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Original Research

Does Pulmonary Hamartoma Increase the Risk of Lung Cancer? Outcomes of 38 Pulmonary Hamartoma Cases

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Abstract

Objectives: Hamartomas are common benign tumors of the lung. Rarely, lung cancer coincidence may occur at the time of diagnosis or in the follow-up period.

Methods: Between 2016 and 2019, 38 patients who underwent a surgical procedure and diagnosed with lung hamartoma were retrospectively evaluated regarding clinicopathological features. Cases were analyzed according to age, sex, radiological findings, localization of nodules, surgical methods, and the coincidence of lung cancer.

Results: The mean age was 50.2±11.1 (range 28–76 years). There were 23 male (60.5%) and 15 female (39.5%) patients. Mean size was 2.7±1.8 (range 0.8–10 cm). In 28 patients, hamartoma was <3 cm in diameter (73.6%). Eighteen hamartomas were localized in the upper lobe (47.4%). Only 6 cases (15.8%) were localized at the central part of the lung. Multiple nodules were reported in 10 cases (26.3%). In 4 cases (10.5%), lung carcinoma and hamartoma were seen together at the time of diagnosis. Video-assisted thoracoscopic surgery (VATS) has been performed in 29 cases (76.3%). As a surgical method, enucleation was performed in 4 cases (10.5%), wedge resection in 28 cases (73.7%), and lobectomy in 6 cases (15.8%). No post-operative mortality appeared in the early follow-up.

Conclusion: Pulmonary hamartomas are usually present as solitary pulmonary nodules with benign radiological findings. VATS wedge resection is a method that can be used safely in diagnosis and treatment. Hamartomas may be associated with lung cancer at the time of diagnosis or follow-up, so it should be kept in mind that a different nodule seen in patients diagnosed with hamartoma may be associated with lung cancer.

Keywords: Lung cancer; pulmonary hamartoma; solitary pulmonary nodule.

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Introduction

Lung hamartomas are the most common benign tumors of the lung.[1] They originate from mesenchymal cells. It consists of varying amounts of mature cartilage, fat, respiratory epithelial cells, osteoid, and smooth muscle tissues. According to the dominant component, they can be divided into subgroups such as chondromatosis, leiomyomatous, lymphangiomyomatous, adenofibromatous, and fibroleiomyomatous.[2] Chondromatosis hamartoma is

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the most common subtype.[3] Hamartomas constitute 6% of solitary pulmonary nodules (SPN) and are often seen in peripheral intraparenchymal and rarely in endobronchial localization.[4,5] As can be seen in many different parts of the body, they are mostly seen in the lung. There are publications showing that the risk of developing lung cancer during diagnosis or follow-up is 6% higher than the entire population.[6]

In this study, we evaluated the clinicopathological features of pulmonary hamartomas and investigated whether pulmonary hamartomas increase the risk of lung cancer.

Methods

We reviewed the hospital charts of 38 pulmonary hamartoma patients who underwent non-anatomic or anatomical resection between 2016 and 2019. Only operated patients were included in the study. Patients under clinical and radiological follow-up are absent in this study. Thoracic contrast computed tomography (CT) was routinely requested in all patients. Positron emission tomography (PET-CT) was used as an additional imaging method in patients with suspected malignancy in the CT reports (spicular enlargement, irregular shape). Fiber-optic bronchoscopy (FOB) and/or transthoracic needle aspiration (TTNA) biopsy was performed in patients suspected of being malignant for diagnostic purposes.[7] Pulmonary function tests were performed routinely before surgery. To operate, the patients were required to have forced expiratory volume in 1 seconds (FEV 1) values suitable to tolerate a minimum lobectomy (FEV1 >60% of the expected value), and those with fit general condition for thoracic surgery according to cardiac values were operated. The surgical approach and resection method planned to be applied to the patients were decided in the surgical councils before surgery. In cases with high benignity criteria, it was decided to apply only wedge resection without applying frozen section method.

As a surgical approach; video-assisted thoracoscopic surgery (VATS) or posterolateral/lateral thoracotomy methods were used. Localization and diameter of the lesion were decisive in the choice of surgical approach. Thoracotomy was preferred for lesions greater than 5 cm and with central localization.

VATS procedure was performed uniportal or biportal according to the surgeon's preference. During the operation, according to palpation findings, nodule enucleation method was used in peripheral cases known to be highly calcified. In cases with high suspicion of malignancy, the diagnosis was confirmed by frozen section method during surgery. In cases where the lesion was centrally localized, frozen examination material was obtained by punch biopsy. Despite the frozen examination, a lobectomy decision was made in two cases. One was due to central localization, and the second was because the pathologist suspected malignancy. In addition, lobectomy was performed in three patients with endobronchial localization and in one tumor case. In pre-operative examination, more than 1 nodule was detected in 10 cases. Frozen section examination was reported as lung malignancy in four cases. In these cases, the second nodule was in the same lobe in one patient, in the different lobe in the other two patients, and in the contralateral lung in the fourth patient. The preoperatively focused nodules in these four lung cancer patients were actually malignant nodules. In ipsilateral cases, the other nodule was diagnosed with hamartoma with a frozen section. None of these patients were diagnosed with lung cancer before surgery.

