hematol Oncol*. 2003;20(5):399-402.
10. Yang KY, Chen YM, Huang MH, Perng RP. Revisit of primary malignant neoplasm's of the trachea: clinical characteristics and survival analysis. *Jpn J Clin Oncol*. 1997;27:305-309.
11. A predictive model for aggressive non-Hodgkin's lymphoma The International Non-Hodgkin's Lymphoma Prognostic Factors Project. *N Eng J Med*. 1993;329:987-994.
12. Freeman C, Berg JW, Culter SJ. Occurrence and prognosis of extranodal lymphomas. *Cancer*. 1972;29:252-260.
13. Wellmann A, Otsuki T, Vogelbruch M, Clarck HM, Jaffe ES, Raffeld M. Analysis of the T (2;5) (p 23; q 35) translocation by reverse transcription polymerase chain reaction in CD 30 +, anaplastic large-cell lymphomas, in other non-Hodgkin lymphoma of T-cell phenotype, and Hodgkin disease. *Blood*. 1995;86:23218.
14. Delsol G, Ralfkiaer E, Stein H, Wright D, Jaffe E. Anaplastic large cell lymphomas, Primary systemic (T/Null cell type). World Health Organization (WHO) Classification of Tumors. Pathology and Genetics of tumours of Haematopoietic and Lymphoid Tissues. 2001 pp 230-235
15. Nassiri M, Byrne GE, Clarence C, Whitcomb CC, Byrne JJ. Synchronous Null-cell anaplastic large cell lymphoma and multiple myeloma. *Ann Hematol*. 2009;88:923-925
16. Stein H, Mason DY, Gerdes J, O'Connor N, Wainscoat J, Pallesen G, Gatter K, Falini B, Delsol G, Lemke H, Schwarting R, Lennert K. The expression of the Hodgkin's disease associated antigen Ki-1 in reactive and neoplastic lymphoid tissue: evidence that Reed-Sternberg cells and histiocytic malignancies are derived from activated lymphoid cells. *Blood*. 1985; 66:848-858.
17. Rizvi MA, Evens AM, Nelson BP, Rosen TS. T cell lymphoma, In: *Lymphoma: pathology, diagnosis and treatment*, Cambridge University Press, (1 ed), New York, 2007;P: 224.
18. Filippa DA, Lardanyi M, Wollner N, Straus DJ, O' Brein JP, Portlock C, Gangi M, Sun M. CD 30( Ki-1)-positive malignant lymphomas: clinical, immunophenotypic, histologic, and genetic characteristics and differences with Hodgkin disease. *Blood*. 1996; 87:2905-2917.
19. Non-Hodgkin Lymphoma Classification Project. A clinical evaluation of the International Lymphoma Study Group Classification of non-Hodgkin lymphoma. *Blood*. 1997;89:3909-3918.
20. Tan DS, Eng PC, Lim ST, Tao M. Primary tracheal lymphoma causing respiratory failure. *J Thorac Oncol*. 2008; 8:929-930.