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Case report

Rare Case of Malignant Transformation of Pulmonary Hamartoma

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Abstract

We reported a rare case of malignant transformation in a pulmonary hamartoma observed in a 48-year-old female. The hamartoma was incidentally identified with the presence of fat attenuation component. Subsequent imaging during follow-up revealed a significant loss of fat content accompanied by an increase in solid components within the nodule. The patient remained asymptomatic for respiratory or systemic issues. An interventional radiology-guided CT biopsy was performed, and histopathological analysis confirmed the presence of a lipid-rich adenocarcinoma. This case underscores the importance of vigilant monitoring and consideration of malignant transformation in pulmonary hamartomas.

Keywords: *Pulmonary hamartoma, Fat, Adenocarcinoma.*

Introduction

Pulmonary hamartoma (PH) is a commonly encountered benign lung tumor, representing 77% of all benign lung tumors and accounting for 4% of solitary lung nodules [1]. It primarily manifests in the lung parenchyma, with potential involvement in the endobronchial region to a lesser extent, with a prevalence ranging from 3% to 12% among all lung hamartomas [2]. The lesion comprises an abnormal mixture of tissue components such as cartilage, epithelium, fat, or muscle, and is typically discovered incidentally as solitary pulmonary nodules, with the majority of patients remaining asymptomatic. They generally have a favorable prognosis, often managed through observation without surgery due to their slow annual growth [3]. However, giant pulmonary hamartomas [4] and cases with rapid growth are documented, [4,5] although malignant transformation of PH is extremely rare.

Here, we present the case of a 48-year-old asymptomatic woman who was incidentally found to have a lung nodule with features suggestive of a hamartoma, displaying multiple densities on a chest CT scan. During follow-up, the patient remained asymptomatic; however, imaging revealed an increase in the size of the lung nodule, mainly in the solid component, with the loss of fat content. She was subsequently referred to a CT-guided biopsy of the lesion, and histopathological studies revealed lepidic pulmonary adenocarcinoma. The patient was then referred to thoracic surgery for a right upper lobectomy after a multidisciplinary lung cancer team meeting.

Case report

A 48-year-old woman, non-smoker with an unremarkable medical history, referred to the pulmonary outpatient clinic due to an abnormal chest X-ray performed for immigration purpose and it reveals a faint nodular opacity in the right upper zone. Upon initial evaluation in the pulmonary clinic in March 2020, she reported no respiratory symptoms, including cough, shortness of breath, or wheezing. Additionally, she denied experiencing fever, weight loss, night sweats, or signs of connective tissue disease. A subsequent chest CT scan was performed, revealing an ill-defined lobulated nodule in the apical segment of the right upper lobe, measuring approximately 2.4 x 2.3 x 2 cm in craniocaudal (CC), transverse, and anteroposterior (AP) dimensions, respectively, with multiple densities, predominantly soft tissue density. The solid part measured 15 x 11 x 16 mm, and a small fatty component was

observed medially (mean density of -170 HU). The characteristics suggested a pulmonary hamartoma (Figure 1).

