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Coexistence of Pulmonary Langerhans Cell Histiocytosis and Bronchial Carcinoid Tumor in Systemic Lupus Erythematosus: Coincidence or Autoimmune Association?

Sara Ibrahim Al Hamal[1], Mustafa Al Nasser[1], Zahra Zaki Al Zahir[2*]

[1]Department of Internal Medicine, Qatif Central Hospital, Qatif, Saudi Arabia
[2]Department of Rheumatology, University of Toronto, Toronto, ON, Canada
Email: *dr.zahrazz@gmail.com

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Abstract

Background: Pulmonary Langerhans cell histiocytosis (PLCH) and bronchial carcinoid tumors are both rare pulmonary neoplasms. Their coexistence in patients with systemic lupus erythematosus (SLE) has not been previously reported. Chronic autoimmune-mediated inflammation in SLE may contribute to pulmonary neoplasia. **Case Presentation:** We report a 39-year-old male active smoker with a 23-year history of SLE, who presented with respiratory symptoms. Chest imaging revealed diffuse cystic and nodular lesions with upper lobe predominance, consistent with PLCH, and an endobronchial mass in the right lower lobe. Bronchoscopy confirmed a well-circumscribed lesion, and histopathology established the diagnosis of a bronchial carcinoid tumor. The patient was treated with Video-assisted thoracoscopic (VAT) lobectomy of a bronchial carcinoid tumor, prednisone, hydroxychloroquine, inhaled bronchodilators, and supportive care, in conjunction with smoking cessation counseling. At the 12-month follow-up, there was no recurrence of the tumor. **Conclusion:** This case highlights a rare coexistence of PLCH and bronchial carcinoid tumor in SLE. While the association may be coincidental, chronic autoimmune inflammation and smoking may contribute to pulmonary neoplasia. SLE patients presenting with respiratory symptoms warrant a comprehensive pulmonary evaluation and long-term surveillance to identify potential overlapping pathologies and guide optimal management.

Keywords

Systemic Lupus Erythematous, Langerhans Cell Histiocytosis, Bronchial Carcinoid Tumor

1. Introduction

Patients with systemic lupus erythematosus (SLE) have altered malignancy risks, with increased incidence of lung cancer, lymphoma, and other malignancies, partly due to smoking and immune dysregulation [1]-[4]. Endobronchial carcinoid tumors are rare, accounting for less than 5% of bronchopulmonary tumors, with typical carcinoids comprising 80% - 90% of the cases [5].

Pulmonary Langerhans cell histiocytosis (PLCH) is an uncommon adult lung disease, most frequently seen in young smokers, and may present with cough, dyspnea, or constitutional symptoms [6]. Moreover, pneumothorax accounts for 10% - 20% of PLCH cases, particularly in young males [6].

The coexistence of SLE, PLCH, and carcinoid tumor may share overlapping pathogenic pathways. Chronic inflammation in SLE and MAPK mutation in PLCH (BRAF and V600E), along with smoking, promote clonal proliferation and tumorigenesis [7]-[11]. Shared NF-κB, STAT3, and MAPK signaling may explain their rare coexistence.

2. Case Presentation

We report a 39-year-old male active smoker who presented with a chronic productive cough, worsening dyspnea with minimal effort, and pleuritic chest pain exacerbated by deep inspiration. He denied hemoptysis, wheezing, fever, night sweats, weight loss, recent travel, or contact with people with tuberculosis.

He was diagnosed with Systemic Lupus Erythematosus (SLE) at the age of 16 years old, initially presenting with constitutional symptoms, joint pain, and renal involvement. The laboratory showed positive Anti-Nuclear Antibodies (ANA), elevated anti-ds DNA titer, and low complement levels, while a renal biopsy confirmed class I lupus nephritis. Although the patient's serology showed elevated anti-ds DNA and hypocomplementemia, his most recent serological results showed normal anti-ds DNA and normal complement, consistent with low disease activity-remission at the time of presentation. His SLE course was characterized by intermittent mild flares, manifesting primarily as arthralgia and transient fatigue, without major organ involvement. These episodes were managed with a short course of corticosteroid, in addition to his baseline hydroxychloroquine 200 mg twice daily, without escalation to immunosuppressive therapy. Additional history included a pneumothorax secondary to a stab wound and a rib fracture following a fall from height.

