EJCRIM
European Journal
of Case Reports
in Internal Medicine

RESPIRATORY-PREDOMINANT RELAPSING POLYCHONDRITIS: THE ROLE OF PET SCAN IN MAKING THIS CHALLENGING DIAGNOSIS

Daniela Alves, João Fonseca, Miguel Martins, Valter Duarte, Gisela Gonçalves, Pedro Lopes

Department of Internal Medicine, Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal

Corresponding author's e-mail: dralves94@gmail.com

Received: 16/07/2025
Accepted: 04/08/2025
Published: 08/09/2025

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: Written informed consent was obtained from the patient to publish his clinical history.
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How to cite this article: Alves D, Fonseca J, Martins M, Duarte V, Gonçalves G, Lopes P. Respiratory-predominant relapsing polychondritis: the role of PET scan in making this challenging diagnosis. *EJCRIM* 2025;**12**:doi:10.12890/2025_005677

ABSTRACT

Relapsing polychondritis is a rare, immune-mediated, multisystemic disease characterized by recurrent inflammation of cartilaginous and proteoglycan-rich tissues. Its diagnosis may be challenging due to its rarity and wide clinical variability. It can be primary or associated with other autoimmune conditions. Recently, it has been associated with an autoinflammatory disease known as vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic syndrome. We present a case of a 65-year-old man with respiratory-predominant relapsing polychondritis. This case illustrates the diagnostic complexity of relapsing polychondritis, where multiple initial investigations were inconclusive. We highlight the pivotal role of the fluorine-18 fluorodeoxyglucose positron emission tomography scan, which provided the key evidence of cartilaginous inflammation, ultimately guiding the diagnosis in this atypical presentation.

KEYWORDS

Myelodysplasia, autoinflammatory disease, VEXAS syndrome, respiratory-predominant, relapsing polychondritis

LEARNING POINTS

- Atypical presentations of relapsing polychondritis may present with isolated respiratory symptoms and constitutional signs in the absence of auricular or nasal chondritis.
- In older male patients with relapsing polychondritis features and myelodysplastic syndromes, vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic syndrome must be considered, requiring detection of somatic ubiquitin-like modifier-activating enzyme 1 gene mutations.
- When histopathology is unavailable, positron emission tomography imaging and clinical criteria are key to diagnosis.

INTRODUCTION

Relapsing polychondritis (RP) is a rare, chronic, immune-mediated disease primarily affecting cartilaginous structures such as the ears, nose, joints and the respiratory tract. The disease is marked by episodic and progressive cartilage inflammation, potentially leading to its permanent destruction and functional compromise. Due to its varied clinical presentation and lack of specific diagnostic tests, RP

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remains a diagnostic challenge and may be misdiagnosed or diagnosed late[1]. This report describes a case of respiratory-predominant RP in a male patient initially evaluated for chronic cough and systemic symptoms. Here we describe the diagnostic journey demonstrating how positron emission tomography (PET) scan was instrumental in reaching the correct diagnosis when conventional methods and initial biopsies were unrevealing.

CASE DESCRIPTION

A 65-year-old man, independent in activities of daily living, with a medical history of bipolar disorder and myelodysplastic syndrome, under treatment with valproic acid, lamotrigine and quetiapine, presented with a 3-month history of persistent dry cough, worse in the supine position, associated with chest pain, which worsened with palpation, odynophagia and hoarseness. He delayed seeking medical attention until the onset of fever, anorexia and weight loss.

In the emergency department, laboratory investigations showed elevated C-reactive protein (CRP) (9.5 mg/dl) and pancytopenia. Empirical antibiotic therapy was initiated, however he returned several days after due to persistent fever, asthenia and night sweats, prompting hospital admission for further evaluation.

Upon admission, he was hemodynamically stable, although febrile. Physical examination revealed tenderness over the costochondral junctions, sternal manubrium and mucocutaneous pallor, with no other abnormalities. Laboratory studies showed low haemoglobin and persistently elevated CRP. Autoimmune screening, microbiological cultures (blood, urine and bronchoalveolar lavage), multiplex CRP respiratory panel and viral and bacterial serologies were negative.

A total-body computed tomography scan revealed diffuse thickening of the tracheal and main/lobar bronchial walls, without additional abnormalities *(Fig. 1)*. Bronchoscopy with transbronchial mucosa biopsy revealed no significant cytologic or histological changes.

