Multiple relapses of cryptogenic organizing pneumonia: A case report

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Abstract. Cryptogenic organizing pneumonia (COP) is an important subtype of idiopathic interstitial pneumonia, triggered by abnormal inflammatory responses of the lung to unknown stimuli. The disease shows good initial sensitivity to glucocorticoid therapy, but ~50% of patients experience recurrence after glucocorticoid dose reduction or withdrawal. Cases of multiple recurrences (≥3 times) are rarely reported clinically, and no unified consensus has been formed on their diagnosis and treatment strategies, making clinical management challenging. In the present study, a 53-year-old female patient was admitted to hospital for the first time, presenting with a recurrent cough for >1 month. Chest computed tomography (CT) revealed multiple areas of increased density in both lungs, with no notable absorption of the lesions following antimicrobial therapy. A CT-guided percutaneous lung biopsy revealed widened alveolar septa with numerous fibroblast clusters and foam cells within the alveolar spaces, consistent with a diagnosis of COP. Following treatment with methylprednisolone combined with anti-infective therapy, the lesions largely resolved. The patient was discharged on a tapering regimen of oral prednisone, completing a total treatment course of 2 months. After discontinuing medication for 18 months, the patient was readmitted due to chest tightness. CT revealed recurrence of the bilateral pulmonary lesions. Treatment with methylprednisolone combined with anti-infective therapy was administered. Following discharge, oral methylprednisolone therapy for 5 months resulted in complete resolution of the lesions. After 16 months of low-dose oral methylprednisolone maintenance therapy, the patient presented for a third visit with a cough and chest tightness. Chest CT confirmed recurrence of the COP. Symptoms improved after oral prednisone administration, but radiographic changes remained minimal. Multiple recurrent COP has clinical characteristics of migratory lesions, glucocorticoid sensitivity and easy recurrence, and a pathological biopsy is the key to its diagnosis. Long-term glucocorticoid maintenance and individualized dose reduction regimens may reduce the risk of recurrence, but the optimal treatment plan still needs to be explored in further clinical studies. The present case can provide a practical reference for the diagnosis and treatment of multiple recurrent COP.

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Introduction

Organizing pneumonia is a group of interstitial lung diseases characterized pathologically by the proliferation of fibroblasts in the alveolar lumen forming polypoid lesions. According to the etiology, it can be divided into cryptogenic organizing pneumonia (COP) and secondary organizing pneumonia; the former has an unknown etiology, while the latter is mostly secondary to definite causes such as infection, drugs, connective tissue diseases, tumor radiotherapy and chemotherapy (1,2). Large population-based epidemiologic studies for COP remain scarce globally. To date, no updated large-scale original investigations with new prevalence or incidence estimates of COP have been published in 2025 or 2026. The best available population-level epidemiological evidence to date comes from a retrospective study spanning 2016 to 2019, which reported an estimated 14,210 hospitalizations for organizing pneumonia during the study period, including 5,145 COP cases. The annual incidence of COP was 0.51 per 100,000 people, rising markedly with age, and was highest among individuals aged ≥70 years (3).

COP usually has a subacute onset with non-specific clinical manifestations. Patients often seek medical attention 2-3 months after the onset due to a low-grade fever, dry cough, shortness of breath after activity, fatigue and weight loss. A few may present with hemoptysis, a pneumothorax or respiratory failure (4,5). The pathological features of COP include fibrinous exudate with polypoid organization in the alveolar ducts, respiratory bronchioles and alveolar lumen, accompanied by a small amount of infiltration of macrophages, lymphocytes and eosinophils. The lung tissue structure is basically preserved without advanced fibrosis changes (4,6).

Due to the overlap of COP symptoms with infectious pneumonia, lung cancer and other diseases, it is prone to misdiagnosis clinically. Comprehensive judgment should be combined with imaging, bronchoalveolar lavage (BAL) and pathological biopsy to form a diagnosis. High-resolution CT typically shows multifocal consolidation shadows (with air bronchograms), ground-glass opacity or small nodular shadows distributed in the peripheral parts of both lungs (7,8). BAL fluid cell classification is mainly characterized by elevated lymphocytes or neutrophils, which can rule out secondary factors such as infection and tumor (9), while lung biopsy (percutaneous puncture or surgical lung biopsy) is the gold standard for diagnosis (10,11).

