Case Report

# Anaplastic large cell lymphoma presenting as bilateral endobronchial tumor in a young boy

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## ABSTRACT

A 15-year-old boy presented to us with a 4-month history of fever with worsening dyspnea since 1 month. His contrast-enhanced computed tomography scan of the thorax showed bilateral endobronchial lesions with complete collapse-consolidation of the left lung and partial collapse of the right lower lobe. His fiberoptic bronchoscopy guided biopsy had been reported in outside hospital as a neuroendocrine tumor. Due to worsening breathlessness, he had to be intubated. We repeated the endobronchial biopsy and combined with outside slides and blocks, was diagnosed to have an anaplastic lymphoma kinase-1 positive anaplastic large cell lymphoma (ALCL). We started the patient on chemotherapy to which he had a dramatic response radiologically and clinically. ALCL presenting as endobronchial mass is an extremely rare occurrence and it presenting with bilateral endobronchial masses has not been reported yet in literature. Pathologists and clinicians should be aware of this presentation as prompt diagnosis and treatment give promising results.

**KEY WORDS:** Anaplastic large cell lymphoma, endobronchial tumor, non-Hodgkin's lymphoma

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## INTRODUCTION

Endobronchial tumors are rare in pediatric age group and are seen in only 0.2% of all pediatric malignancies.[1] They can be benign or malignant of which benign endobronchial tumors include hamartoma, hemangioma, papilloma, plasma cell granulomas, leiomyomas, and mucus gland tumor and malignant tumors include bronchial adenoma, carcinoids, mucoepidermoid carcinoma, and adenoid cystic carcinoma.[1] The most common endobronchial tumor in childhood is carcinoids followed by mucoepidermoid carcinoma.[1-3]

Lymphoma presenting as an endobronchial tumor is a rare entity. Papaioannou and Watson reported only one endobronchial lesion among 93 cases of primary lymphoma involving the lungs.[4] Non-Hodgkin's lymphoma (NHL) involves thoracic structures in about 43% of cases, especially the mediastinum and pulmonary parenchyma at any time in the course of the disease. Anaplastic large cell lymphoma (ALCL) is a type of NHL, seen in childhood. ALCL presenting as endobronchial lesion with no disease elsewhere is even rarer with very few reports in literature.[5]

Bilateral endobronchial lesions in ALCL present as a challenge to treating physician as most of the time they are often deemed as incurable due to bilaterality. Surgery which is most effective treatment modality in benign endobronchial lesions becomes difficult if the disease is bilateral.

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## CASE REPORT

A 15-year-old undernourished boy presented to our outpatient department with a 1-month history of progressive breathlessness on exertion. He had a history of intermittent fever of mild to moderate grade and dry cough since 4 months. His breathlessness had progressed relatively rapidly over 1 month and now limited his daily activities. He also had associated anorexia and weight loss. He had been treated symptomatically by his local physician and later underwent investigations for the persistence of symptoms. A chest X-ray [Figure 1] showed a complete white-out of the left lung with ipsilateral mediastinal shift suggesting complete lung collapse. A contrast-enhanced computed tomography of the thorax showed an endobronchial lesion in the left main bronchus with complete collapse-consolidation of the left lung; it also showed an endobronchial lesion in the right lower lobe [Figure 1]. He underwent a fibreoptic bronchoscopy which confirmed a left main bronchial growth and a right lower lobar bronchial growth and a guided biopsy of these endobronchial lesions [Figure 2] was done. The histopathology report of the left sided lesion was necrotic tissue and the right sided lesion was reported as a neuroendocrine tumor (carcinoid tumor).

