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**Title:** Diagnostic challenges in pulmonary hamartomas: a case series.
**Short title:** Diagnostic challenges in pulmonary hamartomas.

**Abstract**

Pulmonary hamartoma, although its benign nature, it can pose diagnostic challenges due to imaging findings that mimic malignancy. This case serie discusses the diagnostic and therapeutic difficulties in pulmonary hamartomas. These three cases which presented here were surgically managed under suspicion of malignancy and one case diagnosed as a typical carcinoid tumor postoperatively. The study retrospectively evaluated four cases referred for surgery due to suspected malignancy. The cases were analyzed in terms of radiological, surgical, and pathological findings. Three cases showed benign features but were operated on due to suspected malignancy and former history of malignancy were confirmed as hamartomas on pathology. One case, despite radiological features suggesting benignity, was identified as a typical carcinoid tumor postoperatively. Pulmonary hamartomas, despite their benign nature, can mimic malignancy and rarely undergo malignant transformation. Therefore, a multidisciplinary approach, surgical resection, and histopathological examination are essential for accurate diagnosis. Incorporating genetic analyses could enhance the diagnostic process further.

**Keywords:** Pulmonary hamartoma, malignancy, surgical resection, histopathology, multidisciplinary approach.

**Makale başlığı:** Pulmoner hamartomlarda tanısal zorluklar: vaka serisi.

**Kısa başlık:** Pulmoner hamartomlarda tanısal zorluklar.

**Öz**

Pulmoner hamartomlar, benign olmalarına rağmen maligniteyi taklit eden görüntüleme bulguları nedeniyle tanısal zorluklar yaratabilir. Bu çalışmada, malignite şüphesiyle cerrahiye alınan üç hamartom vakası ve cerrahi sonrası tipik karsinoid tümör tanısı alan bir vaka sunularak, pulmoner hamartomların tanı ve tedavisinde karşılaşılan güçlükler tartışılmıştır. Çalışma, malignite şüphesi nedeniyle cerrahiye yönlendirilen dört vakanın retrospektif olarak değerlendirilmesiyle gerçekleştirilmiştir. Vakalar radyolojik, cerrahi ve patolojik bulgular açısından incelenmiştir. Üç vaka, benign özellikler göstermesine rağmen malignite şüphesiyle opere edilmiş ve patoloji sonucunda hamartom olarak raporlanmıştır. Bir vaka ise, radyolojik olarak benign özellikler taşımasına rağmen cerrahi sonrası tipik karsinoid tümör olarak tanımlanmıştır. Pulmoner hamartomlar, benign görünümlerine rağmen maligniteyi taklit edebilir ve nadiren malign transformasyon gösterebilir. Bu nedenle, multidisipliner bir yaklaşım, cerrahi rezeksiyon ve histopatolojik inceleme, kesin tanı için vazgeçilmezdir. Genetik analizlerin eklenmesi, tanı sürecini daha kapsamlı hale getirebilir.

**Anahtar kelimeler**: Pulmoner hamartom, malignite, cerrahi rezeksiyon, histopatoloji, multidisipliner yaklaşım.

## Introduction

Pulmonary hamartomas are benign lesions that account for approximately 8% of lung tumors and represent 75-77% of this benign group [1, 2]. Although these lesions are often detected incidentally and rare malignant potential, they can pose significant diagnostic challenges by mimicking lung cancers, metastases, and tuberculosis in radiological imaging [3]. Imaging characteristics, particularly misleading parameters such as low FDG uptake values, may raise suspicions of malignancy [4].

The literature indicates that 91% of pulmonary hamartomas contain cartilaginous components and typically appear as well-defined nodules with clear borders [5]. However, in cases lacking lipomatous or calcified content, findings resembling malignancy or malignant transformation may be observed [6]. Consequently, a multidisciplinary approach and, when necessary, surgical intervention are critical for accurate diagnosis and management [7].

