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Isolated pediatric endobronchial primary anaplastic large cell lymphoma

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ABSTRACT

Anaplastic large cell lymphoma (ALCL) is rare, accounting for 10–15% of all childhood non-Hodgkin's lymphomas. We present a case of primary isolated ALCL in the lung of a 5-year-old boy. An asymptomatic 5-year-old boy had absent breath sounds over his right hemithorax on routine physical exam. Chest X-ray showed complete white-out of the right hemithorax. Chest CT scan demonstrated a mass occluding the right mainstem bronchus. The first bronchoscopic biopsy was reported as an endobronchial neoplasm with an immunophenotype consistent with Ewing's sarcoma/PNET. One week later, a repeat second bronchoscopy with re-biopsy confirmed the correct diagnosis of ALCL, null phenotype. Clinical and radiological staging revealed no evidence of extrathoracic disease in the past, present, or for three-months after presentation, confirming isolated primary endobronchial ALCL. Complete remission at 6-months with polychemotherapy was achieved. Although a rare tumor of the lung, ALCL should be considered in the differential diagnosis of 'unusual lung neoplasms' in children.

Non-Hodgkin's lymphoma (NHL) of the lung encompasses 3.6% of extranodal lymphomas, and only 0.3% of primary lung neoplasms [1]. These tumors may be classified into two types: a) Type 1: submucosal infiltrates originating from hematogenous or lymphangitic spread in the presence of systemic lymphoma, or b) Type 2: adjacent airway involvement by a localized mass due to direct spread from adjacent lymph nodes [2]. Pediatric non-Hodgkin's lymphoma most commonly affects the lymph nodes and may be associated with mediastinal involvement and hepatosplenomegaly, with extranodal sites of involvement including the skin, bone, muscle, and lung parenchyma [3].

Anaplastic large cell lymphoma (ALCL), representing 10–15% of pediatric lymphomas, occurs most commonly in children and young adults with a bimodal age distribution [2]. ALCL most commonly affects the sinusoids of lymph nodes, and is often associated with involvement of the mediastinum and hepatosplenomegaly. Extranodal ALCL may involve the skin, bone marrow, soft tissue, pelvis, central nervous system, bone, gastrointestinal tract, lung, pleura, breast, chest wall, retroperitoneum, and spleen [3]. When ALCL involves the lung, it is most commonly the result of advanced disseminated disease. Dissemination is hypothesized to occur via direct invasion from adjacent mediastinal or parenchymal disease, or by lymphatic spread, and/or hematogenous spread. Primary isolated endobronchial ALCL in the pediatric population is exceedingly rare, with very few reports in the published English literature.

We herein report the case of a 5-year-old boy with primary isolated endobronchial ALCL.

1. Case report

A 'healthy' asymptomatic 5-year-old boy was discovered, on routine physical examination, to have absent breath sounds over his right hemithorax.

On chest X-ray there was a complete white-out of the right hemithorax with a shift of the mediastinum toward the side of the opacification (Fig. 1A). A chest CT scan revealed the presence of a mass obstructing the right mainstem bronchus with occlusion and surrounding edema (Fig. 1B). Bronchoscopy revealed a soft white fleshy tumor arising from the lumen of the right upper lobe bronchus that was biopsied (Fig. 1C).

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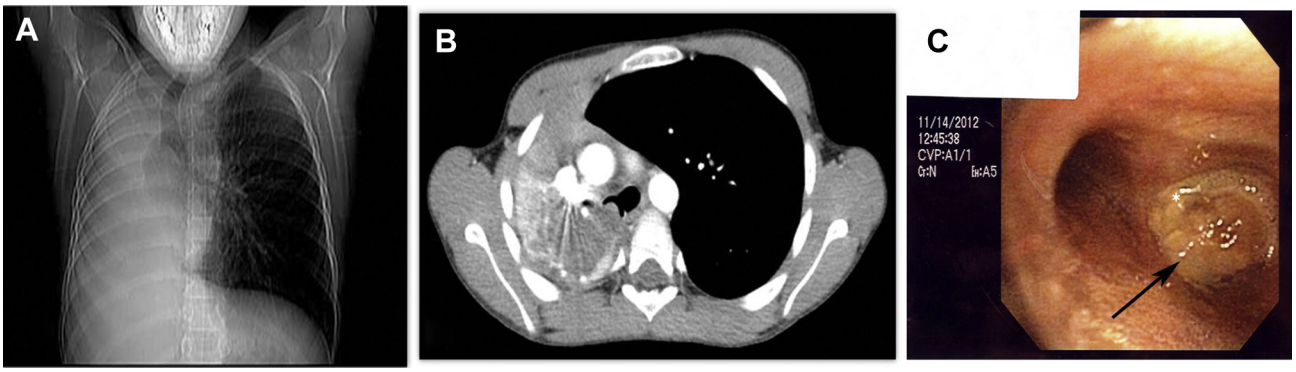

Fig. 1. A) Plain radiograph of the chest reveals complete whiteout of the right hemithorax. B) Computed tomography (CT) scan identifies a mass in the right mainstem bronchus with occlusion and surrounding edema. C) Bronchoscopy image shows the presence of an obstructive mass lesion within the right mainstem bronchus (black arrow).

On histopathological evaluation, a tumor composed of sheets of uniform neoplastic "small blue cells" with no characteristic growth pattern was identified (Fig. 2A and B). Tumor cells were strongly positive to CD99 (Fig. 2C) with a Ki67 labeling index estimated at 90%. Tumor cells were negative for S100, CD3, CD20, CD79a, MPO, TDT, PLAP, LMKT, AFP, Synaptophysin, chromogranin, TTF-1, CK7, CD1a, myogenin, pan-keratin, WT-1, and HCG (Fig. 2D). The pathological diagnosis was a neoplasm with an immunophenotype consistent with Ewing's sarcoma/primitive neuroectodermal tumor (PNET).