Glucocorticoids are the first-line treatment for COP. The initial dose is usually 0.5-1 mg/kg/day prednisone, which is gradually reduced after symptom relief, with a typical total course of 6-12 months (5,12). However, ~50% of patients experience recurrence clinically, and 20% of patients have multiple recurrences. Currently, there are no guideline recommendations for the glucocorticoid maintenance dose, course of treatment and combined treatment plan for multiple recurrent COP (12,13). The present study reports the diagnosis and treatment process of a patient with COP who relapsed three times, and discusses its clinical characteristics, diagnosis and treatment strategies combined with data from recent literature reviews in order to provide a reference for clinical practice.

Case report

Baseline characteristics. Baseline demographic and clinical characteristics are summarized in Table I.

First onset. A 53-year-old female patient with no history of smoking or dust exposure, and no family history of autoimmune diseases was admitted to the Affiliated Hospital of Qingdao University (Qingdao, China) for the first time in February 2022 due to a recurrent dry cough that had persisted for >1 month and fatigue after activity. The patient reported no afternoon fever, night sweats or hemoptysis, and no other clinical manifestations.

Physical examination. Upon physical examination, the patient's body temperature was 36.2˚C, pulse rate was 95 times/min, breathing rate was 16 times/min and blood pressure was 122/77 mmHg. The patient was 159 cm in height and weighed 60 kg (body mass index, 23.7 kg/m^2). No dermatomyositis rash, Gottron's sign or Shawl sign was present. The respiratory sounds of both lungs were clear, and scattered moist rales could be heard in both lower lungs, without dry rales or pleural friction sounds. No pathological murmurs were heard over the cardiac valve auscultation areas. The patient had a soft abdomen, with no tenderness, the liver and spleen were not palpable, and there was no edema in either lower extremity.

Auxiliary examinations. i) Laboratory examinations. Blood routine showed the following results: White blood cell count, 7.79x10^9/l (reference value, 3.5-9.5x10^9/l); neutrophil ratio, 72.1% (reference value, 40-75%); hemoglobin, 98 g/l (reference value, 115-150 g/l; mild anemia); platelet count, 621x10^9/l (reference value, 100-300x10^9/l, elevated); and C-reactive protein, 76.8 mg/l (reference value, 0-10 mg/l; significantly elevated). Blood gas analysis (oxygen inhalation, 2 l/min) revealed the following results: pH, 7.47 (reference value, 7.35-7.45); partial pressure of oxygen, 70 mmHg (reference value, 80-100 mmHg; mild hypoxemia); partial pressure of carbon dioxide, 39 mmHg (reference value, 35-45 mmHg); and actual bicarbonate, 28.4 mmol/l (reference value, 22-27 mmol/l). Tests for tumor markers (for example, carcinoembryonic antigen, squamous cell carcinoma antigen, neuron-specific enolase and cytokeratin 19 fragment 21-1), acid-fast bacillus detection (sputum smear + culture), autoantibodies [antinuclear antibodies, extractable nuclear antigen (ENA) antibody profile and antineutrophil cytoplasmic antibodies], sputum culture, COVID-19 nucleic acid, infectious markers (hepatitis B, hepatitis C, syphilis and human immunodeficiency virus), liver and kidney function, and electrolytes were all normal. Pulmonary function tests showed decreased vital capacity (VC), forced VC (FVC), forced expiratory volume in 1 sec and diffusing capacity of the lungs for carbon monoxide, suggesting restrictive ventilatory disorder.

ii) Imaging examinations. Chest CT showed multiple patchy increased density shadows in both lung fields, mainly in the peripheral parts of the lower lungs on both sides, and some lesions were accompanied by air bronchograms, suggesting inflammatory lesions (Fig. 1A and B).

iii) Pathological examinations. To confirm the diagnosis, a CT-guided percutaneous lung biopsy of the right lower lung was performed. The biopsy specimens were fixed in 10% neutral buffered formalin at room temperature for 6-12 h, sectioned at a thickness of 4 μm, and stained with hematoxylin and eosin according to standard clinical pathology protocols. The slides were observed under a light microscope. Pathological results (Fig. 1C and D) showed a small amount of lung tissue with chronic inflammatory changes, mild widening of alveolar septa, a large number of proliferated fibroblast foci and foam cells in the alveolar lumen. No tumor cells or pathogens were found, which was consistent with the pathological diagnosis of COP (4,6).