Subsequent to these investigations, he was transferred to our hospital for increasing the severity of his symptoms. He presented to our hospital in respiratory distress and required endotracheal intubation with mechanical ventilation. We performed a bronchoscopy which confirmed the outside report and repeated endobronchial biopsies. Review of these and the external biopsies showed a high-grade malignant tumor composed of sheets ofhighly pleomorphic cells containing a moderate amount of eosinophilic cytoplasm and eccentrically placed hyperchromatic nuclei and prominent nucleoli. Few cells showed wreath like/horseshoe-shaped nuclei [Figure 3a]. On immunohistochemistry (IHC) the tumor cells were strongly and diffusely positive for leukocyte common antigen, while negative for cytokeratin [Figure 3d], desmin and CD3 and CD20. On additional IHC the tumor revealed strong positivity for CD30 [Figure 3b] and anaplastic lymphoma kinase-1 (ALK-1) [Figure 3c]. Mib-1 (Ki-67)labelling index was approx. 40-50%. Systemic examination and other investigation did not revealed any evidence of the disease elsewhere. Hence the diagnosis of primary endobronchial Alk-1positive anaplastic large cell lymphoma null cell type was rendered. His cerebrospinal fluid (CSF) cytology was also positive for NHL. We started him on CHVbP protocol chemotherapy, and he showed dramatic improvement in his ventilatory parameters and was extubated in 3 days after initiating chemotherapy. He also received G-CSF prophylactically to prevent neutropenia which is not uncommon and sometimes fatal in these settings. His chest X-ray which had shown complete collapse before treatment also showed dramatic improvement [Figure 4].

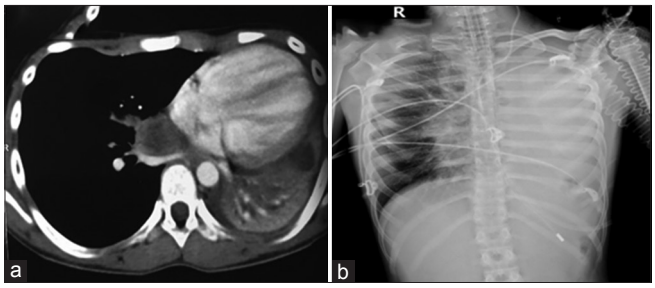


**Figure 1:** (a) Computed tomography scan image showing endobronchial mass with collapse-consolidation of left lung with mediastinal shift, (b) chest X-ray image showing complete white-out of left lung

## DISCUSSION

First case of endobronchial NHL was described in 1955 by Dawe *et al*.[6,22] ALCL is a type of NHL, seen in childhood. In 1985, Stein *et al*. identified a subset of NHLs characterized by anaplastic large lymphoid cells that expressed CD30, had a tendency to grow cohesively, and also had a predilection for invading lymph node sinuses.[7] ALCL as per WHO classification is divided into two categories, most common being ALK-positive and others into less common ALK-negative[8] Systemic ALCL is an aggressive variant of ALCL. Most common sites to be involved are skin, bone, soft tissue, and lung.[9,10] The treatment protocol or systemic ALCL consist of CHOP-like regimen, with high dose methotrexate and or cytarabine included in pediatric protocols.[11,12] ALCL very rarely presents as an endobronchial lesion. L'Hoste *et al*. have proposed the following criteria for diagnosing primary pulmonary lymphoma: (i) involvement of lung, lobar or primary bronchus, with or without mediastinal involvement; (ii) no evidence of extrathoracic lymphoma at the time of diagnosis or for 3 months thereafter.[12,23] ALCL presenting as primary bilateral endobronchial tumor has not been reported so far in literature

ALCL, T-/null-cell type is a rare disease which has been described only since the last two decades. Its peak incidence is seen in childhood, and the disease has male

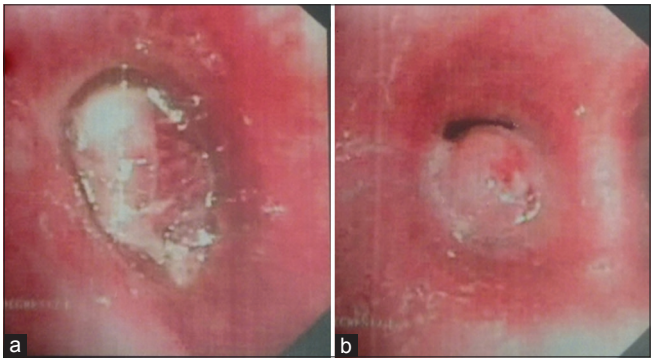


**Figure 2:** Bronchoscopic images of tumor, (a) the left main bronchial tumor completely obstructing the left main bronchus, (b) the right lower lobe endobronchial tumor almost completely obstructing the right bronchus intermedius