In this case serie the diagnostic and therapeutic challenges of pulmonary hamartomas was discussed through the presentation of three cases surgically managed under suspicion of malignancy and one case diagnosed postoperatively as a typical carcinoid tumor.

## Case presentations

### Case 1

A male patient with a prior diagnosis of rectal adenocarcinoma, aged 59, was referred to our clinic for evaluation due to findings in (Computed tomography) CT, which revealed a 16x13 mm nodular lesion in the right middle lobe (Figure 1). Radiological findings based on tomography and suspicous of metastasis; however positron emission tomography (PET) showed on no evidence of uptake. Consequently, right middle lobectomy was performed. Pathological examination identified the mass as a hamartoma. The patient remains under routine oncological follow-up.

### Case 2

A male patient with a prior diagnosis of osteosarcoma in the right maxilla, aged 62, underwent PET-CT follow-up. A subsolid nodule in the right lower lobe showed an increased FDG uptake (SUV max: 2.09) was revealed (Figure 2). Seconder malignancy or metastasis could not be excluded, a right lower lobe superior segmentectomy was performed. Pathology confirmed the diagnosis of chondroid hamartoma. The patient is under oncological follow-up.

**Case 3**

A male patient with a previous diagnosis of laryngeal cancer, aged 64, was referred to our clinic with PET-CT, which revealed a spiculated, hypermetabolic nodule in the left upper lobe. Follow-up CT demonstrated an increase in the solid component, prompting surgical intervention, no SUV uptake was detected (Figure 3). A left upper lobe wedge resection revealed a hamartoma on pathology. Additional findings included bronchiectasis and fibrotic changes.

**Case 4**

A 65-year-old male presented with a nodular lesion in right lower lobe with benign FDG enhancement on PET-CT (SUV max: 2.73). Due to its size, lobulated appearance and proximity to inferior pulmonary vein, a right lower lobectomy performed (Figure 4). Pathology identified the mass as a typical carcinoid tumor and cartigenous osseoz metaplasia seconder to bronchiectasis; surgical margins were reported as clear. The patient is under regular follow-up period.

**Discussion**

Pulmonary hamartomas, can mimic malignancy on radiological imaging despite their benign nature, as evidenced by our cases. For instance, in Case 1, a lesion suspicious for malignancy on PET-CT was ultimately diagnosed as a hamartoma pathologically. While low SUV values generally suggest benignity, these parameters alone are insufficient to exclude malignancy [4]. This highlights the critical role of a multidisciplinary approach and surgical evaluation in clarifying diagnoses. Lung nodule which was detected in patients especially who have prior history of malignancy, yields high suspicous for metastasis. Particularly lesions well shaped and round featured such as hamartoma may be interpreted seconder malignancy of lungs.

Case 4 underlines the rare but documented association between hamartomas and malignancy. In this case, a lesion considered as benign on imaging was diagnosed as a typical carcinoid tumor on pathological examination after lobectomy. Similar findings have been reported in the literature, where lesions resembling hamartomas were subsequently identified as malignant [3, 8, 9]. This emphasizes the importance of not to neglecting the potential for malignant transformation in hamartomas which may result a significant diagnostic and therapeutic errors. This patient's pathological findings reported as cartigenous osseoz metaplasia consistent with radiologic image characteristics which assumed hamartoma.

**1. Surgical approaches and clinical findings**

In our series, surgical resection was main choice of diagnosis and treatment modality. In Case 2, a subsolid nodule suspected of malignancy on PET-CT necessitated a segmentectomy, leading to a diagnosis of chondroid hamartoma. Segmentectomy is a valuable surgical technique for achieving complete resection and also diagnostic procedure while preserving lung function. VATS-based segmentectomies, in particular, are associated with lower complication rates and shorter recovery times [10]. Similarly, in Case 3, wedge resection provided both diagnostic clarity and symptomatic relief.