Treatment and outcome. After diagnosis, 40 mg/day intravenous methylprednisolone was administered for 7 days in combination with 4.5 g intravenous piperacillin-tazobactam every 8 h for 7 days for anti-infective treatment, together with oxygen inhalation and symptomatic cough relief. After 1 week of treatment, the chest CT was reviewed, and the bilateral lung lesions had been markedly absorbed (Fig. 2A and B). The symptoms of coughing and fatigue were relieved, and the patient was discharged. Oral prednisone acetate tablet treatment (5 mg/tablet) was administered outside the hospital. The dose of prednisone (45 mg/day) was calculated according to the standard of 0.75 mg/kg/day; however, considering the patient's age and sex, in order to reduce the occurrence of side effects of prednisone, the dose was adjusted to 40 mg/day, with the initial 40 mg/day reduced to 35 mg/day after 1 week of discharge, then reduced to 30 mg/day after 2 weeks of discharge, reduced to 5 mg per week, reduced to 5 mg/day for 1 week, and then reduced to 2.5 mg/day for maintenance treatment. The total course of treatment was >2 months. A total of 1 month after drug withdrawal, the outpatient review showed that the patient had no respiratory symptoms, and chest CT showed that the bilateral lung lesions were nearly completely absorbed (Fig. 2C and D).

Table I. Baseline demographic and clinical characteristics of the patient.

Parameters	Results	Reference range
Demographics		
Age, years	53	-
Sex	Female	-
Height, cm	159	-
Weight, kg	60	-
BMI, kg/m^2	23.7	-
Past history		
Smoking history	No	-
Dust exposure	No	-
Autoimmune disease family history	No	-
Vital signs		
Body temperature,˚C	36.2	36.0-37.2
Pulse, beats/min	95	60-100
Respiratory rate, breaths/min	16	12-20
Blood pressure, mmHg	122/77	90-140/60-90
Physical examination		
Lung auscultation	Scattered moist rales in both lower lungs	Clear breath sounds
Skin manifestations	No dermatomyositis rash, Gottron's sign or Shawl sign	-
Cardiac auscultation	No pathological murmurs	-
Abdomen	Soft, no tenderness, liver and spleen not palpable	-
Lower extremities	No edema	-