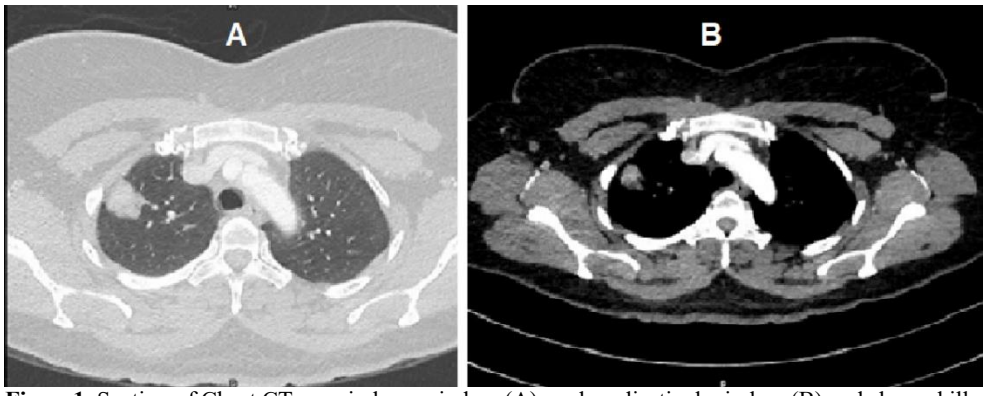

Figure1. Section of Chest CT scan in lung window (A), and mediastinal window (B) and showed ill-defined lobulated nodule in the apical segment of the right lung upper lobe laterally measuring about 2.4 x 2.3 x 2 cm in CC, transverse and AP diameters respectively. The lesion shows multiple densities with predominantly soft tissue density, small fatty component medially (mean density of -170 HU). It is seen abutting the adjacent pleural surface.

A follow-up chest CT scan in October 2020 demonstrated no significant change in the size of the right upper lobe lesion with no new changes. Unfortunately, the patient was lost to follow-up during the COVID-19 pandemic. Upon reevaluation in March 2023, the patient again denied any new respiratory or constitutional symptoms, Vital signs showed a blood pressure of 125/72 mmHg, heart rate of 88 beats/min, temperature of 36.8°C, and oxygen saturation of 99% with room air. Physical examination was unremarkable. Laboratory investigations revealed hemoglobin of 11.7 g/dL, white blood cell count of 6100/μL, and platelet count of 174,000/μL. Serum creatinine was 56 μmol/L; potassium 4.4 mmol/L; sodium 137 mmol/L; C-reactive protein 5.9 mg/L; alanine transaminase, 14 U/L; and aspartate transaminase 13 U/L.
A new chest CT scan was requested and revealed an interval increase in size of the right upper lobe lesion, measuring about 24 x 25 x 26 mm, with an interval increase in the size of the solid part of the lesion (now measuring 20 x 18 x 24 mm) (Figure 2).

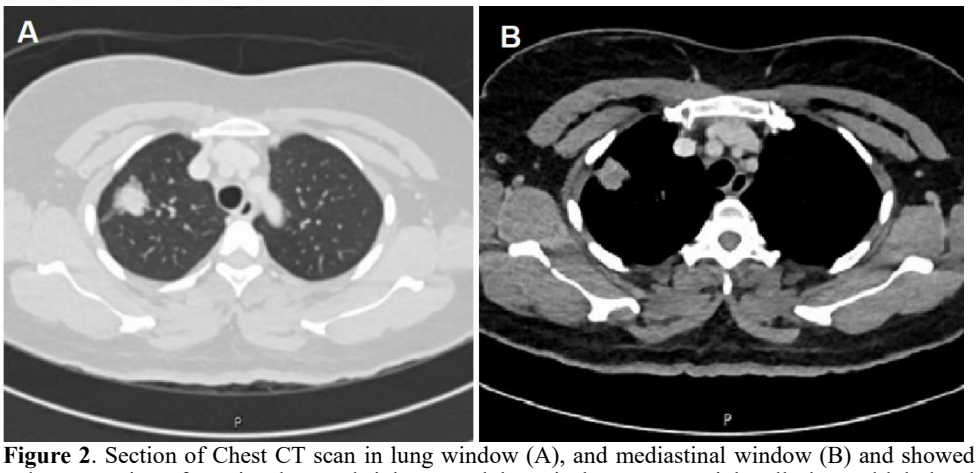

Figure 2. Section of Chest CT scan in lung window (A), and mediastinal window (B) and showed redemonstration of previously noted right upper lobe apical segment peripherally located lobulated lesion, predominantly solid with internal bubble-like lucency and surrounding halo of groundglass opacity and speculations now measuring about 24 x 25 x 26 mm in overall size. There appears to be interval increase in size of the solid part of the lesion which now measures 20 x 18 x 24 mm compared to 15 x 11 x 16 mm in figure 1.

