



## ANAPLASTIC LARGE CELL LYMPHOMA IN THE LUNG DIAGNOSED BY CYTOLOGY

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<p><b>Article Info</b></p> <p><i>Received 02/07/2015</i> <i>Revised 30/07/2015</i> <i>Accepted 19/08/2015</i></p> <p><b>Key words:</b> Anaplastic large cell lymphoma, Lung, ALK1, Cytology.</p>	<p><b>ABSTRACT</b></p> <p>Anaplastic large cell lymphoma (ALCL) is one of the common forms of peripheral T cell lymphomas (PTCL) that usually presents as painless lymphadenopathy. Extra nodal presentations are common in the skin but rare in the lung (1). In this article we present the case of a 21 years old male who had no significant previous medical history but recently started complaining from shortness of breath, cough and white sputum. CT scan with IV contrast of the chest revealed an ill-defined heterogeneous mass approximately 6 cm in size, protruding into the lumen of the right main bronchus. Endobronchial ultrasound guided fine needle aspiration (FNA) was performed. Cytology revealed numerous large and highly atypical malignant cells. Further evaluation via bronchoscopy also showed an endobronchial nodular mass. A biopsy taken from the mass confirmed the diagnosis of ALCL. The clinical and pathological features of this rare pulmonary presentation of ALCL are described together with literature review.</p>
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### CASE REPORT

A 21 years old male with no significant past medical history presented with shortness of breath and productive cough of more than one month duration. He also complained from fever, 6 to 7 kilograms of weight loss and night sweats. He had a few episodes of hemoptysis. Physical examination showed normal vital signs but with decreased breath sounds over the entire right chest. Laboratory investigations revealed low hemoglobin (109 g/L), low RBC count (3.9 x10.e12/L) and prolonged partial thromboplastin time (55.7 seconds). Other parameters were, however, unremarkable. Chest X-ray showed complete whiteness of the right hemithorax. After primary evaluation, a chest CT scan with IV contrast was done. This revealed an ill-defined and heterogeneous mass protruding into the lumen of the right main bronchus (Figure 1). Endobronchial ultrasound guided fine needle aspiration (FNA) was performed and showed malignant cells suggestive of ALCL (Figure 2). Further evaluation

via bronchoscopy and biopsy showed large malignant cells with prominent nucleoli, irregular nuclear membrane and vesicular chromatin (Figure 3). Immunohistochemical stains showed that the tumor cells are positive for CD30 (Figure 4), ALK1 (Figure 5), CD4, CD43 and CD45, which confirmed the diagnosis of ALCL. During his admission the patient had an episode of respiratory distress, which required intubation and mechanical ventilation. The patient subsequently received one cycle of CHOP chemotherapy (Cyclophosphamide, Adriamycin, Vincristine and Prednisone) and he is currently stable and awaiting his second dose of chemotherapy.

### DISCUSSION

Anaplastic large cell lymphoma (ALCL) was first described by Stein and colleagues in 1985 [2]. It is one of the most common forms of the peripheral T cell lymphomas (PTCL) [1]. A large part of ALCLs are associated with translocations involving ALK, the



Anaplastic Lymphoma Kinase gene, located on chromosome 2p23 [1]. These ALK+ tumors have a distinctly better clinical outcome than ALK- systemic ALCLs [3]. ALCL is composed of two subtypes, primary systemic ALCL and primary cutaneous ALCL [4]. As the name implies, primary systemic ALCL presents as systemic, extracutaneous disease and may be ALK positive or ALK negative. However, primary cutaneous ALCL is confined to the skin of patients without a pre-existing lymphoproliferative disorder and lacks ALK translocations [5, 6].