On examination, he was a young male, alert, oriented, not cachectic, with no cyanosis or acute distress. Vital signs revealed a heart rate of 95 beats per minute, blood pressure 132/80 mm Hg, temperature 37.5˚C, and respiratory rate of 19 breaths per minute. He appeared mildly pale, with no alopecia, malar rash, oral or nasal ulcers, or peripheral edema. Chest examination showed normal chest shape, decreased chest expansion with scattered fine crackles, no wheezes, or decreased breath sounds. Normal heart sounds, no murmur or signs of heart failure were noted. The abdomen was soft, lax, with no tenderness or organomegaly. No skin

lesions or telangiectasia were observed. Joint examination showed preserved full range of motion, with no swelling, tenderness, or deformities. No digital clubbing or hypertrophic osteoarthropathy was present. No palpable cervical, axillary, or inguinal lymphadenopathy was detected.

Laboratory results showed no peripheral eosinophilia, relative lymphopenia, and a mild elevation in ESR (Table 1). The autoimmune profile showed fine speckled, nuclear positive ANA. Normal anti-dsDNA and complements.

Table 1. Laboratory investigations.

	Reference Rang	Patient Investigation
WBC	(4 - 10) × 10^3/uL	9.08
HBG	(13 - 17) g/dL	4.86
HCT	49% - 54%	14.7
MCV	(78 - 96) fL	46.9
MCH	(27–32) PG	99.1
MCHC	(31.5 - 34.5) g/dL	30.5
RDW	11.6% - 14%	30.8
Platelet Count	(150 - 340) × 10^3/uL	285
Neut %	40% - 70%	75.7
Lymp %	20% - 45%	15.1
Mono %	2% - 10%	6.63
Eso %	1% - 6%	1.12
Baso %	0% - 2%	0.97
Bilirubin (Total)	(0 - 1.2) mg/dL	12.32
Bilirubin (Conjugated)	(0 - 0.3) mg/dL	3.36
ALT	(30 - 65) U/L	19.2
AST	(15 - 37) U/L	14.3
LDH	(81 - 230) U/L	234
Glucose Fasting	(3.89 - 6.11) mmol/L	5.14
Creatinine	(53 - 106) umol/L	71
PT	(11.5 - 15.5) sec	15.2
INR	(0.85 - 1.15) N	1.13
PTT		30.5
CRP	0 - 5	0.61
ESR		46.6

Continued

ANA		Positive, fine speckled, nuclear +2
Anti-ds-DNA (IFA) and (ELISA)		Negative
C4	90 - 180 mg/dL	92.3
C3	10 - 40 mg/dL	11.1
Anti-RNP	0	Negative
Anti-SM	0	Negative
Anti-SSA (RO)	0	Negative
Anti-SSB (LA)	0	Negative
Beta2-Glycoprotein 1 IgG		Negative
Anti-Cardiolipin IgG and IgM		Negative
Microalbumin in Urine	(1.3 - 100)	1.27
Urine Creatinine	(2652 - 110,50) umol/l	8923
Albumin-Creatinine Ratio (ACR)	(0 - 2.9) m/mmol	0.14
Urine Analysis	Negative for protein, blood, and RBC casts	
CK	(39 - 308) U/L	896
CK-MB	(7 - 25) U/L	39

The chest X-ray showed reticulonodular and cystic-like changes in the upper and mid lung fields, with the hilum and mediastinum widened, corresponding with a bronchial carcinoid tumor (Figure 1).

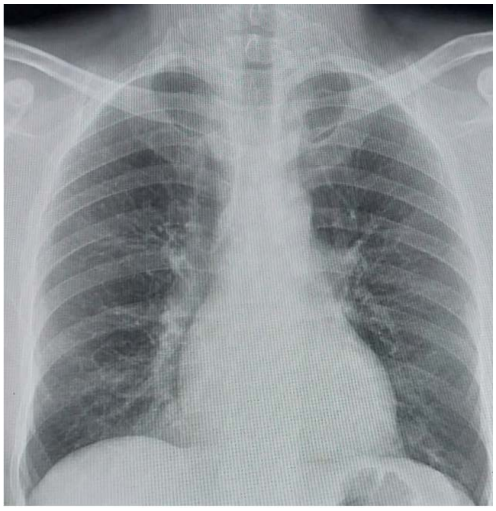

Figure 1. CXR showed reticulonodular and cystic-like changes in the upper and mid lung fields, with the hilum and mediastinum widened, corresponding with a bronchial carcinoid tumor.