Due to inconclusive findings, a PET scan was conducted, revealing a metabolic uptake in the vocal cords, trachea, main bronchi and costal cartilage, findings suggestive of cartilaginous inflammation *(Fig. 2)*. Given the bronchial and costochondral involvement in a 65-year-old man with a medical history of myelodysplastic syndrome, vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic (VEXAS) syndrome was suspected, but ubiquitin-like modifier-activating enzyme 1 (UBA1) gene mutation was negative, excluding this diagnosis hypothesis. Based on the clinical picture, the PET scan findings, the exclusion of VEXAS syndrome and applying the diagnostic criteria proposed by Damiani et al.[2], a diagnosis of the respiratory-predominant variant of idiopathic RP was suspected. This diagnosis was further supported by the patient's clinical response to corticosteroid therapy (prednisolone 0.5 mg/kg/day), leading to total resolution of symptoms and progressive normalization of CRP levels *(Table 1)*. At 6-month follow-up, the patient remains asymptomatic, with persistently undetectable CRP.

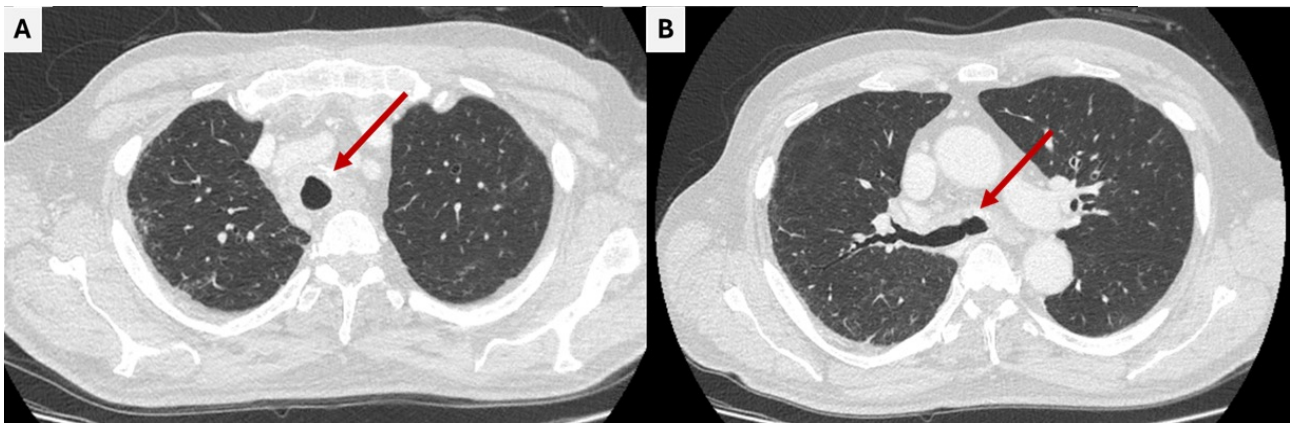


Figure 1. Total-body computed tomography scan showing A) diffuse thickening of the tracheal and B) main/lobar bronchial walls. Arrows highlight the thickened wall.

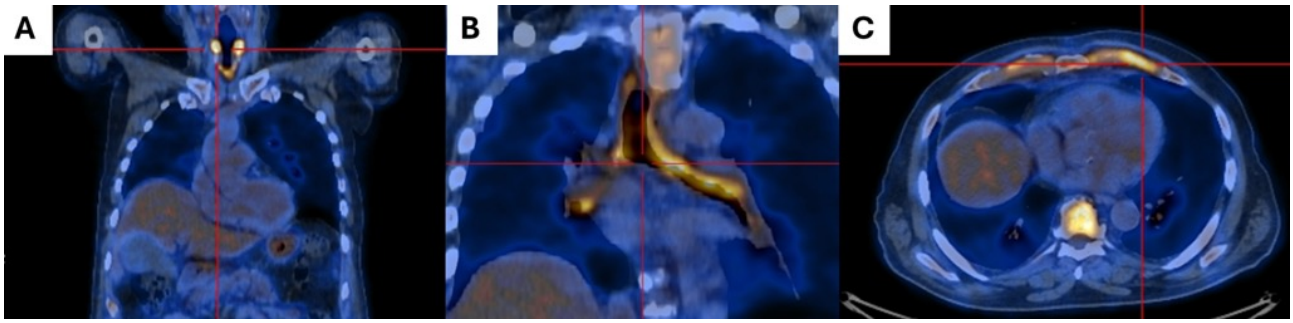


Figure 2. Fluorine-18 fluorodeoxyglucose positron emission tomography scan showing A) an increased metabolic uptake in the vocal cords, B) in the trachea and main bronchi and C) in the costal cartilage.

