 doi: 10.5146/tjpath.2010.01033

Coexistence of Atypical Adenomatous Hyperplasia and Hamartoma of the Lung

Akciğerde Atipik Adenomatöz Hiperplazi ve Hamartom Birlikteliği

Ahmet MİDİ[1], Rahmi ÇUBUK[2], A. Neşe YENER[1], Alpay ÖRKİ[3], Bülent ARMAN[3]

Departments of [1]Pathology, [2]Radiology and [3]Thoracic Surgery, Maltepe University, Faculty of Medicine, İSTANBUL, TURKEY

ABSTRACT

Atypical adenomatous hyperplasia is considered to be a preliminary lesion for pulmonary adenocarcinoma while lung hamartomas (mesenchymomas) are non-neoplastic, tumor-like malformations. A patient underwent transthoracic fine-needle aspiration biopsy for a pulmonary mass and then lingulectomy following a diagnosis of adenocarcinoma. The surgical specimen was solid and 25 mm in diameter. Microscopic investigation revealed that the mass was a hamartoma with an atypical adenomatous hyperplasia focus at the periphery. We believe that the cells leading the cancer diagnosis had come from the atypical adenomatous hyperplasia focus around the hamartoma. We presented this case as atypical adenomatous hyperplasia contains atypical epithelium and can be diagnosed as a malignancy on fine needle aspiration biopsy and the coexistence of atypical adenomatous hyperplasia and hamartoma has not been reported previously.

Key Words: Lung, Hyperplasia, Hamartoma

ÖZ

Atipik adenomatöz hiperplazi akciğer adenokarsinomu için öncü lezyon olarak kabul edilmektedir. Akciğer hamartomu (mezenkimom) non-neoplastik tümör benzeri malformasyondur. Akciğerinde kitle nedeniyle trans torasik ince iğne aspirasyon biyopsisi yapılan ve adenokarsinom tanısı alan olguya lingulektomi operasyonu yapılmıştır. Bu materyalin incelenmesinde 25 mm çapta solid kitle izlenmiştir. Mikroskopik incelemede bu kitlenin hamartom olduğu görülmüş ve çevresinde atipik adenomatöz hiperplazi odağı izlenmiştir. Karsinom tanısı almasına neden olan hücrelerin ise, hamartom çevresinde bulunan atipik adenomatöz hiperplazi odağından geldiği düşünülmüştür. Atipik adenomatöz hiperplazinin atipik epitel içermesi nedeniyle ince iğne aspirasyon sitolojisinde malignite tanısı alabilmesi ve literatürde atipik adenomatöz hiperplazi ve hamartom birlikteliği bildirilmemiş olması nedeniyle olgumuz sunulmaya değer bulunmuştur.

Anahtar Sözcükler: Akciğer, Hiperplazi, Hamartom

INTRODUCTION

Atypical adenomatous hyperplasia (AAH) is considered to be a preliminary lesion for pulmonary adenocarcinoma (1-4). It has been defined by the World Health Organization (WHO) as a noninvasive lesion where the alveolus wall generally <5 mm in thickness is lined by a single row of atypical epithelium (5). Atypical columnar epithelial cells that line the alveolus-like spaces are seen histologically. The pattern resembles bronchoalveolar carcinoma. The presence of atypical epithelium may lead to a diagnosis of malignancy on fine needle aspiration biopsy (FNAB). Lung hamartoma (mesenchymoma) is a non-neoplastic tumor-like malformation and is generally diagnosed in the 5th and 6th decades (6,7). It has a peripheral localization in the lung parenchyme but can also be seen in an endobronchial location. It is usually single and rarely multiple. Radiologically it is seen as a round, homogenous opacity in the lung parenchyme. It has regular borders macroscopically but is seen to have irregular extensions of fibroblastic proliferation into the peripheral pulmonary parenchyme. Calcification may be observed at the periphery of the lesion(8-10). There have been no previous reports of AAH and hamartoma coexistence. We present a case where AAH and hamartoma of the lungcoexisted.

