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CASE REPORT

Extremely Rare Coexistence of Peripherally Located Mucous Gland Adenoma and Pulmonary Chondroid Hamartoma

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Abstract

Pulmonary mucous gland adenomas (MGAs) originating in mucous-secreting cells in the bronchi are extremely rare benign tumours. Pulmonary chondroid hamartomas (PCHs) are the most common benign neoplasms of mesenchymal origin of the lung. This study reports an unusual case where MGA and PCH coexisted in a peripheral intra-parenchymal location. A patient with a 1-cm non-specific nodule in the left lung on a computed tomography scan underwent wedge resection. Microscopically, mesenchymal elements consisting of fat and cartilage tissue were observed. Mucous glands were present around these mesenchymal elements. No cellular atypia or mitosis was observed. This allowed for complete treatment without the need for a segmentectomy.

Key words: adenoma; hamartoma; lung; mucous gland

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Introduction

Mucous gland adenoma (MGA) is defined as a benign salivary gland-type tumour thought to arise from the seromucous submucosal lining glands of the bronchus (Zhang et al, 2018). An MGA is usually located as an intraluminal exophytic mass in the proximal airways and presents with obstructive symptoms or nonspecific symptoms, whereas there are no specific symptoms, especially for peripherally located MGAs, and they are detected incidentally (Zaleski et al, 2020; Zhang et al, 2018). To the best of our knowledge, only a few studies in the literature have reported that MGAs are located in the periphery of the lung (Sasaki et al, 2023; Zhang et al, 2018).

Pulmonary chondroid hamartomas (PCHs) are the most common benign tumours of the lung composed of mesenchymal components such as bone, cartilage, fat, and smooth muscle (Yamada et al, 2018). Although PCHs are endobronchial in 1%–8% of cases, they are usually intraparenchymal, asymptomatic, and often detected incidentally (Yamada et al, 2018; Zhang et al, 2018). However, considering all lung lesions, their incidence is reported as 0.025%–0.32% (Ahn et al, 2023).

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The present study reports an association of MGA presenting as a single nodule simultaneously with chondroid and adipose tissue predominant pulmonary hamartoma. In addition to histomorphological and immunohistochemical findings of this rare association, the study also discusses the points to be considered in the differential diagnosis.

Methods

For routine follow-up, samples were fixed with formaldehyde solution (LOT: 100724, Facepath, İzmir, Turkiye). They were then embedded in paraffin blocks and 4 mm thick sections were taken on slides. Paraffin was removed from slides using xylene (LOT: 1811230132, Biorad, Istanbul, Turkiye) and rehydrated using alcohol (Absolute Ethanol >99.5%, LOT: 1203240059, Biorad, Istanbul, Turkiye). The sections were stained with Haematoxylin (LOT: ZC200802 403, Merck KGaA, Darmstadt, Germany) and Eosin (LOT: FN1317035 623, Merck KGaA, Darmstadt, Germany) (H&E) stain for histological evaluation. The slides were also administered histochemical staining using Mucicarmine Mayer's (LOT: 052023.085, Histo-Med, Ankara, Turkiye). Immunohistochemistry was performed with antibodies to thyroid transcription factor-1 (TTF-1) (anti-thyroid transcription factor-1, 8G7G3/1, Mouse Monoclonal Primary Antibody, LOT: K20218, Ventana, Switzerland) and Napsin A (MRQ-60, Mouse Monoclonal Primary Antibody, LOT: V0 004015, Cell Marque, Los Angeles, CA, USA) using diaminobenzidine substrate (Ultraview Universal DAB detection kit, LOT: K20488, Ventana, Switzerland).

Case Report

Clinical History

A 61-year-old male patient with no previous complaints, no known disease, and no history of drug use had been complaining of chest pain for the last two months. The patient had a history of appendectomy 3 years ago. The patient's vital signs were stable. In the physical examination, no findings were detected by inspection, palpation, percussion, and auscultation in the thorax examination. No additional findings were detected in the head-neck, heart, abdomen, genitourinary, and extremity examinations. The patient's history, vital signs, and physical examination findings are shown in Table 1. The haemogram and biochemistry results of laboratory tests are within normal limits (Table 2).