**2. Radiological and pathological evaluation**

Hamartomas are typically characterized by benign features such as calcification, fat content, and well-defined borders. However, these findings can sometimes resemble malignancy [2]. In Case 3, for instance, a spiculated, hypermetabolic nodule was initially interpreted as metastatic, yet pathology confirmed it as a hamartoma. This aligns with literature emphasizing that, despite their benign features, hamartomas have the potential to mimic malignancy [5]. On PET-CT, hamartomas typically show minimal or no FDG uptake, supporting their benign nature [11].

**3. Molecular and genetic insights**

Understanding the genetic basis of pulmonary hamartomas is essential for evaluating malignancy risk. Mutations in the HMGA2 gene are implicated in hamartoma pathogenesis and may indicate malignant transformation risk [1]. However, genetic analyses were not performed in our cases, highlighting a potential area for further evaluation.

**4. Importance of a multidisciplinary approach**

All cases in our series underlines the value of multidisciplinary approach. Cases were assessed by a thoracic oncology council before surgery, demonstrating the pivotal role of collaborative evaluation in achieving accurate diagnoses emphasize the importance of multidisciplinary assessment and surgical intervention for pulmonary lesions with suspected malignancy [9].

In conclusion, this case series illustrates that pulmonary hamartomas, despite their benign nature, can mimic malignancy and, in rare instances, undergo malignant transformation. Patients who have lung nodules with a history of prior malignancy or new diagnosed lung cancer undergo a challenging process to discriminate benign or malign. Our findings highlight the critical role of multidisciplinary approaches and surgical pathology in the diagnostic and therapeutic process. In such cases, reliance solely on radiological findings is insufficient; surgical resection and histopathological examination

remain indispensable. Additionally, integrating genetic analyses could provide a more comprehensive understanding of these lesions.

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**Author contributions:** A.K. have constructed/constructed the main idea and hypothesis of the study. A.K., E.Z. They developed the theory and arranged/edited the material and method section. G.Ö. has/have done the evaluation of the data in the Results section. Discussion section of the article. Written by E.Z., Ü.A. reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.

**Conflict of interest:** No conflict of interest was declared by the authors.

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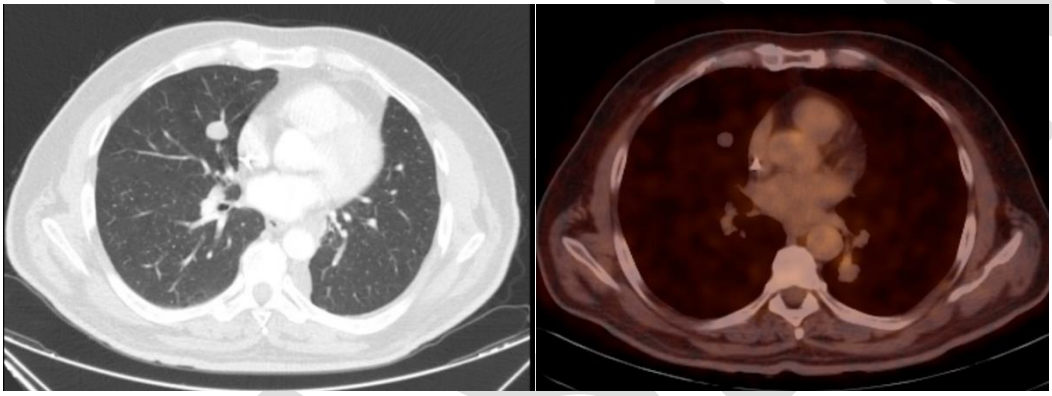