The patient reported no exposure history, and had no family history of lung malignancy, she was subsequently referred to interventional radiology (IR) for a CT-guided biopsy, confirming the diagnosis of pulmonary adenocarcinoma lepidic subtype. PET scan showed an intensely metabolically active right upper lobe nodule with no metabolically active nodal or

distant metastatic disease. The patient was then referred to right upper lobectomy by Video-Assisted Thoracoscopic Surgery (VATS), after A multi-disciplinary lung cancer team meeting (MDT).

Discussion

Hamartoma was first described by the pathologist Eugen Albrecht in 1904, and since that time, it has been reported in various anatomical sites, encompassing organs such as the lung, heart, liver, kidneys, and other visceral structures [6]. PH is the most common benign lung lesion, with an overall incidence of 0.025–0.32% [2]. Hamartomas are more common in males than females, with an incidence ratio of 2-3:1, with an average age of 50 [7]. Lung hamartomas are usually asymptomatic and are found incidentally during imaging performed for various reasons, as in our patient, or for lung cancer screening. Obstructive pulmonary symptoms related to hamartomas, such as atelectasis, pneumonia, cough, hemoptysis, and chest pain, have been reported in endobronchial hamartomas [3,8,9]. The majority of lung hamartomas are solitary; however, multiple hamartomas are very rare and reported in a few case reports [10,11,12]. In one single-center series including 59 patients, multiple hamartomas were detected in 6.8% of the cases [13]. The mean transverse diameter of the hamartomas at discovery was 2.72 cm (in our patient, 2.4 cm) and found mainly in the periphery, particularly in the right lower lobe [14]. The average total duplication time (TDT) of hamartomas was calculated to be 581.2 days [15], though rapid growth was reported, with a mean TDT of 132.2 days [5].

Pathologically, pulmonary hamartoma [PH] contains a mixture of soft tissues, including cartilage, fat, smooth muscle, fibromyxoid tissue, bone, undifferentiated mesenchyme, and less frequently smooth muscle growing in the interstitium and entrapping regular bronchioli and/or alveoli with hyperplastic pneumocytes [16]. Radiologically, PH appears on chest CT scan as well-circumscribed nodules 2-3 cm in diameter, with calcification or fat content [17]. Though intranodular fat and popcorn-like chondroid calcifications are considered reliable markers to diagnose pulmonary hamartoma, it's found that the fat content is only seen in about 35.6% of hamartomas, whereas calcifications along with fat are present in about 27.1%, with typical popcorn calcification occurrence in 10.2% of the cases [13]. In our case, the diagnosis of pulmonary hamartoma was supported by the presence of fat content in the initial chest CT scan. Although the definitive diagnosis of pulmonary hamartoma necessitates histopathological analysis, biopsy is not performed in all cases, and the diagnosis can be made through chest CT scan characterization. In a study that compared the histological and radiological images of hamartomas in 54 patients, the radiological images enable a high accuracy diagnosis, provided that the nodule is round with smooth contours, smaller than 3 cm, shows the presence of 'popcorn' calcifications, or of adipose tissue, and is well-circumscribed from the surrounding tissues. [18]

Hamartoma is a benign tumor and has a good prognosis; most cases are followed up by observation without the need for surgery due to slow annual growth [19]. However, the risk of pulmonary malignancy is higher than in the general population. In one study, the estimated risk was 6.3 times after adjustment for age, sex, and ethnicity. Malignancy can occur either on the same side as the hamartoma or in the contralateral lung [17]. In another study that included 96 patients, 18 patients (18.75%) of the hamartoma patients were found to have concomitant malignancies, including squamous carcinoma, adenocarcinoma, typical carcinoid, and mixed mesothelioma [20]. Smoking and environmental carcinogenic factors have been identified as important risk factors for the development of lung malignancy, [14], Avraham et al. [21] detected 6 cases of bronchial carcinoma in 52 patients with hamartoma during follow up period between 1960 and 1975, and four of these cases were reported at the same lobe with the hamartoma.