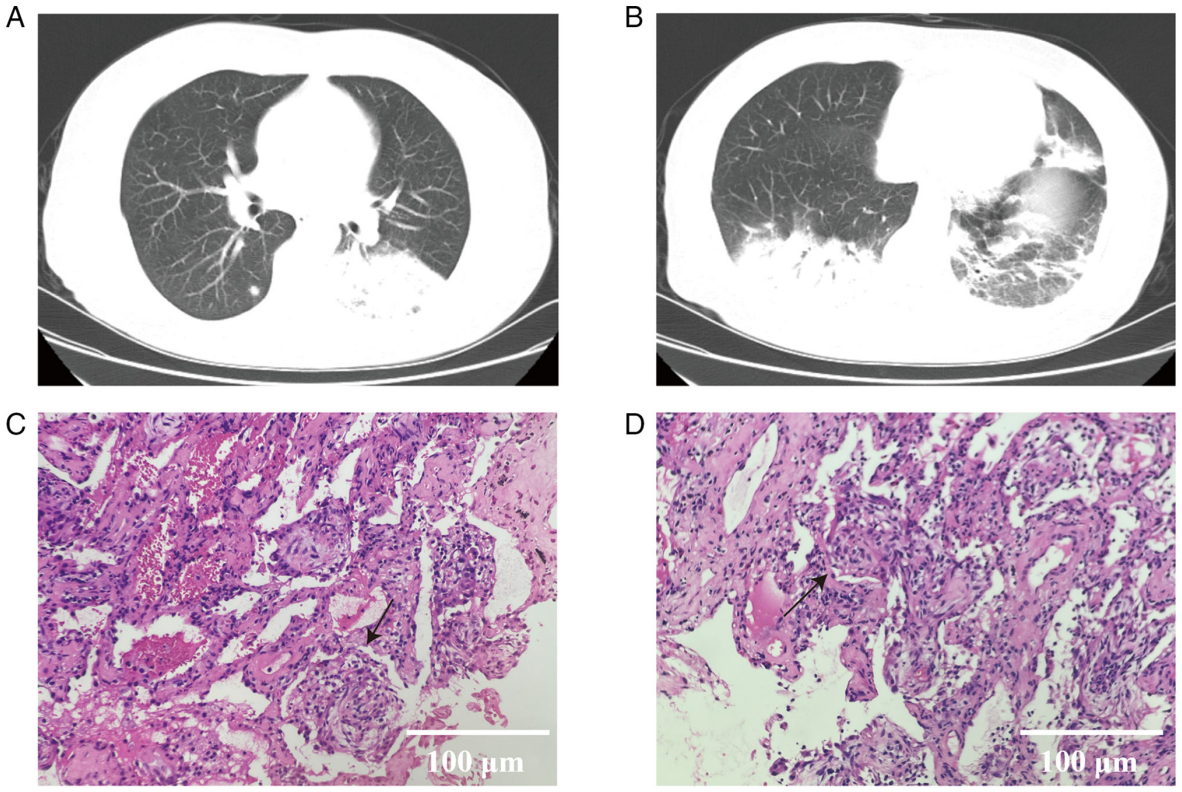

Figure 1. (A and B) Imaging findings of chest computed tomography at admission. (A) Axial chest CT at the level of the upper-middle lung lobes, showing patchy consolidation in the left lower lobe and a small nodular opacity in the right lower lobe. (B) Axial chest CT at the level of the lower lung lobes (near the diaphragm), showing multifocal patchy consolidations and ground-glass opacities with subpleural distribution in both lungs. (C and D) Histopathological examination of percutaneous lung biopsies showed that a small amount of lung tissue showed chronic inflammatory changes, the alveolar septum was slightly widened, and a large number of proliferating fibroblast clusters (arrows) and foam cells were apparent in the alveolar space (hematoxylin and eosin staining; x200 magnification). CT, computed tomography.

