A Case of T/null Anaplastic Large Cell Lymphoma Arising in Lung

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Abstract

Anaplastic large cell lymphoma (ALCL) is a rare non-Hodgkin, T-cell lymphoma, representing only 2-3% of all lymphoid neoplasm's in adults according to World Health Organization (WHO). CD30 antigen-positive, large neoplastic cells characterize ALCL. We present here a 46-year-old male with pulmonary ALCL previously diagnosed with Hodgkin disease. Microscopically, atypical bi-and multinucleated cells with frequent mitoses were present. The neoplastic cells were large and had clear cytoplasm, large vesicular nuclei, and prominent nucleoli. Immunophenotypic analysis revealed LCA, vimentin and CD30 positivity. ALK immunostaining was negative. Immunohistochemical profile was consistent with ALK negative ALCL. The progression of Hodgkin lymphoma to aggressive non-Hodgkin lymphoma (ALCL in this case) is well known entity. After the diagnosis was established, our patient immediately had been referred to the Department of Hematology in order to get appropriate chemotherapy, necessary in such cases.
KEY WORDS: lung, anaplastic large cell lymphoma

Introduction

Anaplastic large cell lymphoma (ALCL) is a rare non-Hodgkin, T-cell lymphoma, representing only 2-3% of all lymphoid neoplasm's in adults according to World Health Organization (WHO) (1). CD30 antigen-positive, large neoplastic cells characterize ALCL (1). ALCL is a highly aggressive T cell lymphoma that requires aggressive treatment, particularly in case of anaplastic lymphoma kinase (ALK) down regulation (2). ALK (2p23), is a receptor tyrosine kinase gene, involved in chromosomal t (2,5) translocation that causes the anaplastic lymphoma kinase (ALK) gene on chromosome 2 to fuse with the NPM gene on chromosome 5.17. This leads to formation of chimeric genes encoding self associating, constitutively active ALK fusion proteins that activate a number of downstream effectors, including phospholipase C-gamma, phospho-inositol 3'-kinase, RAS, and signal transducer

and activator of transcription proteins, all of which seem potentially important in cellular transformation (2-4). t(2,5) is also the most common mutation in ALK+ ALCL (3). Clinical presentation of ALCL is primarily based on specific genetic alterations (4). Thus, ALK+ ALCL is a specific clinicopathological entity, distinct from ALK- systemic or ALK- cutaneous ALCL. Besides, ALK– ALCL is more prevalent among alder patients (4). Clinical presentation frequently involves both nodal and extranodal sites, including (in decreasing order of frequency) skin, bone, soft tissue, lung, and liver (4). The lung variant of ALCL is a rare entity that usually presents with mediastinal lymphadenopathy..

Case Report

A 46-year-old male was admitted to the Department of Thoracic Surgery because of mediastinal lymph node enlargement and involvement of right lung. The patient has previously been diagnosed with Hodgkin lymphoma and has been treated by chemotherapy at the Department of Hematology. In past six months nodular abnormalities of the mediastinum and his right lung have been observed on chest X -ray. Computed tomography (CT) of chest (Figure 1) and Chest X -ray (Figure 2) showed nodular infiltrations of the lung, and multiple enlarged lymph nodes in the mediastinum. Ultrasonography of abdomen also revealed changes in patient's liver (hypoechogenic area measured 48 mm) and enlargement of retroperitoneal lymph nodes (Figure 3). The surgical procedure was performed and a nodular infiltration of the lung was removed with using atypical resection of the lung. On gross pathologic examination lung tissue was like bacon, inflexible with node measuring 12x10 mm. Microscopically, atypical bi-and multinucleated cells with frequent mitoses were present. The neoplastic

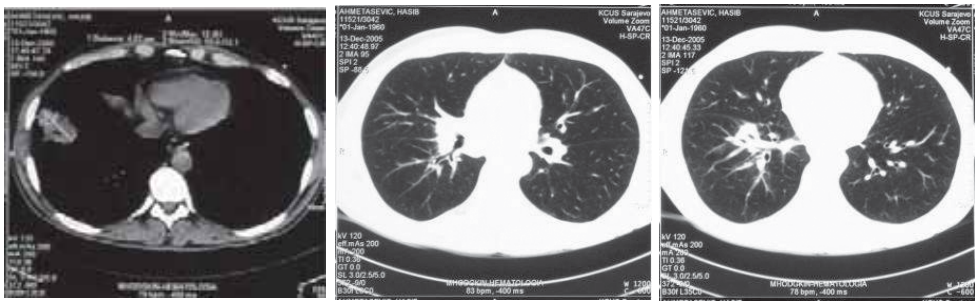

FIGURE 1.
Computed tomography (CT) of chest (a, b, c) nodular infiltrations of the lung, and multiple enlarged lymph nodes in the mediastinum

