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

Abhijeet Dharmaji Sawant, Vijayraj S Patil, Pranjal M Gugalia1, Rajiv Kumar1, Sabita Jiwnani, George Karimundackal, CS Pramesh
Departments of Thoracic Oncosurgery and 1Pathology, Tata Memorial Hospital, Mumbai, Maharashtra, India

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

INTRODUCTION

Endobronchial tumors are rare in pediatric age group and are seen in only 0.2% of all pediatric malignancies. 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.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms. For reprints contact: reprints@medknow.com

How to cite this article: Sawant AD, Patil VS, Gugalia PM, Kumar R, Jiwnani S, Karimundackal G, et al. Anaplastic large cell lymphoma presenting as bilateral endobronchial tumor in a young boy. Lung India 2018;35:66-9.
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 of highly 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-1 positive 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].

DISCUSSION

First case of endobronchial NHL was described in 1955 by Dawe et al. 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. ALCL as per WHO classification is divided into two categories, most common being ALK-positive and others into less common ALK-negative. Systemic ALCL is an aggressive variant of ALCL. Most common sites to be involved are skin, bone, soft tissue, and lung. The treatment protocol or systemic ALCL consist of CHOP-like regimen, with high dose methotrexate and or cytarabine included in pediatric protocols. 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. 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 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

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. 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. Endobronchial involvement has been reported sparsely in adults, only four case reports of primary isolated endobronchial ALCL have been reported in pediatric age group. 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. 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, and positron emission tomography.

**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 CECT - mass in right main bronchus with distal collapse Bronchoscopy - mass in right main bronchus Biopsy - aspergilloma 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 CT scan - mass in right main bronchus with surrounding edema Bronchoscopy - fleshy tumor in right upper lobe bronchus Biopsy - ALCL | Positive   | Chemotherapy Complete remission |
| [19]             | Guerra et al.     | 9/female| Dry cough, dyspnea, chest pain, fever | Chest X-ray - left upper lobe lingular segment opacification. CT scan - 9 cm × 6.5 cm × 12 cm left upper lobe mass with necrosis that encased the hilum Bronchoscopy and biopsy - lesion in left main bronchus Biopsy - ALCL | Positive   | Chemotherapy Complete remission |
| [20]             | Pavlov et al.     | 13/female| Dyspnea, wheezing Progressive dyspnea | Chest X-ray, bronchoscopy, pulmonary function test | Positive   | Chemotherapy Complete remission |
| [21]             | Bhalla and McClure| 17/female| Dyspnea, wheezing Progressive dyspnea | Chest X-ray - increased density in left hilum with volume loss CT scan - 3-4 cm mass in left main bronchus with left lung consolidation Bronchoscopy with washings and biopsy - ALCL Bronchoscopy and biopsy, chest X-ray | Positive   | Chemotherapy Complete remission |
| Our patient      |                   | 15/male | Dyspnea, fever         |                                                                                           | Positive   | Chemotherapy Complete remission |