The International T cell Lymphoma Project is a retrospective study done to estimate the incidence of ALCL in which 1314 cases of peripheral lymphoma of T cell or NK cell origin from 22 centers worldwide diagnosed between 1990 and 2002 were assessed [7]. Approximately 6.6 percent were classified as ALK+ ALCL. The majority of adults with ALK+ ALCL present with painless lymphadenopathy [4]. Both peripheral and retroperitoneal adenopathy are common. While a majority has systemic symptoms (eg, fever, weight loss), patients may present with isolated lymphadenopathy or with extranodal disease in any site, including the gastrointestinal tract, breast, spleen, liver, and bone [3, 8-10]. In the International T cell Lymphoma Project [7], the lymph nodes were the only site of disease in 54%, while 19% had involvement of more than one extranodal site. Bulky lymphadenopathy (>10 cm) was present in 21 percent. The most common sites of extranodal involvement were bone (14%), bone marrow (12%), subcutaneous tissue and spleen (10% each), skin and lung (8% each), and liver (3%).

The Classical variant of ALCL is composed of large cells with round or pleomorphic, often horseshoe-shaped or "embryoid" nuclei with multiple (or single) prominent nucleoli [4]. The cells have abundant cytoplasm, which gives them an epithelial or histiocyte-like appearance. The "hallmark cell" which is classically identified with ALCL, has an eccentric nucleus and a

prominent, pale Golgi region, or paranuclear hof [11]. Normal and atypical appearing mitoses are common [1]. Approximately 70 to 80 percent of ALCL demonstrate classical morphology [4]. Other atypical variants comprise approximately 20 percent of ALCL [1] with the following being the most common morphologic variants: small cell variant (the majority of cells are small to medium in size and have clear cytoplasm and irregular nuclei) [4], lymphohistiocytic variant (large numbers of histiocytes mixed with the neoplastic cells) [1] and monomorphic variant (the tumor cells have a more monomorphous appearance, with round to oval nuclei and no Reed-Sternberg-like cells; as in the more anaplastic cases, there is abundant cytoplasm with a frequent cohesive, often sinusoidal growth pattern) [12].

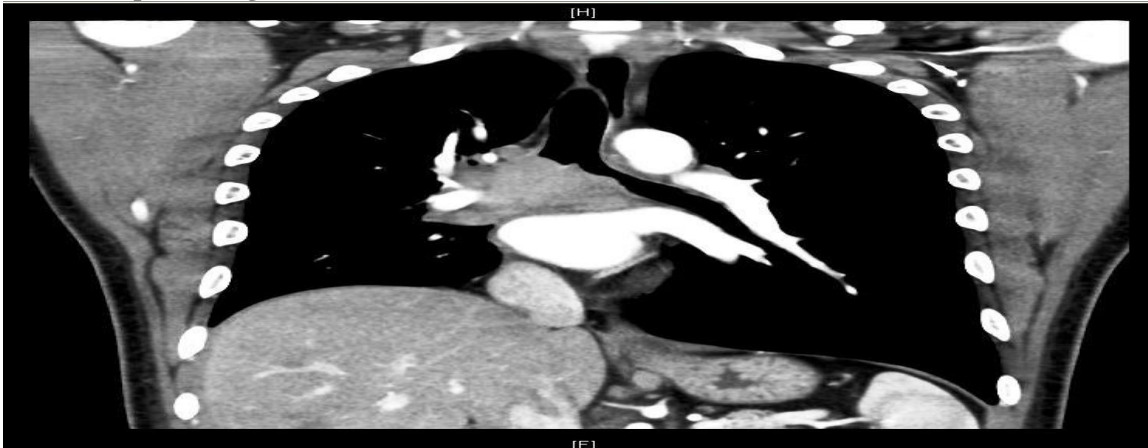
ALK+ ALCL tumor cells are universally positive for both CD30 and ALK and negative for B cell surface markers (eg, CD19, CD20, CD22) [4]. Most tumors have phenotypes consistent with an origin from a mature activated T cell (HLA-DR+, CD25+, and variable positivity for one or more T cell markers), but some belong to the so-called null cell type, in which the tumor cells fail to express any B or T lineage markers [1].

The differential diagnosis of ALK+ ALCL includes other lymphoid neoplasms of T or null cell origin and some B cell neoplasms, such as the anaplastic type of diffuse large B cell lymphoma (DLBCL) and Hodgkin lymphoma, which may have similar morphologic features [1].