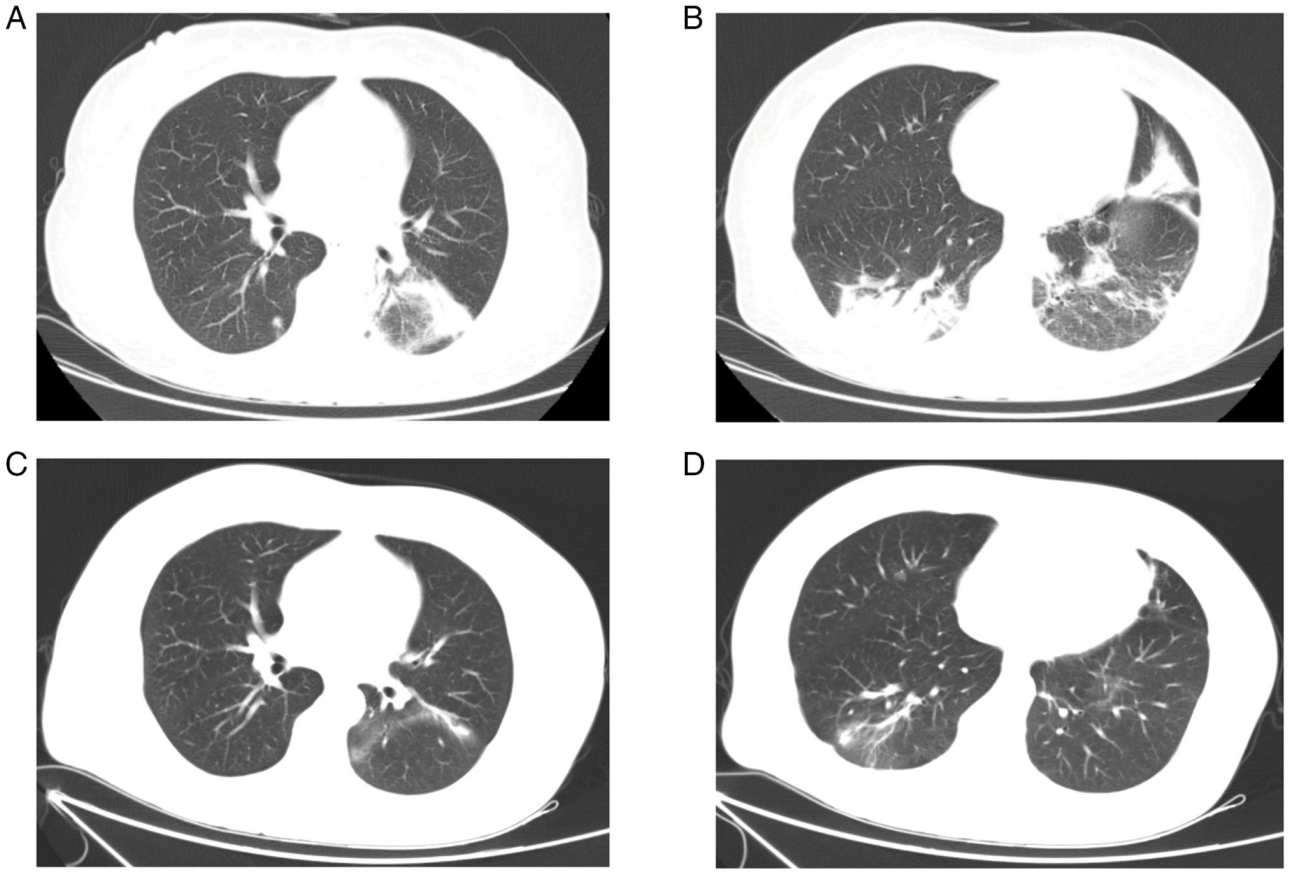

Figure 2. Chest CT findings at different follow-up stages. (A and B) Chest CT images before discharge, showing partial resolution of bilateral pulmonary lesions compared with baseline images at admission. (C and D) Chest CT images after discharge, showing complete resolution of the pulmonary lesions. CT, computed tomography.

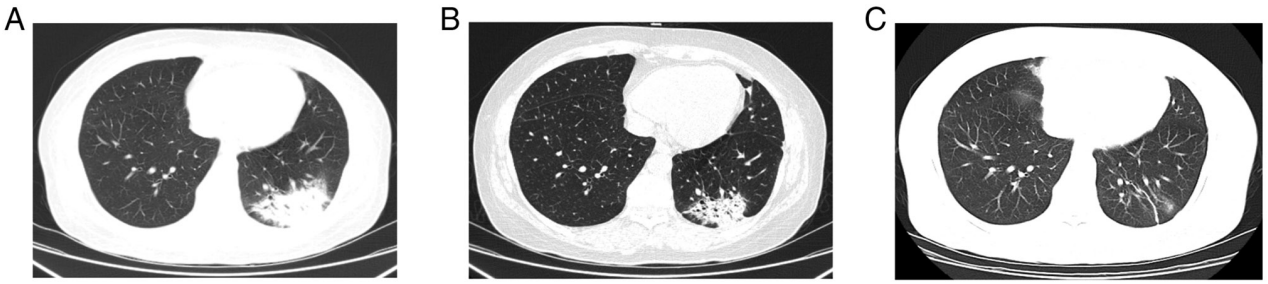

Figure 3. (A, B and C) Chest computed tomography manifestations from the second onset to almost complete absorption.

Second recurrence. At 18 months after the first drug withdrawal, the patient was readmitted due to chest tightness without obvious inducement for 1 week, which was aggravated after activity.

Auxiliary examinations. Chest CT showed new multiple patchy consolidations in the periphery of both lungs, which were different from the distribution of the first-onset lesion (migratory characteristics), and COP recurrence was considered (Fig. 3A). There were no abnormalities in tests for anti-nuclear antibody, ENA, anti-neutrophil cytoplasmic antibody, anti-cyclic citrullinated peptide antibody, antistreptolysin O and rheumatoid factor. Electronic bronchoscopy showed no airway stenosis, new organisms or bleeding. BAL fluid cell classification revealed the following results: Neutrophils, 8.00% (normal reference range, 0-5%); macrophages, 82.00% (normal reference range, 80-90%); lymphocytes, 10.00% (normal reference range, 5-15%); gram staining of BAL liquid showed a small amount of Gram-positive cocci and Gram-negative bacilli, and no pathogenic bacteria were cultured. BAL liquid acid-fast bacilli were negative; there were no malignant tumor cells in the BAL fluid cell pathology. There were no abnormalities in the blood routine, C-reactive protein or autoantibodies.

Treatment and outcome. Considering the possibility of atypical pathogens and subclinical infection, on the basis of intravenous infusion of 40 mg/day methylprednisolone combined with intravenous infusion of 400 mg moxifloxacin