CASE REPORT

A 76-year-old female received a diagnosis of bronchitis and antibiotic treatment was started at another center where she had presented with intensive sputum production, pain radiating to the back, dyspnea, cough and weight loss. Her symptoms persisted and a left lower pulmonary mass was found on further investigation, leading to referral to our hospital. Thorax CT showed a parenchymal lesion with regular borders, 2 cm in diameter, located at the periphery of

Received : 08.02.2010
Accepted : 08.03.2010

Correspondence: Ahmet MİDİ
Department of Pathology, Maltepe University, Faculty of Medicine, İSTANBUL, TURKEY
E-mail: ahmetmidi@yahoo.com Phone: +91 216 399 97 50

the left lower pulmonary lobe and FNAB was recommended. The transthoracic FNAB was performed at the radiology clinic under observation by a pathologist and adequacy was decided upon beside the patient. Microscopic investigation showed scattered cell groups that had prominent nucleoli in places with faint cilia and gland-like structures (Figure 1A-C). The result was reported as a malignant tumor consistent with non-small cell carcinoma and intraoperative pathology consultation was recommended. The patient then underwent open left lateral pulmonary lingula resection and mediastinal lymph node dissection (no. 5-7,9 and 10) by open thoracotomy. Macroscopy revealed a hard white nodule 3x3x2.5 cm in size that had regular borders and a homogenous cut surface on the pulmonary tissue section 11x6x3 cm in size. Microscopical examination of the solid lesion showed a tumor with regular borders and no capsule (Figure 2A). The lesion consisted of spindle cells in large areas and there were many gland-like structures with narrow spaces in between resembling a deer's antlers (Figure 2B). There were also bronchus-like structures, mucinous in character, lined with pseudostratified ciliated columnar epithelium (Figure 3A). There were focal areas of peribronchial acinar mucinous structures and occasional myxoid areas (Figure 3B). Foci of cartilage were also seen around the bronchus-like structures at the periphery (Figure 3C). There was an "atypical adenomatous hyperplasia" focus where bronchial structures lined with atypical columnar epithelial cells had created a 3 mm nodular structure around the hamartoma (Figure 4A, B). The diagnosis with these findings was coexisting pulmonary hamartoma and atypical adenomatous hyperplasia.

DISCUSSION

AAH is rarely seen and may lead diagnostic difficulties as they contain atypical epithelium. The presence of the atypical epithelium can lead to a diagnosis of adenocarcinoma especially on FNAB, as in our case. Our case had a hamartamatous lesion with regular borders and an AAH focus at its periphery. The FNAB provided a diagnosis of adenocarcinoma as cells from this area were aspirated and atypical cells consisted of groups in places. The atypical cells can have the phenotype of Clara cells, type II pneumocytes or columnar cells (5) Our case had the columnar cell phenotype. The presence of smaller nuclei is important in the differential diagnosis with bronchoalveolar and other carcinomas. AAH was not considered in the differential diagnosis in our case as the lesion was smaller than 3 cm radiologically. Adequacy was certified during the evaluation beside the patient, believing that the cells had been obtained from a solid lesion, and the case reported as a malignant.

Molecular studies show that AAH is a precancerous lesion. AAH lesions are usually seen around pulmonary carcinomas. They are more rarely found around metastases and benign lesions (2,3). AAH has been reported to coexist with non-malignant tumors as well as malignant tumors but there are no reports of coexistence with a hamartoma (11,12).

A hamartoma (mesenchymoma) usually shows parenchymal development while endobronchial development is seen in 10-20% of cases. The treatment is tumor enucleation or wedge resection (7-10). The cancer risk is 6.3 times higher than that of the normal population in hamartoma cases (8).

They are said to make up 7-14% of pulmonary coin lesions in large series (8,13,14)

Radiologically, they are generally seen as a round homogenous opacity at the lung periphery. They rarely have a lobulated appearance and peripheral calcification is found in 10% of cases.

Our case was radiologically consistent with a hamartoma. Informing the pathology department of the clinical and radiological preliminary diagnosis of hamartoma in such cases will decrease the possibility of misdiagnosis. Hamartomas are hard lesions and hypocellularity is therefore expected at FNAB. The hard mass will be resistant to the needle and the mass will move and make needle penetration difficult due to the characteristics of the pulmonary parenchyma, leading the cells from the peripheral pulmonary parenchyma entering the needle. Keeping hamartoma in mind in the radiological differential diagnosis of pulmonary coin lesions and cooperation between clinical, radiological and pathological evaluations will decrease the possibility of misdiagnosis. The presence of ciliated cells in such lesions should also bring to mind that the material was obtained from the perilesional pulmonary parenchyme. Consultation by a pathologist experienced in pulmonary lesions will be appropriate for cases where the diagnosis is difficult, as in our case. AAH treatment is usually surgical. Our case did not receive any further surgery than necessary despite the preoperative misdiagnosis..