preponderance.[9] Though lung is one of the common sites involved in ALCL, endobronchial involvement by ALCL has not been frequently reported. The endobronchial location of the lesion causes postobstructive intrinsic collapse which in its initial phases may be mistaken to be a consolidation. Isolated occurrence of chest symptoms such as cough, chest pain, and dyspnea without any systemic manifestation may be even more misleading. After the first case report in 1955, less than five cases have been reported from India.[13] Endobronchial involvement has been reported sparsely in adults, only four case reports of primary isolated endobronchial ALCL have been reported in pediatric age group.[14] Three other pediatric cases with endobronchial ALCL were noted but had extrapulmonary disease in form of lymphadenopathy. In India, less than five cases of endobronchial lymphoma have been reported.[15] However, ALCL or NHL presenting as bilateral endobronchial tumor in pediatric age group has not been reported in literature. Table 1 gives details of patients with primary endobronchial tumours.

Endobronchial ALCL presents with progressive dyspnea and atelectasis. Basic investigations needed include peripheral blood smears, bone marrow aspirate smears, CSF cytology, ultrasonography, computed tomography

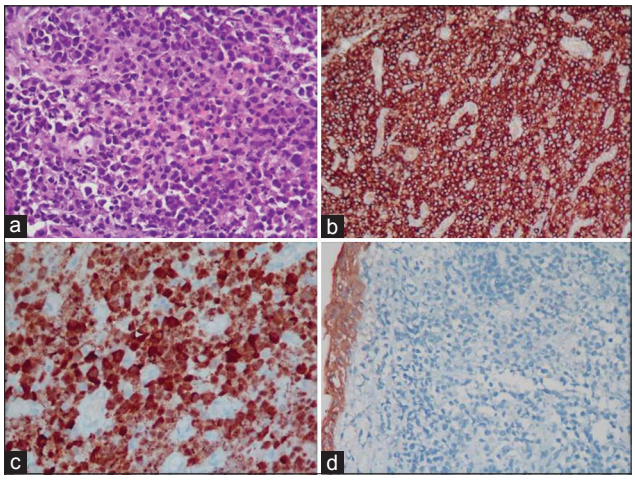


**Figure 3:** Histopathological examination revealed population of highly pleomorphic malignant cells arranged in diffuse sheets (a: H&E-400X). These tumor cells were immunopositive for CD30 (membranous positivity)(b: DAB;200x) and ALK-1(nuclear as well as cytoplasmic positivity) (c: DAB;400x) while negative for AE1/AE3 (d: DAB;200x) confirming the diagnosis of Alk-positive Anaplastic large cell lymphoma