The study was approved by the Institutional Review Board and was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

The data were entered into the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 25.0, Armonk, NY, United States). In the data analysis, mean±standard deviation and minimum-maximum values were used for continuous variables (age and tumor diameter) as descriptive data. Frequencies and percentages were calculated for categorical variables (gender, presence of more than one nodule, accompanying lung cancer, etc.).

Results

The mean age was 50.2±11.1 (range 28–76 years). There were 23 men (60.5%) and 15 women (39.5%). The average size was 2.7±1.8 (range 0.8–10 cm). Hamartoma was <3 cm in diameter in 28 patients (73.6%) and >3 cm in 10 patients (26.4%). In thorax CT, calcification was observed in 15 cases (39.5%). There was more than 1 nodule in 10 cases (26.4%). Four (40%) of these cases were diagnosed with lung cancer during surgery. Three (33.3%) of other multiple nodules were under 1 cm at the contralateral lung and these nodules were decided to be followed up. Last three (33.3%) nodules were sampled during surgery and diagnosed anthracotic lymph nodes. Lung cancer was diagnosed in 10.5% in all patient populations. In lung cancer cases, the diagnosis was reported as adenocarcinoma in three of them, while in one case, the diagnosis was carcinoid tumor. All four cases diagnosed with lung cancer were male and the mean age was 67.7 (range 51–69 years). Two cases were in different lobes (Figs. 1 and 2), one was in the same lobe (Fig. 3), and one was in the contralateral lung which was diagnosed as

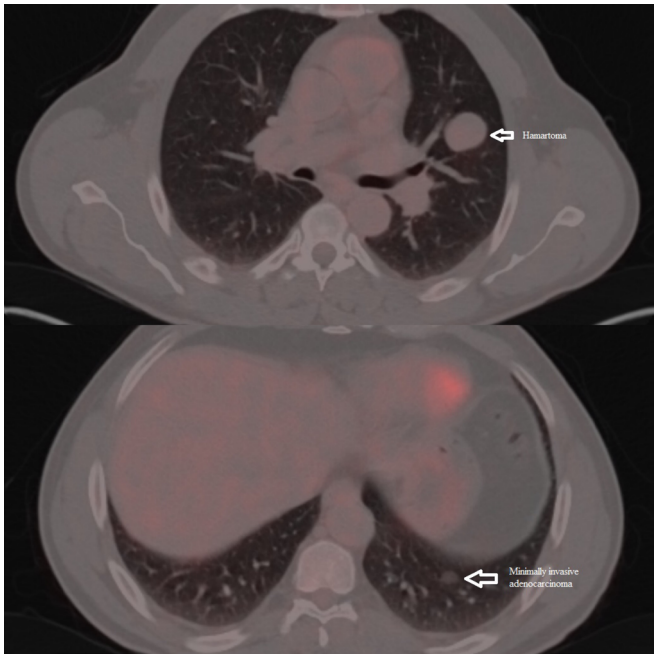

Figure 1. Patient 1 – Andeocarcinoma-hamartoma ipsilateral different lobe.

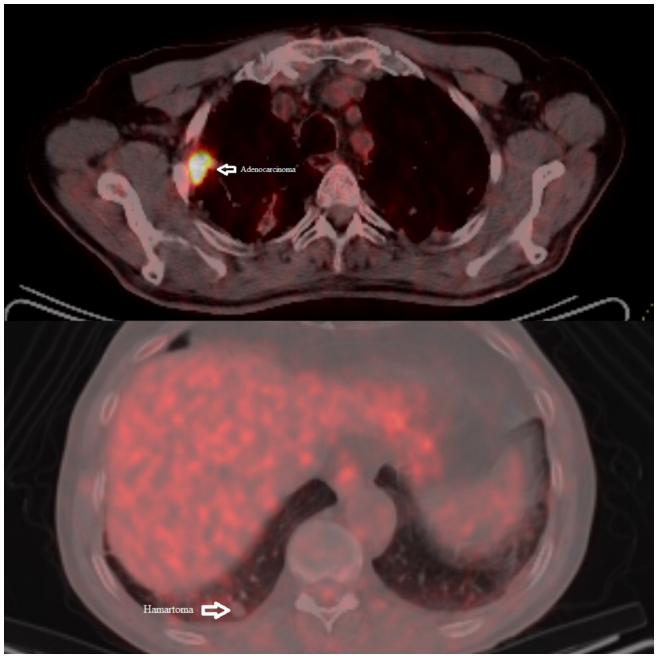

Figure 2. Patient 2 – Andeocarcinoma-hamartoma ipsilateral different lobe.