The lingulectomy procedure performed on our patient is therefore appropriate. We presented this case as it had mistakenly been diagnosed as carcinoma due to the AAH focus around the hamartomatous lesion.

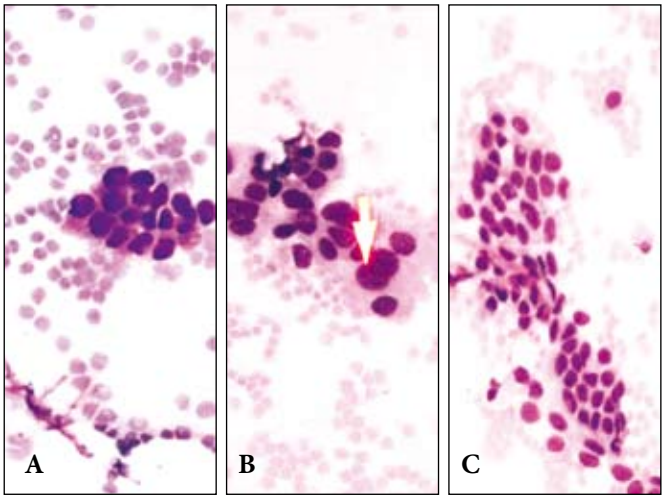

Figure 1: (A) Normal bronchial epithelial cells with cilia, **(B)** Prominent nucleolus in epithelial cell, **(C)** Group of epithelial cells with large nuclei (Giemsa, x400).

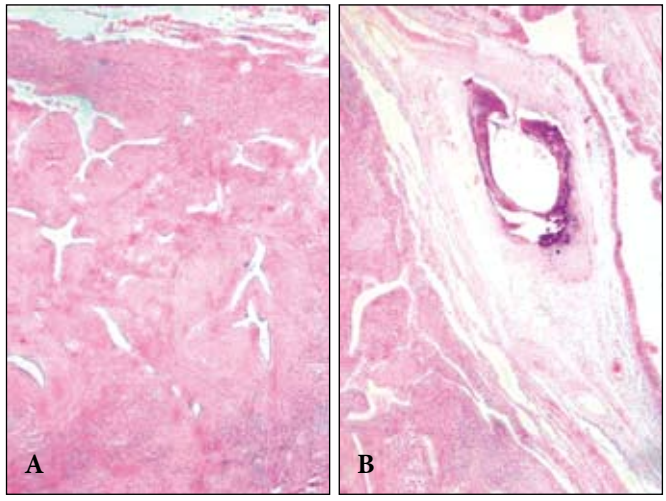

Figure 2: (A) Hamartoma focus with no capsule at top, clearly demarcated from the lung parenchyma (H&E, x40), **(B)** Gland-like structures shaped like a deer antler within the hamartoma (H&E, x40).

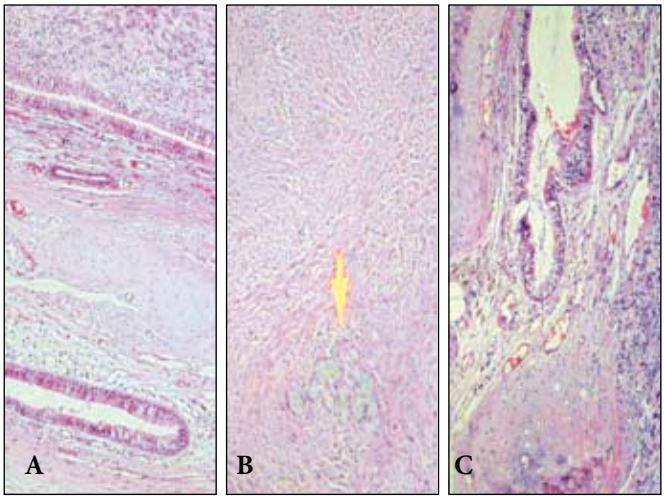

Figure 3: (A) Bronchial structures lined with ciliated epithelium in the hamartoma (H&E, x200), **(B)** Acinary mucinous structures (H&E, x40), **(C)** Cartilage foci around bronchus-like structures (H&E, x200).