A 12-lead ECG and echocardiogram showed normal sinus rhythm and normal ejection fraction.

The chest CT showed a small pericardial effusion. There was diffuse bronchial wall thickening suggestive of airway disease. Moderate centrilobular emphysema was noted. Multiple bilateral pulmonary nodules were identified, with the exception of 4 mm nodules in the left lower lobe. The lung parenchyma demonstrated diffuse micronodules and irregularly shaped cysts of variable sizes. There is an endobronchial/central enhancing mass in the right lower bronchus consisting of a bronchial carcinoid tumor. These findings, with a characteristic upper lobe predominance and sparing of the costophrenic angles, are consistent with pulmonary Langerhans's Cell Histiocytosis (Figure 2).

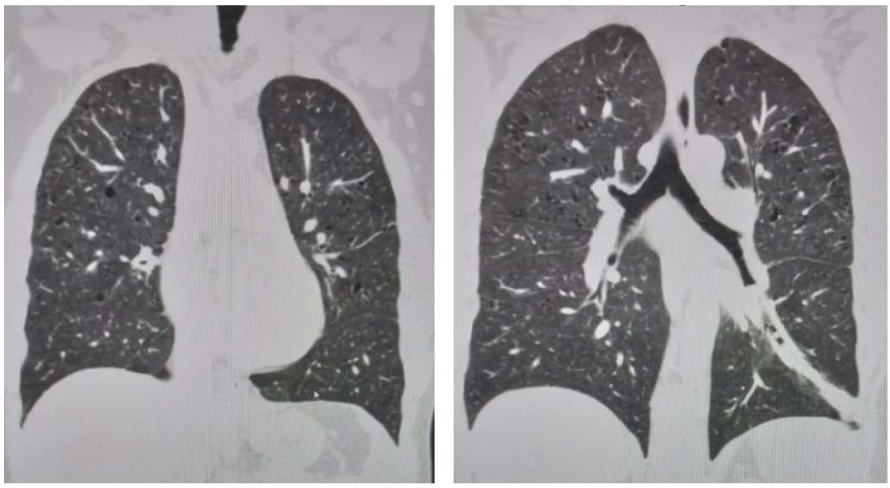

Figure 2. Chest CT showed multiple cystic changes and nodular lesions predominantly in the upper and mid lung zones. There is an endobronchial/central enhancing mass in the right lower bronchus consistent with a bronchial carcinoid tumor.

Bronchoscopy revealed a well-defined endobronchial lesion at the roof of the basal segments, between the anterior and lateral segments.

Biopsy of the pulmonary lesion confirmed the diagnosis of a pulmonary carcinoid tumor on histopathology.

Pulmonary function tests demonstrated a normal FEV1/FVC ratio. Both FVC and FEV1 were slightly reduced but remained within normal limits (>80% predicted). Maximum voluntary ventilation (MVV) was reduced to 80%, possibly reflecting suboptimal effort or mild respiratory muscle weakness. Peak expiratory flow (PEF) was slightly reduced at 84%, likely effort-dependent. The flow-volume loop appeared normal. Overall, there was no clear evidence of obstructive or restrictive lung disease; however, only mild restriction or submaximal effort was suggested.

The patient was commenced on prednisone 5 mg once daily, hydroxychloroquine 200 mg twice daily (weight-based dose), salbutamol (2 puffs twice daily), and Relvar (1 puff at night), as well as calcium and Vitamin D3 supplementation.

Smoking cessation was discussed with the patient, and annual prophylactic influenza and pneumococcal vaccinations were advised.

On the follow-up visits, no tumor recurrence was detected on annual serial chest CT, and his lupus disease activity remained well controlled on stable doses of prednisone 5 mg daily, hydroxychloroquine 200 mg twice daily, and as-needed salbutamol.