carcinoid tumor (Fig. 4). Bilateral surgery was performed in this case with an interval of 2 months. All tumor diameters were under 3 cm and lobectomy was performed in three cases and segmentectomy was performed in one case. The accompanying hamartoma nodules were removed by

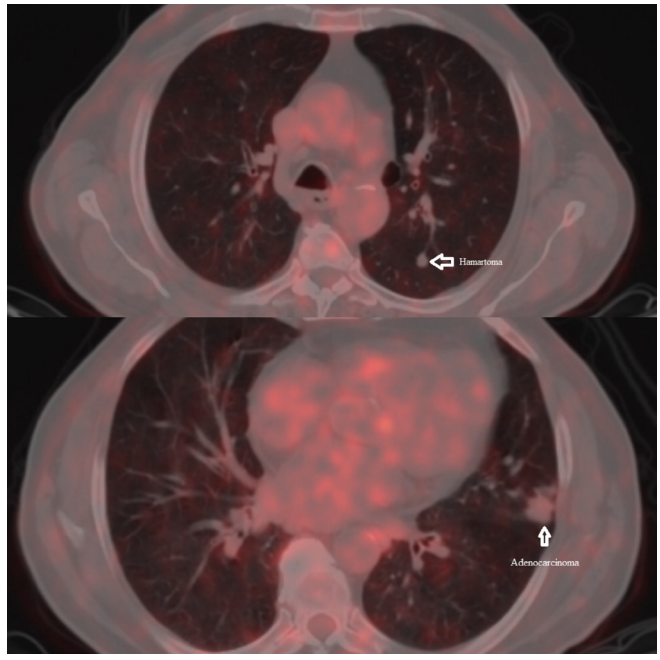

Figure 3. Patient 3 – Andeocarcinoma-hamartoma ipsilateral same lobe.

wedge resection in three cases and enucleation was performed in one case.

Diagnostic methods were applied to 16 patients (42%). FOB was performed in 13 patients and TTNA was performed in nine patients. Only five cases have been diagnosed with hamartoma before surgery (two with TTNA and three with FOB). PET-CT was used for diagnosis in 17 malign suspicious patients (77.7%). The mean suv max value was 1.4 (range 0–3). In lung cancer, cases mean suv max value was 3.8 (range 3–5.4). VATS has been performed in 29 cases (76.3%). As a surgical method, enucleation was performed in four cases (10.59%), wedge resection in 28 (73.7%), and lobectomy in 6 (15.8%) cases. In 20 suspicious cases (52.6%), the diagnosis was made by the frozen section method during the surgical procedure. Eighteen hamartomas were localized in the upper lobe (47.4%), 24 cases (63.2%) were localized at the right hemithorax, and 35 cases (92.1%) had extra bronchial localization. Only 6 cases (15.8%) were localized at the central part of the lung. There was only one post-operative complication requiring rethoracotomy (hemorrhage of thoracotomy lobectomy patient with intrabronchial localization). No post-operative mortality appeared in early follow-up.

Discussion

Goldsworthy used hamartoma term for benign cartilage and adipose tissue tumors that originated in the lung in 1934.[8]

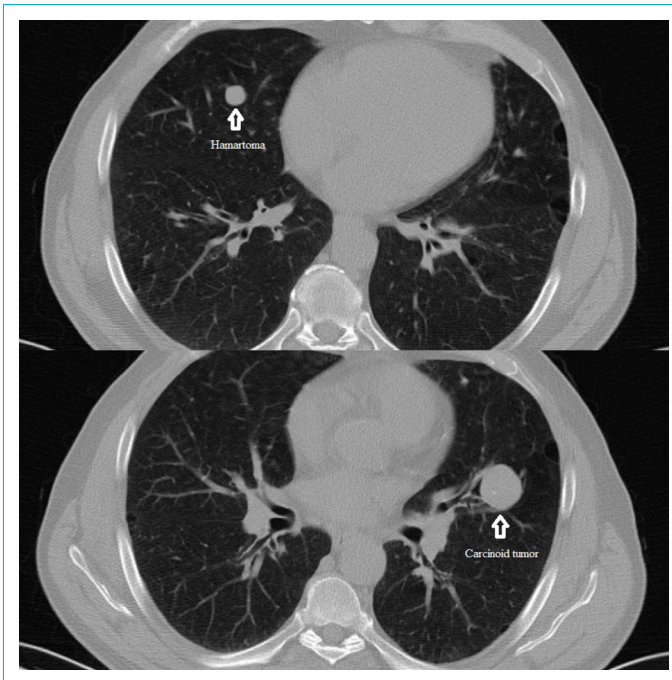

Figure 4. Patient 4 – Carcinoid tumor-hamartoma contralateral lung.