A week later the bronchoscopy was repeated to plan for operative resection of the tumor (right upper lobectomy ± sleeve resection of the bronchus intermedius) and additional tumor debulking was performed with the tissue being sent for pathological evaluation. Histopathology of this tissue showed uniform polygonal dark blue cells with fine granular chromatin and scant-to-moderate amounts of eosinophilic cytoplasm (Fig. 2E and F). Lesional cells were strongly positive to CD45, with some expression of CD99, which was inconsistent with the previous reported diagnosis of Ewing's sarcoma. Additionally, the cells were strongly positive to CD30 (Fig. 2G), ALK-1 (Fig. 2H), EMA, TIA-1, and Granzyme. Moderate expression of KP1CD68 was noted, and cells were negative for CD10, CD4, CD8, CD1a, TDT, CD117, and CD34. This immunophenotype favored the diagnosis of anaplastic large cell lymphoma (ALCL). External pathological review of the biopsy material confirmed this suspicion, and the patient was diagnosed with ALCL ALK+ null phenotype. FISH for ALK translocation revealed an abnormal pattern in 54% with evidence of aneuploidy and clonal evolution.

A detailed staging work-up including complete blood count, bone marrow, CSF, plain X-rays ultrasonography, CT, MRI, and skeletal scintigraphy was undertaken. There were no B-symptoms and no extrathoracic involvement was detected. It was therefore determined that this lesion was isolated to the right upper lobe of the lung.

The patient was started on chemotherapy in accordance with the Children's Oncology Group protocol including intrathecal methotrexate, IV vincristine, IV doxorubicin, and PO prednisone. At

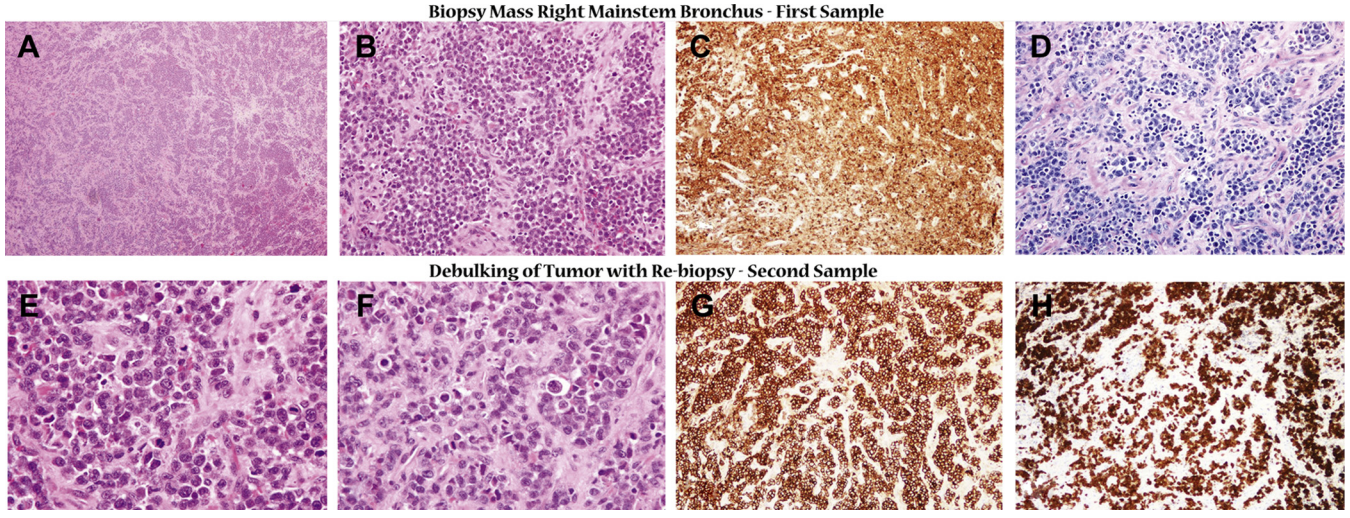

Fig. 2. A–D) Histopathological evaluation of the first biopsy sample from the right mainstem bronchus. A) Photomicrograph of hematoxylin & eosin stained slide at low power shows sheets of uniform small "blue cells." B) Photomicrograph of hematoxylin & eosin stained slide at medium power shows no characteristic growth pattern. C) Photomicrograph of immunohistochemically stained slide at medium power shows strong expression for CD99. D) Photomicrograph of immunohistochemically stained slide at medium power shows no expression of S100, CD3, CD20, CD79A, MPO, TDT, PLAP, LMKT, AFP, Synaptophysin, CGA, TTF1, CK7, Myogenin, pankeratin, WT1, and HCG. E–H) Histopathological evaluation of the second biopsy sample obtained at debulking of the tumor with re-biopsy. E) Photomicrograph of hematoxylin & eosin stained slide at medium power shows uniform polygonal dark blue cells with fine granular chromatin, inconspicuous nucleoli and scant cytoplasm. F) Photomicrograph of hematoxylin & eosin stained slide at high power shows abnormal dense hyperchromatic cells with increased mitoses and apoptosis. G) Photomicrograph of immunohistochemically stained slide at medium power shows strong positive staining to CD30. H) Photomicrograph of immunohistochemically stained slide at medium power shows strong expression with ALK-1 antibodies. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)