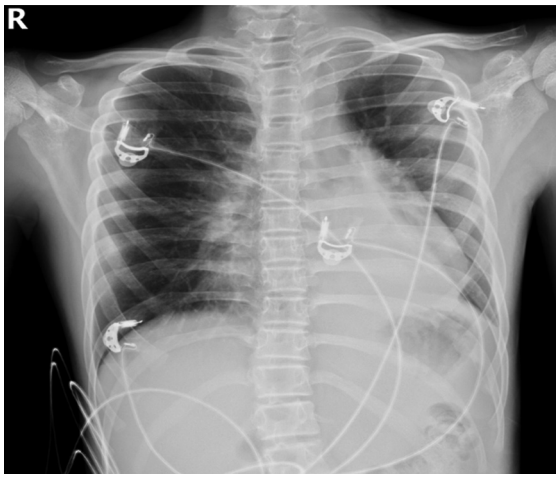


**Figure 4:** Chest X-ray showing complete expansion of previously collapsed left lung after starting chemotherapy

**Table 1: Primary endobronchial anaplastic large cell lymphoma**

| Reference number | Author | Age/sex | Initial presentation | Investigations | ALK status | Treatment and response |
|---|---|---|---|---|---|---|
| [6] | Chand *et al*. | 24/male | Breathlessness, cough, fever | Chest X-ray - right lower lobe collapse<br>CECT - mass in right main bronchus with distal collapse<br>Bronchoscopy - mass in right main bronchus<br>Biopsy - aspergilloma<br>HPR - ALCL with aspergilloma | Positive | Right lower lobectomy in view of diagnosis being aspergilloma |
| [15] | Kanthan | 5/male | Asymptomatic, unexplained collapse of lung | Chest X-ray - white out of right hemithorax with mediastinal shift<br>CT scan - mass in right main bronchus with surrounding edema<br>Bronchoscopy - fleshy tumor in right upper lobe bronchus<br>Biopsy - ALCL | Positive | Chemotherapy<br>Complete remission |
| [19] | Guerra *et al*. | 9/female | Dry cough, dyspnea, chest pain, fever | Chest X-ray - left upper lobe lingular segment opacification.<br>CT scan - 9 cm×6.5 cm×12 cm left upper lobe mass with necrosis that encased the hilum<br>Bronchoscopy and biopsy - lesion in left main bronchus<br>Biopsy - ALCL | Positive | Chemotherapy<br>Complete remission |
| [20] | Pavlov *et al*. | 13/female | Dyspnea, wheezing | Chest X-ray, bronchoscopy, pulmonary function test | Positive | Chemotherapy<br>Complete remission |
| [21] | Bhalla and McClure | 17/female | Progressive dyspnea | Chest X-ray - increased density in left hilum with volume loss<br>CT scan - 3-4 cm mass in left main bronchus with left lung consolidation<br>Bronchoscopy with washings and biopsy - ALCL | Positive | Chemotherapy |
| | Our patient | 15/male | Dyspnea, fever | Bronchoscopy and biopsy, chest X-ray | Positive | Chemotherapy |

ALCL: Anaplastic large cell lymphoma, CT: Computed tomography, CECT: Contrast-enhanced computed tomography, ALK: Anaplastic lymphoma kinase, HPR: Histopathology report

scan and skeletal scintigraphy. Diagnosing ALCL is a challenge for both the pathologist and the clinician, but this diagnostic dilemma has been eliminated partly by progress made in immunophenotyping and cytogenetic studies. IHC plays a vital role in diagnosing ALCL as it helps us in distinguishing ALCL from other histopathological diagnosis of undifferentiated carcinoma, rhabdomyosarcoma, other NHL like diffuse large B-cell lymphoma and recently described entity NUT midline carcinoma. IHC is mandatory to obtain the definitive diagnosis. Presence or absence of ALK protein is the most important prognostic factor, with a reported 5 years survival of 93% in patients who were ALK positive in contrast to 37% in ALK-negative patients.[16] Various novel prognostic markers like epithelial membrane antigen, MUC and survivin have been studied.[17,18]

Histological diagnosis with appropriate immunochemistry is a must to achieve a correct diagnosis. In addition, lymphoma must be considered as a differential diagnosis in patients with endobronchial lesions. In a patient like ours, who was on mechanical ventilation (precluding endobronchial therapy), it is crucial to get a definitive diagnosis, as virtually any other diagnosis would have been untreatable, and possibly fatal. Our initial clinical impression of a neuroendocrine tumor (carcinoid), which is far more common with endobronchial polypoid growths in this age group, would have been possibly impossible to treat as his ventilatory supports were such that we would not have time to perform endobronchial laser or other ablative therapy.

## CONCLUSION

Clinical suspicion and prompt diagnosis are of utmost importance in treating such complicated cases. Swift, accurate diagnosis is crucial especially in critically ill patients like ours, as it dictates the final treatment-carcinoids would need surgery and patients with lymphoma would respond very well to chemotherapy.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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