Although the exact etiological cause is unknown, many theories have been proposed, such as congenital malformation, hyperplasia of normal structures, cartilage-associated benign tumor, and response to inflammation. No specific risk factor for pulmonary hamartoma has been identified.[9]

Pulmonary hamartomas are more common in middle and older age groups and mostly in males.[10,11] In our study, we found an average age of 50, and also similar to the literature, there was male dominance. A SPN is a name given to radiologically marked opacity, normal lung tissue around it and lesions less than 3 cm in diameter. Pulmonary hamartomas are seen radiologically as flat and well-confined, lobulated, peripheral solitary nodules.[12] Popcorn calcification is very typical. However, most are not found in hamartomas.[13] In our case, 39.5% (*n*=15) calcification was detected. In the present study cases, mean size was 2.7±1.8 (range 0.8–10 cm). In 28 patients, hamartoma was <3 cm in diameter (73.6%). Localizations of the lesions were 84.2% (*n*=32) peripheral and 94.7% (*n*=36) extra bronchial. In the series of 215 cases of Gjevre *et al*.[14] determined the localization of the lesions as 90% peripheral and 98.6% extra bronchial similar to our results. When a solitary nodule is detected radiologically, a benign/malignant distinction should be attempted. According to the National Comprehensive Cancer Network guidelines, it is recommended to apply a direct surgical approach in SPN with high malignancy suspicion and to diagnose by the frozen section method preoperatively.[15] Although surgery is controversial in patients diagnosed as hamartoma with TTNA, surgery is recommended in patients with progression during follow-up or in cases larger than 2.5 cm or in patients with pulmonary symptoms.[16] In our patient group, TTNA biopsy was performed in 9 cases (23.6%), but a definitive diagnosis could not be achieved except in two patients.

Although pulmonary hamartomas are benign tumors, they can rarely show malignant transformation.[17] We did not have such a case in our case series experience. The relationship of hamartoma with lung or other cancers has been the subject of many studies.[18] In a study with 215 case series, a concurrent neoplasm (most often lung cancer) in 63 patients (29.3%) was detected at the time of diagnosis or at follow-up.[19] Lung cancers coincidence with chondromatous hamartoma have some of the common features. Male patients above middle age, accompanying lung cancer with a histology of adenocarcinoma, and accompanying cancer in the same lobe.[20] In the present study patient series, we observed the histology of adenocarcinoma in three cases. In two cases, we found synchronous lung cancer in an ipsilateral different lobe and all cases were above middle age. Avraham *et al*.[21] detected six cases of bronchial carcinoma in 52 patients with hamartoma followed between 1960 and 1975, and four of these cases were reported at the same lobe with the hamartoma. They released that two lung cancers developed in years after diagnosis. According to their results, they stated that about the Israel population; hamartoma increased the development of lung cancer 6.3 times. According to cancer statistics in our country, the incidence of trachea, bronchus, and lung cancer ratio is reported as 0.052%.[22] Lung cancer coincidence was detected in 4 (10.5%) of 38 hamartoma cases. Although this rate is much higher than the risk of lung cancer in our country, we think that with clinical follow-ups and with large patient series, the determination of the risk of lung cancer coincidence may be diagnosed more accurately.

The current study has some limitations. First of all, we do not have patient data with long-term follow-up. Therefore, it will be very ambitious to determine the rate of lung cancer coincidence. We think that we document the demographic and pathological features of the patients appropriately. Although there are studies on hamartomas in our country, we have not seen many studies on lung cancer coincidence. We think that we have shown well that lung cancer and hamartoma coincide with a large number of cases.

Conclusion

Although pulmonary hamartomas are benign lesions, determining the diagnosis with VATS wedge resection and

frozen section evaluation is the most accepted form of diagnosis and treatment. As evidence from many studies, the risk of lung cancer in lung hamartoma patients increases at diagnosis or at follow-up. Therefore, hamartoma cases should be carefully evaluated for the presence or development of lung cancer and be kept under follow-up for years. It should be remembered that a second nodule detected at the time of diagnosis may be lung cancer.

Disclosures

Ethics Committee Approval: The study was approved by Istanbul Training and Research Hospital Local Ethics Committee (2281/08.05.2020).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – A.C.K.; Design – A.C.; Supervision – H.A.; Materials – S.E., S.O.; Data collection &/or processing – E.Y.E., N.Y.; Analysis and/or interpretation – V.E., S.E.; Literature search – E.Y.E., S.B.; Writing – V.E., E.Y.E.; Critical review – M.M.

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