3. Discussion and Conclusions

Patients with SLE are associated with altered incidences of certain malignancies compared with the general population. Many studies have shown an increased risk of non-Hodgkin lymphoma, lung, liver, vaginal, and thyroid malignancies, whereas a decreased risk of breast and prostate cancer has been reported [1]. Among these, lung cancer has a notably higher incidence in SLE. The greatest increase in risk has been observed for small cell lung cancer, followed by squamous cell carcinoma, large cell carcinoma, and adenocarcinoma [1] [3] [4]. This association may be explained by the higher prevalence of smoking among SLE patients, as well as the link between smoking, increased disease activity, and malignancy risk in the SLE population [1] [2].

Although lung cancer is more frequently encountered in SLE patients, endobronchial carcinoid tumors remain rare [5]. Bronchial carcinomas are uncommon neuroendocrine tumors, accounting for less than 5% of all bronchopulmonary tumors [5]. The most common primary endobronchial neoplasm is the typical carcinoid, which accounts for 80% - 90% of pulmonary carcinoid tumors [5]. Surgical resection remains the standard and definitive management for these tumors.

Pulmonary Langerhans cell histiocytosis (PLCH) is another rare entity in adults, and precise epidemiological data remain limited. In a large series of patients undergoing open lung biopsy for interstitial lung disease of unknown origin, less than 5% were diagnosed with pulmonary LCH [6]. The disease may be underdiagnosed, as it can be asymptomatic, may spontaneously remit in a subset of patients, and can be difficult to confirm histologically in advanced stages. With the increasing use of high-resolution CT (HRCT), more cases are now being diagnosed [6].

PLCH can affect patients across a wide age range, but occurs most commonly in young adults, with peak incidence between 20 and 40 years [6]. Some studies have reported a male predominance, while other studies have shown a nearly equal sex distribution, with a later onset in females. These differences likely reflect variations in smoking habits [6], since 90% - 100% of pulmonary LCH cases are associated with cigarette smoking. Clinically, approximately two-thirds of patients present with respiratory symptoms, most commonly persistent dry cough and exertional dyspnea. Constitutional symptoms such as fever, weight loss, or night sweats may also occur. Chest pain, when present, is usually related to pneumothorax caused by rupture of subpleural cystic lesions. This complication is observed in 10% - 20% of cases. Pneumothorax occurs at any stage of the disease, can be recurrent or bilateral, and is particularly frequent in young male patients

[6].

The coexistence of SLE, PLCH, and subsequent neoplasia may reflect overlapping pathophysiological pathways. Chronic immune activation in SLE creates a proinflammatory pathway driven by type I interferon, TNF-*α*, IL-6, and IL-17 that can promote both dendritic/Langerhans cell proliferation and tumorigenesis [7] [8]. In PLCH, recurrent MAPK pathway mutations (such as BRA, V600E) highlight the transition from reactive inflammation to clonal neoplasm [9] [10], while environmental triggers such as cigarette smoking and long-term immunosuppressive therapy in SLE further enhance the risk [11]. Shared pathways, including NF-*κ*B, STAT3, and MAPK signaling, thus provide a link that may explain the rare coexistence of autoimmunity and malignancy in the same patient.

Our case report described an unusual presentation of bronchial carcinoid tumor and pulmonary Langerhans cell histiocytosis in a young male with SLE. The patient was managed with Video-assisted thoracoscopic (VAT) lobectomy of a bronchial carcinoid tumor, along with supportive care, bronchodilator, and smoking cessation counseling. During follow-up visits, annual chest CT showed no evidence of tumor recurrence, and his SLE remained well controlled. The patient continued to smoke despite receiving counseling on smoking cessation.

To our knowledge, this rare coexistence of PLCH and bronchial carcinoid tumor in SLE has not previously been reported in the literature. A potential mechanism increasing the risk of carcinoid tumors in autoimmune disease is plausible but requires validation through well-designed studies.

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Authors' Contributions

All authors contributed equally to the manuscript.

Ethical Approval and Consent

Informed consent was obtained from the patient.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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