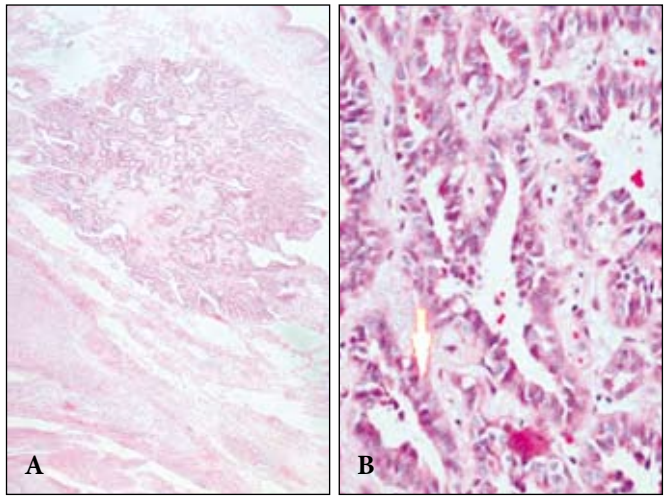

Figure 4: (A) Hamartoma on the left and AAH focus on the upper right (H&E, x40), **(B)** Close-up view of the AAH focus (H&E, x400).

REFERENCES

1. ***Nakahara R, Yokose T, Nagai K, Nishiwaki Y, Ochiai A:*** Atypical adenomatous hyperplasia of the lung: a clinicopathological study of 118 cases including cases with multiple atypical adenomatous hyperplasia. Thorax 2001, 56:302-305
2. ***Morandi L, Asioli S, Cavazza A, Pession A, Damiani S:*** Genetic relationship among atypical adenomatous hyperplasia, bronchioloalveolar carcinoma and adenocarcinoma of the lung. Lung Cancer 2007, 56:35-42
3. ***Sartori G, Cavazza A, Bertolini F, Longo L, Marchioni A, Costantini M, Barbieri F, Migaldi M, Rossi G:*** A subset of lung adenocarcinomas and atypical adenomatous hyperplasia-associated foci are genotypically related: an EGFR, HER2, and K-ras mutational analysis. Am J Clin Pathol 2008, 129: 202-210
4. ***Huo Z, Liu HR, Wan JW:*** Atypical adenomatous hyperplasia of lung: clinicopathologic study of 8 cases and review of literature. Zhonghua Bing Li Xue Za Zhi 2007, 36:292-296
5. ***Müller-Hermelink HK, Möller P, Engel P, Menestrina F, Kuo TT, Shimosato Y, Ströbel PH, Asamura H, Marx A, Masaoka A, Harris NL, Sobin LH:*** Tumours of the thymus. In Travis WD, Brambilla E, Müller-Hermelink HK, Harris CC (Eds). World Health Organization Classification of Tumours. Tumours of the Lung, Pleura, Thymus and Heart. Lyon, IARC Press, 2004, 145-248
6. ***Taniyama K, Sasaki N, Yamaguchi K, Motohiro K, Tahara E:*** Fibrolipomatous hamartoma of the lung: a case report and review of the literature. Jpn J Clin Oncol 1995, 25:159-163

7. ***Wang SC:*** Lung hamartoma: a report of 30 cases and review of 477 cases. Zhonghua Wai Ke Za Zhi 1992, 30:540-542, 571-572
8. ***van den Bosch JM, Wagenaar SS, Corrin B, Elbers JR, Knaepen PJ, Westermann CJ:*** Mesenchymoma of the lung (so called hamartoma): a review of 154 parenchymal and endobronchial cases. Thorax 1987, 42:790-793
9. ***Bateson EM:*** So-called hamartoma of the lung--a true neoplasm of fibrous connective tissue of the bronchi. Cancer 1973, 31: 1458-1467
10. ***Tomashefski JF Jr:*** Benign endobronchial mesenchymal tumors: their relationship to parenchymal pulmonary hamartomas. Am J Surg Pathol 1982, 6:531-540
11. ***Thomas DH, Attanoos RL, Gibbs AR:*** Coexistent atypical adenomatous hyperplasia, primary lung adenocarcinoma and pleural mesothelioma in an asbestos-exposed subject. Histopathology 2004, 45:540-542
12. ***Miller RR:*** Bronchioloalveolar cell adenomas. Am J Surg Pathol 1990, 14:904-912
13. ***Steele JD:*** The solitary pulmonary nodule. report of a cooperative study of resected asymptomatic solitary pulmonary nodules in males. J Thorac Cardiovasc Surg 1963, 46:21-39
14. ***Ray JF 3rd, Lawton BR, Magnin GE, Dovenbarger WV, Smullen WA, Reyes CN, Myers WO, Wenzel FJ, Sautter RD:*** The coin lesion story: update 1976. Twenty years' experience with thoracotomy for 179 suspected malignant coin lesions. Chest 1976, 79:332-336