Bilateral auricular chondritis	Two of seven Mc Adam et al.[7] criteria
Nonerosive seronegative inflammatory	
Polyarthritis	
Nasal chondritis	
Ocular inflammation	
Respiratory tract chondritis	
Audiovestibular damage	
PLUS	
Response to corticosteroids	

Table 1. Criteria by Damiani et al.[2] for diagnosis of relapsing polychondritis.

DISCUSSION

Relapsing polychondritis (RP) is a rare multisystemic disorder characterized by inflammation of cartilaginous tissue, commonly affecting the ears, tracheobronchial tree and joints[1], potentially leading to irreversible damage[3]. Other proteoglycan-rich tissues may also be involved, including the eyes, inner ear, heart, blood vessels and kidneys[1].

The clinical spectrum is broad, but auricular chondritis is most frequent[3]. The auricle becomes red, swollen and tender, sparing the earlobe, lasting for days to several weeks. Nasal chondritis can also occur[4]. Arthralgia and inflammatory seronegative arthritis are the second most common manifestations[3], typically non-erosive, episodic, asymmetric and migratory, affecting both peripheral and axial joints, including sternoclavicular and costochondral[1,4]. Approximately 50% of patients have laryngotracheal involvement, presenting with hoarseness, cough, dyspnoea or wheezing, potentially leading to airway obstruction, a major cause to morbidity and mortality[4].

Other manifestations include ocular, cardiac, dermatologic, neurologic and haematological features[1]. Constitutional symptoms, as fever, fatigue and weight loss, may be part of the initial presentation or accompany disease flares[3].

RP may occur as an isolated condition (primary RP) or in association with other systemic rheumatic diseases[1]. More recently, VEXAS syndrome, an adult-onset autoinflammatory disease, has been described. Caused by somatic UBA1 gene mutations, it primarily affects middle-aged men presenting with recurrent fever, auricular and nasal chondritis, pulmonary involvement, neutrophilic dermatosis and hematologic abnormalities, including myelodysplastic syndrome[5,6].

RP diagnosis relies on clinical features, imaging findings and histological evidence from cartilage biopsies[1], though the latter is no longer essential[4]. Without formal diagnostic criteria, classification is often based on criteria proposed by McAdam et al.[7], Damiani et al.[2] and Michet et al.[8]. Particular attention should be given to upper airway involvement due to the risk of obstruction and collapse, warranting imaging such as chest radiography, pulmonary function testing and high-resolution chest computed tomography. Bronchoscopy can be informative but must be approached with caution due to the risk of exacerbating airway inflammation[4]. PET scan can be a valuable tool in the early diagnosis of RP, especially in patients without organ involvement that is easily accessible for biopsy[1] and genetic screening for UBA1 mutations should be considered to exclude VEXAS syndrome[6].

Treatment aims to control inflammation, alleviate symptoms and prevent structural damage[3]. For mild cases, nonsteroidal anti-inflammatory drugs are used[9]. Corticosteroids are the mainstay for severe acute flares, including ocular or laryngotracheal involvement and systemic vasculitis. Oral prednisolone at 0.5-1 mg/kg/day is commonly employed, with tapering following symptom control, maintaining a low-dose corticosteroid regimen if clinically indicated[3]. Conventional immunosuppressants steroid-sparing agents and biological agents, including tumour necrosis factor alpha inhibitors and the B cell depleting agent, have shown benefit in refractory RP, particularly in systemic or chondritic involvement[9].

Despite not fulfilling three major criteria at onset, the rapid resolution of symptoms and normalization of inflammatory markers with prednisolone (0.5 mg/kg/day), in the setting of laryngotracheal and costochondral inflammation, satisfied Damiani's therapeutic response criteria.

This case highlights the diagnostic value of PET imaging, for identifying cartilaginous inflammation, especially in atypical presentations or when deeper, less accessible sites like the tracheobronchial tree. RP should be considered even without auricular or nasal chondritis, as early diagnosis and treatment can prevent irreversible airway damage and improve outcomes.

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