Radiological Findings

After observing a radio-opaque lesion of approximately 1 cm in diameter located in the left lung on the posteroanterior (PA) chest radiography (Fig. 1A) mimicking lung cancer, a chest computed tomography (CT) was performed. Subsequently, a smooth-edge, homogenous, non-specific nodule with a diameter of 1 cm was observed in the chest CT (Fig. 1B), located in the superior part of the left lower lobe of the lung.

Table 1. Baseline information of the patient.

Items	Specific contents
Age	61
Sex	Male
Presenting medical problem	Chest pain
Vital signs	
Blood pressure (systolic/diastolic)	110/62
Pulse (beats per min)	75
Body temperature (axillary, C)	36.8
History of significant medical problems	Appendectomy (3 years ago)
Physical examination	
Head and neck	Normal appearance
Thorax and lungs	Inspection: bilateral hemithorax participates equally in respiration Palpation: no tenderness, no crepitation Percussion: bilateral sinuses open Auscultation: respiratory sounds bilaterally equal
Heart	S1+, S2+, ejection fraction: 55%, no additional sounds and murmurs, heart rate: 75/min
Abdomen	Normal
Genito-urinary system	Normal
Extremities	Normal

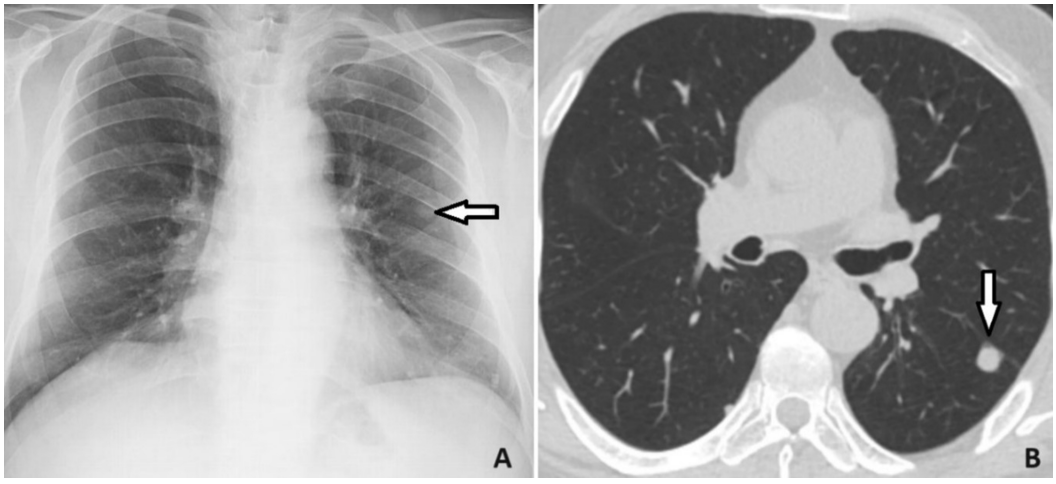

Fig. 1. Radiological findings of the patient. On posteroanterior chest radiography, a homogeneous radio-opaque lesion (white arrow) with smooth margins in the left lung (A). On chest computed tomography, a 1 cm diameter, smooth-edged, homogeneous, soft tissue nodule (white arrow) in the left lower lobe of the lung (B).

Histological Findings

The patient was operated on with these findings for diagnostic and treatment purposes. A left thoracotomy was performed, and the nodule was removed with

Table 2. Laboratory blood panel.

Investigation	Results	Reference range
AST	16.3	0–35 (U/L)
ALT	15.3	0–35 (U/L)
Creatinine	1.02	0.55–1.02 (mg/dL)
Glucose	100.5	74–106 (mg/dL)
Na	142	136–145 (mmol/L)
K	4.27	3.5–5.1 (mmol/L)
Ca	9.3	8.8–10.6 (mg/dL)
TSH	1.44	0.38–5.60 (μIU/mL)
Hb	13.8	11.9–16.3 (g/dL)
Total WCC	6.15	3.9–10.8 (10^3 μL)
Plt	228	145–345 (10^3 μL)

AST, Acetyl Transaminase; ALT, Alanine Transaminase; TSH, Thyroid Stimulating Hormone; Hb, Haemoglobin; WCC, White Cell Count; Plt, Platelet count.