**Figure 1.** CT and PET-CT fusion images showing a nodular lesion in the right middle lobe

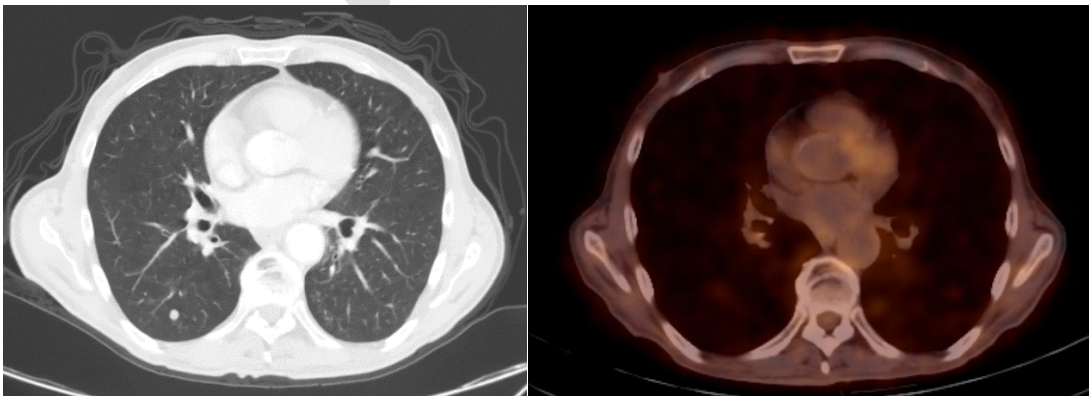

**Figure 2.** CT and PET-CT fusion images of a subsold nodule in the right lower lobe

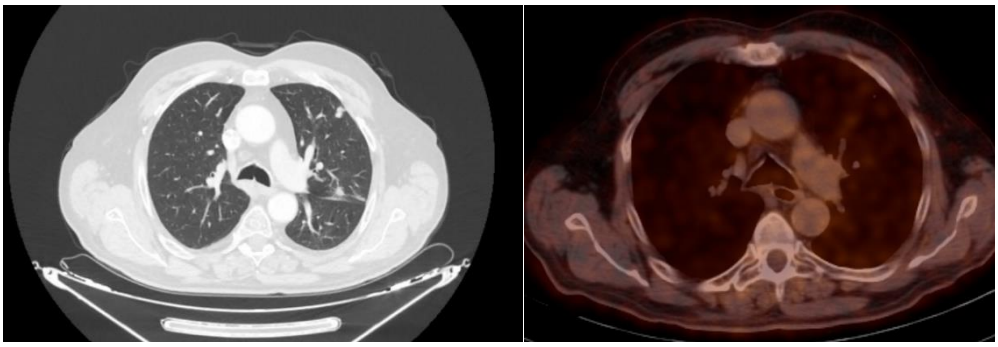

**Figure 3.** CT and PET-CT fusion images demonstrating a lobulated mass in the left upper lobe

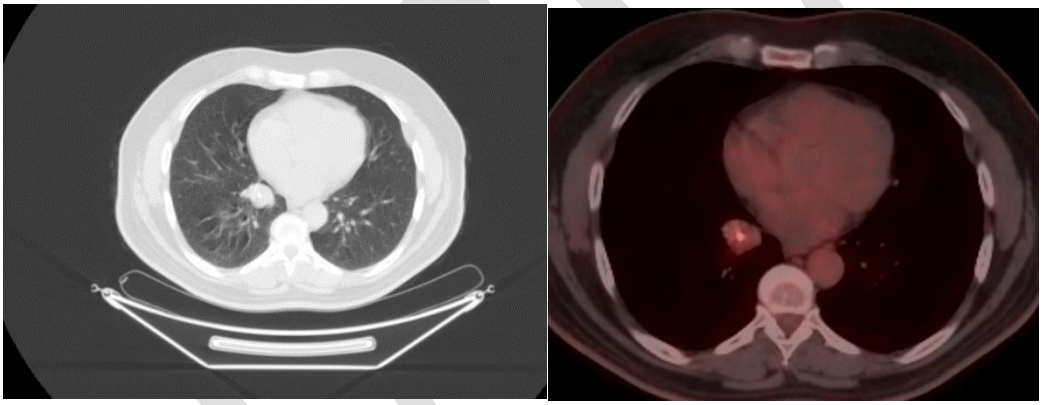

**Figure 4.** PET – CT scan showing a nodular lesion in the right lower lobe

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