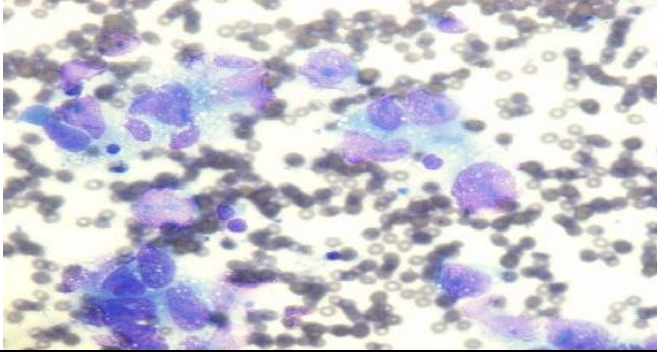
## CONCLUSION

Cytological examination from endobronchial ultrasound guided FNA of the lung mass, which proofed to be a useful and minimally invasive diagnostic tool in this case, revealed multiple large atypical cells; a biopsy was obtained using bronchoscopy. Histopathological examination and immunohistochemical studies were positive for ALK and CD30, which confirmed the diagnosis of ALCL.

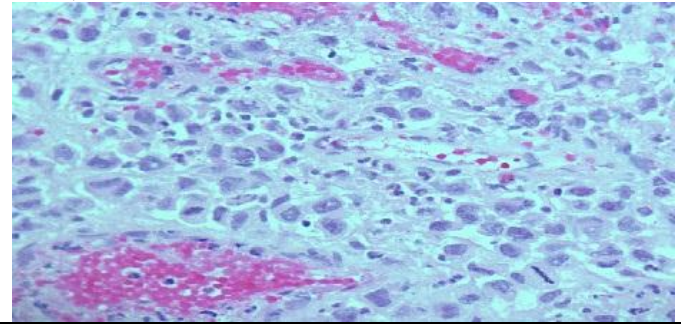
**Fig 1. Coronal view of chest CT scan showing a tumor mass lesion occupying the entire circumference of the right main bronchus and protruding into the lumen**



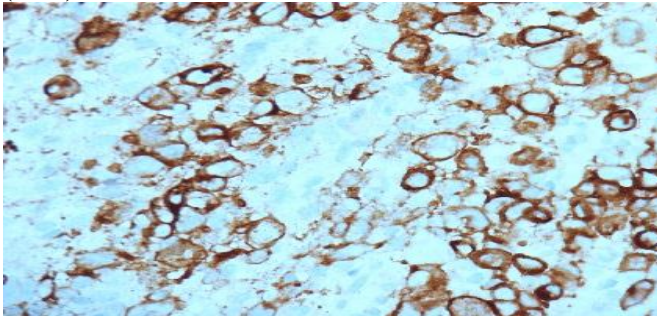
**Fig 2. FNA of the ALCL tumor cells showing nuclear pleomorphism including enlarged nuclei, prominent nucleoli and irregular nuclear contour. (Diff. Quick x400)**



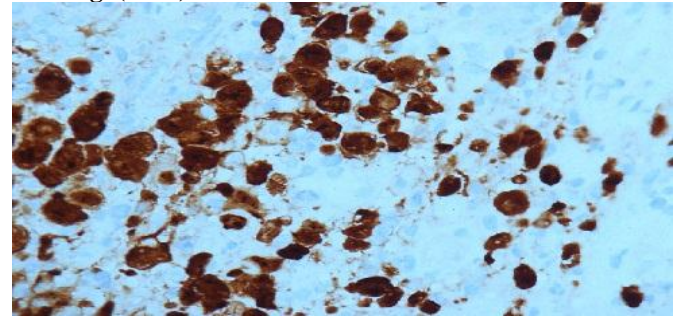
**Fig 3. Permanent sections of the ALCL tumor cells showing nuclear pleomorphism including enlarged nuclei, prominent nucleoli and irregular nuclear contour. (H&E x 200)**



**Fig 4. Immunohistochemical stain showing CD30 staining (x200)**



**Fig 5. Immunohistochemical stain showing ALK1 staining. (x200)**



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