wedge resection for intra-operative consultation. In the gross examination of the removed material, intraparenchymal located, 1 × 0.9 × 0.9 cm grey to white, hard-grained structures without areas of necrosis and haemorrhage were observed. In an intraoperative histopathological examination, hyaline cartilage lined with epithelium without inflammation or atypia on a loose myxoid base was observed. In addition, another lesion was observed with glandular structures formed by columnar cells containing apical intracytoplasmic mucin. No malignancy was detected. Based on these findings, the study reported the intraoperative examination results as a mesenchymal lesion, pulmonary hamartoma, and pulmonary adenoma. A segmentectomy was not performed for this result.

Routine formalin fixation steps were applied to the tissue. Microscopically, fragments of cartilaginous tissue, foci of mature adipose tissue, and hyalinize stroma were the areas where the hamartomas were observed (Fig. 2A,B). In the area of the adenomas, the tumour was composed of abundant mucus-filled cystic areas and mucous glands. These glands were lined with a single layer of tall columnar epithelium and cells with basally located nuclei and mucus-filled cytoplasm (Fig. 2C). There was no cellular atypia or mitotic activity. Although numerous sections were examined, no bronchial origin was detected.

Immunohistochemical and Histochemical Staining

The majority of the observed lumens of glands contained mucus positive for histochemical mucin stain (Fig. 2D). An immunohistochemical analysis for Napsin A and TTF-1 remained unreactive for the mucous glands but positive for the overlying epithelium (Fig. 2E,F).