Pulmonary hamartoma may also manifest as part of Carney triad, often presenting alongside gastric leiomyosarcoma and functional non-surrenal paraganglioma [22].

The transformation of malignant hamartoma to carcinoma or sarcoma was reported in very few cases. Basile et al. [23] reported a pleomorphic sarcoma occurred shortly after resection of a pulmonary hamartoma, while Hayward and Carabasi [24] and Poulsen et al. [25] described a pulmonary hamartoma with synchronous adenocarcinomatous changes. In our case, suspicion of malignant transformation arose due to an increase in the size of solid content within the pulmonary hamartoma and the concurrent disappearance of fat content, which its presence typically indicates the benign nature of the lesion.

At present, there are no established guidelines for the follow-up of patients with pulmonary hamartomas, and the decision for surgical resection is typically guided by expert opinion.

In a retrospective study spanning 20 years, Wei Guo et al. recommended surgical resection for solitary pulmonary lesions with a diameter greater than 2.5 cm; cases imposing a psychological burden; lesions demonstrating a tendency for expansion or recurrence; cases with pulmonary symptoms unresponsive to drug treatment; and particularly when the lesion cannot be confidently differentiated from malignancy [26].
The objective of our case report is to heighten awareness regarding the uncommon but noteworthy occurrence of malignant transformation in pulmonary hamartomas. And the loss of fat content observed during follow-up imaging emerges as a significant indicator warranting consideration for potential malignancy.

Conclusion

Here, we present a rare case of pulmonary hamartoma that has been transformed into malignancy during follow-up imaging. No new symptoms appeared in the patient, and suspicion of malignancy arose when follow-up imaging revealed the loss of the fat component initially seen in the first image, with an increase in the solid component. We aim to raise awareness about this serious transformation and indicate that the loss of fat content in a hamartoma needs further investigation to rule out a sinister cause.