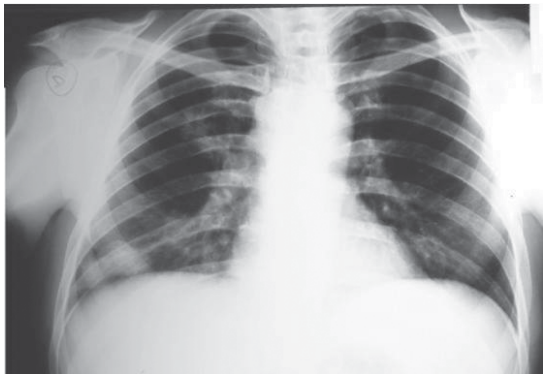

FIGURE 2. Chest X –ray, nodular infiltrations of the lung

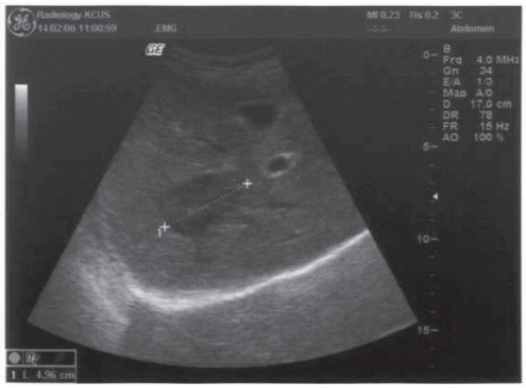

FIGURE 3. Ultrasonography of abdomen, with hypoechogenic area in liver

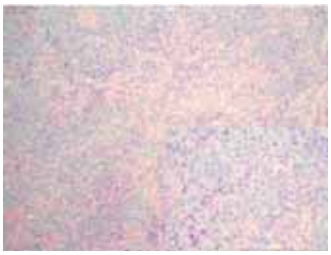

FIGURE 4. a) The neoplasm consisted of noncohesive large cells generally with one nucleus, slightly lobated in some cells, that possessed basophilic nucleoli and eosinophilic cytoplasm (HE x200)

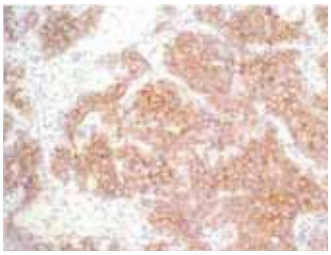

FIGURE 4. b) The tumor was positive for CD30

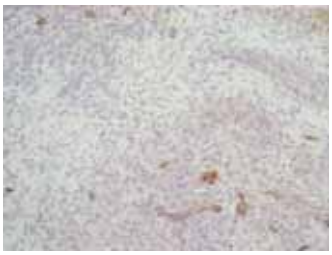

FIGURE 4. c) Only rare cells are positives on EMA

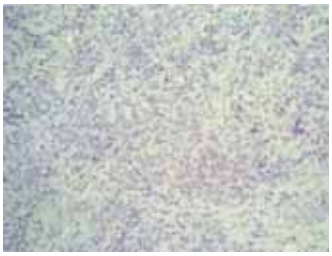

FIGURE 4. d) ALK immunostaining was negative (x 200)

cells were large and had clear cytoplasm, large vesicular nuclei, and prominent nucleoli. Immunophenotypic analysis revealed LCA, vimentin and CD30 positivity. ALK immunostaining was negative. Immunohistochemical profile was consistent with ALK negative ALCL. Below is *immunophenotypic analysis.* The neoplasm consisted of noncohesive large cells generally with one nucleus, slightly lobated in some cells, that possessed basophilic nucleoli and eosinophilic cytoplasm (HE x200) (Figure 4. a). The tumor was positive for CD30 (Figure 4. b). Only rare cells are positives on EMA (Figure 4. c). ALK immunostaining was negative (x 200) (Figure 4. d)

Discussion

This interesting case reports on ALCL with primarily pulmonary and mediastinal involvement. This is usually not case since the most common sites of ALCL include skin, bone, soft tissue, lung, and liver (in decreasing order) (4). The patient has previously been diagnosed with Hodgkin lymphoma. The progression from Hodgkin lymphoma to aggressive non-Hodgkin lymphoma (ALCL in this case) is well known complication of that malignancy (1). The expression of ALK is of high importance, both diagnostically and prognostically. The presence of ALK predicts a good therapeutic response and longer overall survival (4, 5, 6). ALK+ ALCL correlate more positively with higher mitotic activity, higher growth index, fraction of cells expressing cyclin A or B or the cell cycle-regulatory protein p34 (cdc2) than ALK- do (7). This might significantly contribute to better therapeutic response. Our case was ALK negative. This is consistent with other studies according to whom ALK positivity inversely correlated with patient's age (4, 8). The patient did not have B-symptoms. However, the studies have not confirmed correlation between B symptoms and ALK expression (4).

Conclusion

The progression of Hodgkin lymphoma to aggressive non-Hodgkin lymphoma (ALCL in this case) is well known entity. However, pulmonary variant of ALCL is very rare but is important entity because of its aggressive biological and clinical behavior (especially ALK- ALCL) and it requires a caution in both clinicians and pathologists. Unusual clinical presentation of ALCL is particular problem and significantly can delay the diagnosis. This can have the major implications on patient's outcome. After the diagnosis was established, our patient immediately had been referred to the Department of Hematology in order to get an appropriate chemotherapy, necessary in such cases (4).

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