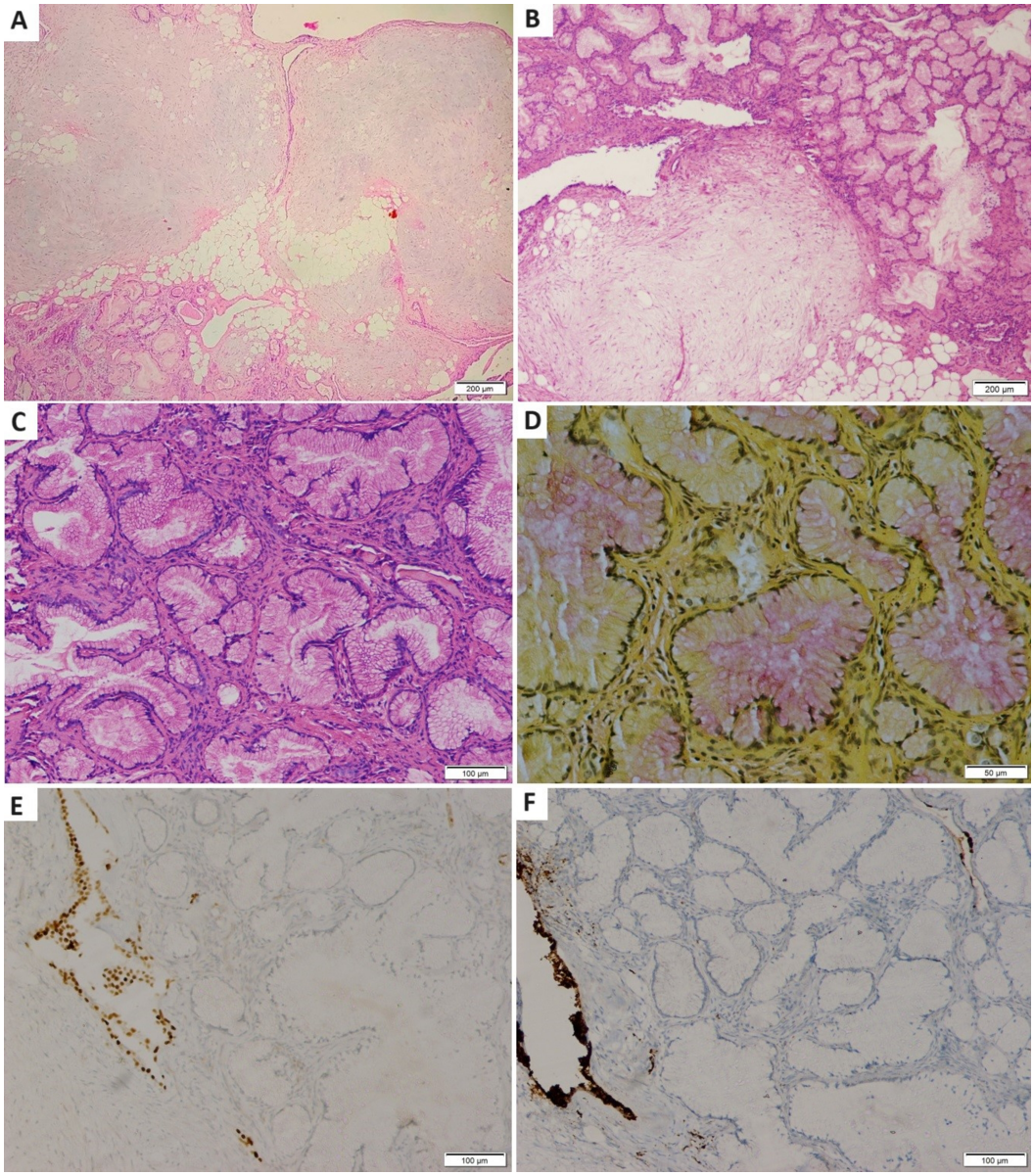

Fig. 2. Histochemical and immunohistochemical findings of the case. Pulmonary chondroid hamartoma: Histologic section demonstrating predominantly hyaline cartilage admixed with amounts of adipocytes (A). Mucous gland adenoma consisting of mucous glands around cartilaginous tissue, some of which contain mucin in the lumen (B). Histologic section of mucous gland adenoma, which consists of single-layered columnar cells and basally sited nucleus (Haematoxylin and Eosin (H&E) stain) (C). Histochemistry demonstrating positivity for mucin (D). Immunohistochemistry staining demonstrating negativity for thyroid transcription factor-1 (TTF-1) (E) and Napsin A (F) in mucous glands and positivity in the surrounding parenchyma.

Follow-up after Operation

The patient's postoperative vital signs were stable. The patient was followed up with daily posteroanterior (PA) chest radiographs for 7 days of hospitalization and no complications were observed. On the 15th day, the patient was called for a follow-up and no additional findings were found on physical examination and PA chest radiography (Fig. 3). With the current diagnosis, the patient achieved full

recovery without the need for additional treatment. The patient has been living for 12 months without any complaints.

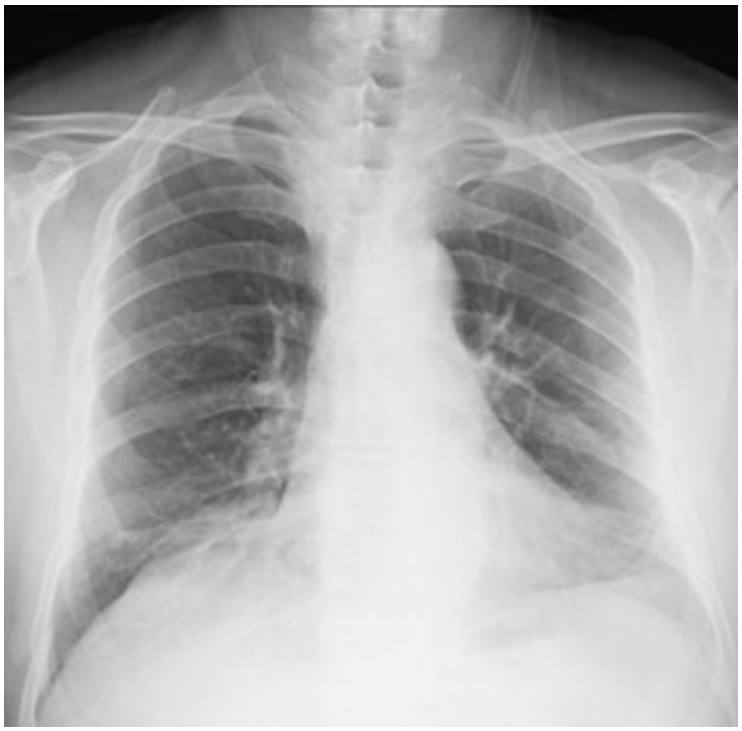

Fig. 3. Post-operative radiological image of the patient. A posteroanterior (PA) chest radiograph taken on the 15th post-operative day showing no nodular lesion.