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. Various novel prognostic markers like epithelial membrane antigen, MUC and survivin have been studied. 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 un treatable, 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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Neville HL, Hogan AR, Zhuge Y, Perez EA, Cheung MC, Koniaris LG, et al. Incidence and outcomes of malignant pediatric lung neoplasms. J Surg Res 2009;156:224-30.
2. Curtis JM, Lacey D, Smyth R, Carty H. Endobronchial tumours in childhood. Eur J Radiol 1998;29:11-20.
3. Bellah RD, Mahboubi S, Berdon WE. Malignant endobronchial lesions of adolescence. Pediatr Radiol 1992;22:563-7.
4. Papaioannou AN, Watson WL. Primary lymphoma of the lung: An appraisal of its natural history and a comparison with other localized lymphomas. J Thorac Cardiovasc Surg 1965;49:373-87.
5. Kilgore TL, Chazen MH. Endobronchial non-Hodgkin’s lymphoma. Chest 1983;84:58-61.
6. Chand T, Bansal A, Dua H, Sharma K. Endotracheobronchial lymphoma: Two unusual case reports and review of article. Lung India 2016;33:653-6.
7. Stein H, Mason DY, Gerdes J, O’Connor N, Wainscoat J, Pilleseg S, et al. The expression of the Hodgkin’s disease associated antigen Ki-1 in reactive and neoplastic lymphoid tissue: Evidence that Reed-Sternberg cells and histiocyitic malignancies are derived from activated lymphoid cells. Blood 1985;66:848-58.
8. Campo E, Swerdlow SH, Harris NL, Pileri S, Stein H, Jaffe ES. The 2008 WHO classification of lymphoid neoplasms and beyond: evolving concepts and practical applications. Blood. 2011 May 12;117(19):5019-32. doi:10.1182/blood-2011-01-393050. Review. PubMed PMID: 21300984; PubMed Central PMCID: PMC3199529.
9. Falini B, Pileri S, Zinzani PL, Carbone A, Zagonel V, Wolf-Peeters C, et al. ALK + lymphoma: Clinico-pathological findings and outcome. Blood 1999;93:2697-706.
10. Kadin ME, Carpenter C. Systemic and primary cutaneous anaplastic large cell lymphomas. Semin Hematol 2003;40:244-56.
11. Williams DM, Hobson R, I'meson J, Gerrard M, McCarty K, Pinkerton CR; United Kingdom Children’s Cancer Study Group. Anaplastic large cell lymphoma in childhood: Analysis of 72 patients treated on the United Kingdom Children’s Cancer Study Group chemotherapy regimens. Br J Haematol 2002;117:812-20.
12. Malur PR, Gaude GS, Bannur HB, Anursheth SB, Suranagi VV, Kangle RP, et al. Primary endobronchial Hodgkin’s disease. Lung India 2009;26:136-8.
13. Upadhyay R, Garg R, Kushwah R, Goel M. A long-standing endobronchial non-Hodgkin’s lymphoma: Designed to be cured. Lung India 2016;33:577-8.
14. Seidemann K, Tiemann M, Schrappe M, Yoksan E, Simonitch I, Janka-Schaub G, et al. Short-pulse B-non-Hodgkin lymphoma-type chemotheraphy is efficacious treatment for pediatric anaplastic large cell lymphoma: A report of the Berlin-Frankfurt-Muenster Group Trial NHL-BFM 90. Blood 2001;97:3699-706.
15. Rani K, Jenna-Lynn S, Miller G. Isolated pediatric endobronchial primary anaplastic large cell lymphoma. J Pediatr Surg Case Rep 2014;2:66-9.
16. Gascoyne RD, Aoun P, Wu D, Chhanabhai M, Skinnider BF, Greiner TC, et al. Prognostic significance of anaplastic lymphoma kinase (ALK) protein expression in anaplastic large cell lymphoma: A report of the Berlin-Frankfurt-Muenster Group Trial NHL-BFM 90. Blood 1999;93:3913-21.
17. Rassidakis GZ, Goy A, Medeiros LJ, Jiang Y, Thomaides A, Remache Y, Janka-Schaub G, et al. Prognostic significance of MUC1 expression in systemic anaplastic large cell lymphoma. Clin Cancer Res 2003;9:2213-20.
18. Altieri DC. Validating survivin as a cancer therapeutic target. Nat Rev Cancer 2003;3:46-54.
19. Guerra J, Echevarria-Escudero M, Barrio N, Velez-Rosario R. Primary endobronchial anaplastic large cell lymphoma: A report of the Berlin-Frankfurt-Muenster Group Trial. J Thorac Cardiovasc Surg 1965;49:373-87.
20. Filho RP, Aoun P, Wu D, Chhanabhai M, Skinnider BF, Greiner TC, et al. Prognostic significance of anaplastic lymphoma kinase (ALK) protein expression in adults with anaplastic large cell lymphoma. Blood 1999;93:3913-21.
21. Bhalla R, McClure S. Pathologic quiz case: A 17-year-old adolescent girl with short history of dyspnea. Endobronchial, anaplastic large cell lymphoma, T-cell phenotype. Arch Pathol Lab Med 2003;127:e430-1.
22. Darwe CJ, Woolner LB, Parkhill EM, McDonald JR. Cytologic studies of sputum, secretions and serous fluids in malignant lymphoma. Am J Clin Pathol 1955;25:480-8.
23. L’Hoste RJ, Fillipa DA, Lieberman PH, Brettsky S. Primary pulmonary lymphoma: A clinicopathological analysis of 36 cases. Cancer 1984;54:1396-406.