References

1. Lu Z, Qian F, Chen S, Yu G. Pulmonary hamartoma resembling multiple metastases: A case report. Oncol Lett. 2014;7(6):1885-1888. doi:10.3892/ol.2014.2043
2. Abu Omar M, Abu Ghanimeh M, Tylski E, Saettele T. Endobronchial hamartoma: a rare disease with more common presentation. BMJ Case Rep. 2016;2016:bcr2016216771. Published 2016 Nov 7. doi:10.1136/bcr-2016-216771
3. Raina N, Kaushal V, Pathania R, Rana A. Pulmonary hamartoma: Case report and brief review of literature. Clinical Cancer Investigation Journal. 2016;5(3):240. doi:https://doi.org/10.4103/2278-0513.182067
4. Hutter J, Reich-Weinberger S, Hutarew G, Stein HJ. Giant pulmonary hamartoma--a rare presentation of a common tumor. Ann Thorac Surg. 2006;82(2):e5-e7. doi:10.1016/j.athoracsur.2006.05.032
5. Itoga M, Kobayashi Y, Takeda M, et al. A case of pulmonary hamartoma showing rapid growth. Case Rep Med. 2013;2013:231652. doi:10.1155/2013/231652
6. E. Albrecht, "Ueber hamartome," Verhandlungen Der Deutschen Gesellschaft Für Pathologie, vol. 7, pp. 153–157, 1904.
7. Erdogu V, Emetli EY, Kutluk AC, et al. Does Pulmonary Hamartoma Increase the Risk of Lung Cancer? Outcomes of 38 Pulmonary Hamartoma Cases. Sisli Etfal Hastan Tip Bul. 2021;55(3):344-348. Published 2021 Sep 24. doi:10.14744/SEMB.2020.06936
8. Choi JC, Yu CM, Ryu YJ, et al. The role of endoscopic surgery for completely obstructive endobronchial benign tumor. Korean J Intern Med. 2006;21(1):15-19. doi:10.3904/kjim.2006.21.1.15
9. Schneider F, Winter H, Schwarz F, et al. Endobronchial lipomatous hamartoma: an incidental finding in a patient with atrial fibrillation-a case report. Case Rep Med. 2012;2012:897581. doi:10.1155/2012/897581
10. Fan M, Lin Y, Liu L. Multiple pulmonary chondroid hamartoma. J Thorac Oncol. 2014;9(7):1053-1054. doi:10.1097/JTO.0000000000000175
11. Nili M, Vidne BA, Avidor I, Paz R, Levy MJ. Multiple pulmonary hamartomas; a case report and review of the literature. Scand J Thorac Cardiovasc Surg. 1979;13(2):157-160. doi:10.3109/14017437909100984
12. 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(10):790-793. doi:10.1136/thx.42.10.790
13. Ulas AB, Aydin Y, Eroglu A. Pulmonary Hamartomas: A Single-Center Analysis of 59 Cases. Eurasian J Med. 2022;54(3):270-273. doi:10.5152/eurasianjmed.2022.21150
14. Esme H, Duran FM, Unlu Y. Surgical treatment and outcome of pulmonary hamartoma: a retrospective study of 10-year experience. Indian J Thorac Cardiovasc Surg. 2019;35(1):31-35. doi:10.1007/s12055-018-0728-x
15. Schwartz M. A biomathematical approach to clinical tumor growth. Cancer. 1961;14:1272-1294.
16. Melocchi L, Cavazza A, Sirolli M, et al. Pulmonary hamartoma: a clinic-pathologic study of 206 consecutive cases focusing on different histologic variants[J/CD]. Chinese Journal of Thoracic Surgery (Electronic Edition), 2022, 9(3): 133-139.
17. Sezer, H. F., Elicora, A., Abdullayev, G., & Topçu, S. Review of 30 pulmonary hamartoma cases: Follow-up and treatment. J Surgery Medicine;2021;5(t4):336-339.
18. Kaznowska E, Guz W, Ramotowski R, Kądziołka W, Kulig A. Histological and radiological diagnostics of the pulmonary hamartomas. Polish journal of radiology. 2007; 72(1): 36-43

19. Lundeen KS, Raj MS, Rajasurya V, et al. Pulmonary Hamartoma. [Updated 2023 Jul 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539806/
20. Ekinci GH, Hacıömeroğlu O, Ersev A, Alpay L, Özgen H, Yılmaz A. The frequency of lung cancer in patients with pulmonary hamartomas: An evaluation of clinical, radiological, and pathological features and follow-up data of 96 patients with pulmonary hamartomas. Rev Port Pneumol (2006). 2017;23(5):280-286. doi:10.1016/j.rppnen.2017.04.008
21. Karasik A, Modan M, Jacob CO, Lieberman Y. Increased risk of lung cancer in patients with chondromatous hamartoma. J Thorac Cardiovasc Surg. 1980;80:217–20
22. Haberal MA, Dikis OS, Erkan A. Pulmonary hamartoma: Retrospectiveanalysis of 24 cases. Dicle Tıp Dergisi 2019;46(1):27-32
23. Miura K, Hori T, Yoshizama K, et al. Cystic pulmonary hamartoma. Ann Thorac Surg 1990;49:828/9.
24. Basile A, Gregoris A, Antoci B, et al. Malignant change in a benign pulmonary hamartoma. Thorax 1989;44:232/3.
25. Poulsen JT, Jacobsen M, Francis D. Probable malignant transformation of a pulmonary hamartoma. Thorax 1979;34:557/8.
26. Guo W, Zhao YP, Jiang YG, Wang RW, Ma Z. Surgical treatment and outcome of pulmonary hamartoma: a retrospective study of 20-year experience. J Exp Clin Cancer Res. 2008;27(1):8. Published 2008 May 31. doi:10.1186/1756-9966-27-8