Discussion

The coexistence of MGA and PCH is very rare in the literature and there is a report of MGA with cartilage islands (Lee et al, 2014). However, there is no definition of the cartilaginous component of MGA in the literature and there is no glandular component in PCH (Lee et al, 2014). These data suggest that these two lesions are two different entities. This study evaluated both lesions separately with their own differential diagnoses.

The most critical point in peripherally located lung nodules is to determine whether this nodule is benign or malignant (Komatsu et al, 2022). Adenocarcinoma and low-grade mucoepidermoid carcinomas (MEC) should be included in the differential diagnosis of MGA, which should be excluded by looking for the presence/absence of atypia, necrosis, mitosis, and infiltration (Uluşan et al, 2018). MEC contains squamous cells and intermediate oval cells in addition to mucus-secreting cells (Karpathiou et al, 2013). Some benign lesions such as papillary adenoma, alveolar cell adenoma, and mucinous cystadenoma must be excluded. However, papillary adenoma consists of a fibrovascular core lined by columnar or cuboidal cells positive for TTF-1 (Karpathiou et al, 2013). Alveolar adenoma contains cyst-like spaces lined by cuboidal cells also positive for TTF-1 (Karpathiou

et al, 2013). In addition, mucinous cystadenoma has true-mucin-filled cysts with variable immunoreactivity of TTF-1 (Karpathiou et al, 2013).

In an immunohistochemical study, TTF-1 was negative in the MGA areas while it demonstrated strong positive staining in the lung parenchyma (Karpathiou et al, 2013). In the present study, TTF-1 and Napsin A were negative in the MGA area.

PCHs are slow-growing tumours considered benign neoplasms (Prasad et al, 2023). Malignant transformation of PCH also exists, which has been reported as sarcoma, carcinoma, and adenocarcinoma (Prasad et al, 2023). PCHs consist of at least two mesenchymal components such as cartilage, bone, fat, and smooth muscle (Prasad et al, 2023). Thus, they are distinguishable from chondroma and lipoma (Prasad et al, 2023). PCHs are detected incidentally during radiological examinations performed for other indications (Ahn et al, 2023). Pulmonary hamartomas very slowly continue to increase in size and rarely cause significant morbidity (Wick, 2019).

Conclusion

Peripherally located MGA can be differentiated from malignant entities with the absence of mitosis, atypia, and necrosis. Careful histomorphological evaluation should be performed in the differential diagnosis to avoid confusion with benign cystic lesions as well as adenomatous lesions or hamartoma. Immunohistochemical markers such as negative TTF-1 and Napsin A in the lesion area may be used to support histomorphological findings.

In conclusion, in addition to the rarity of peripherally localized MGA, the association of MGA and PCH is quite rare and further investigations are needed.

Key Points

- In addition to the extreme rarity of peripherally localized mucous gland adenoma, here, this study described an unusual case of intraparenchymal localized MGA and pulmonary chondroid hamartoma coexisting in the periphery of the lung, of which there are few cases in the literature.
- MGA and PCH can be seen together as a single nodule on both radiologic imaging and macroscopic examination of the resection material.
- It is important to be aware that bronchial mucous glands may also be localized in the periphery of the lung.
- MGA may be confused with adenocarcinoma and low-grade mucoepidermoid lesions, especially in intraoperative consultation sections.
- It should be noted that immunohistochemically TTF-1 and Napsin A are negative in the MGA area. Additional studies are needed for a more detailed immune profile of MGA.

Availability of Data and Materials

All the data of this study are included in this article.

Author Contributions

SÖ, FD, HDT, AK and YA designed the structure of the study. SÖ, FD, and HDT performed the literature research, drafted the manuscript, and revised it for publication. AK and YA provided support with radiological and clinical information. All authors were involved in critical revisions of the paper and contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The procedures are in accordance with the Helsinki Declaration. The patient signed an informed consent form to publish this case report.

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Conflict of Interest

The authors declare no conflict of interest.

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