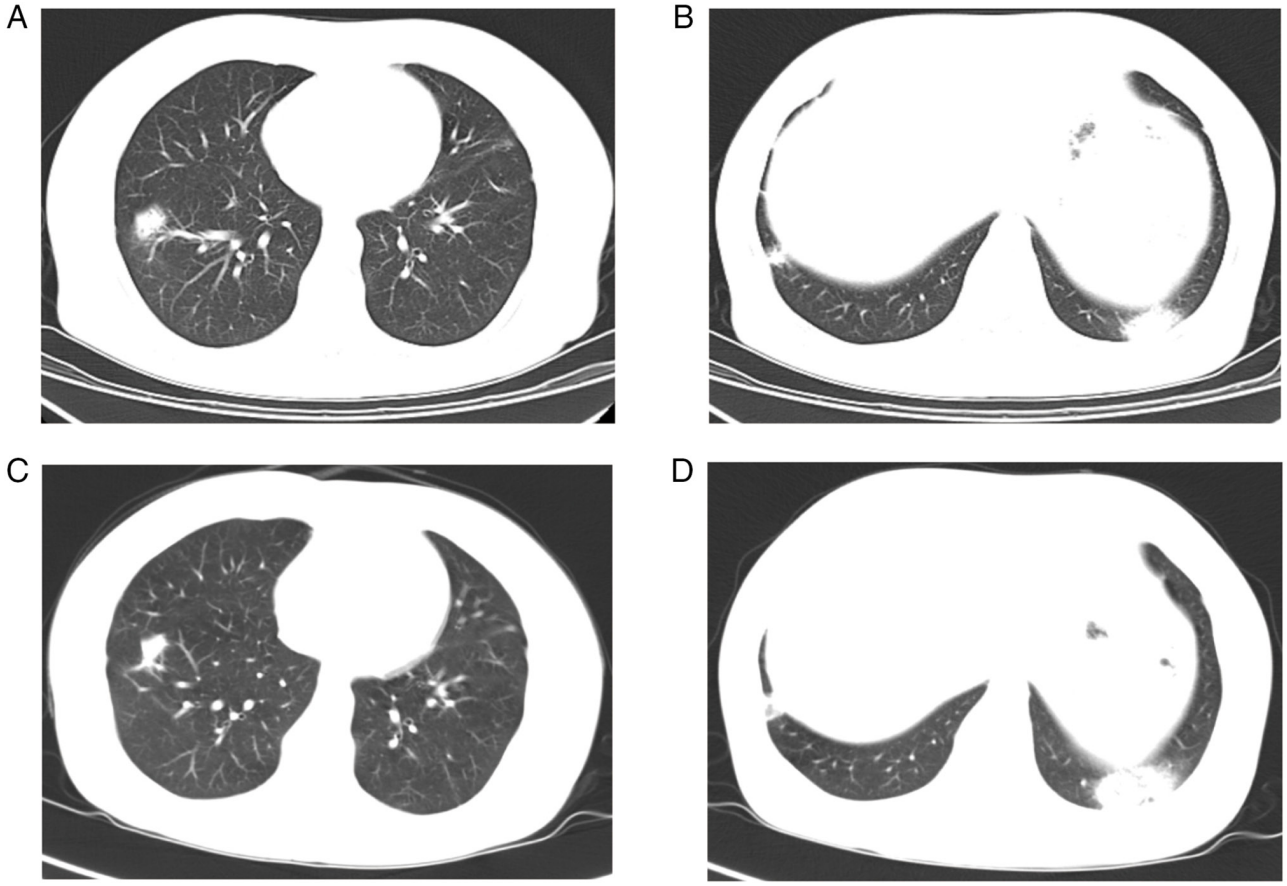

Figure 4. (A and B) Chest CT at the third recurrence, and (C and D) chest CT at the time of reexamination after 2 weeks of treatment. CT, computed tomography.

once daily for anti-infection (a total of 10 days), moxifloxacin was promptly discontinued after infection was excluded, and the patient's chest tightness symptoms were gradually relieved. The chest CT was reviewed before discharge, and the lesion resolved earlier than expected (Fig. 3B). After discharge, oral administration of methylprednisolone, 32 mg/day, reduced to 8 mg/day to maintain treatment for 2 months; the chest CT was reviewed, and the lesions in both lungs were completely absorbed (Fig. 3C). Low-dose methylprednisolone (4 mg/day) was continued for maintenance treatment.

Third recurrence. After 16 months of maintenance treatment with low-dose methylprednisolone (4 mg/day), the patient was admitted to the Outpatient Clinic for a recurrent cough that had persisted for 2 weeks, with mild chest tightness. The patient had no fever, night sweats, fatigue, weight loss, hemoptysis, expectoration, chest pain, joint pain, rash, dry mouth, dry eyes or other clinical manifestations. Chest CT showed new patchy ground-glass opacity and consolidation around the lower lobe of both lungs. Given that the clinical and imaging findings of the patient were generally consistent with previous COP episodes, it was consistent with the third recurrence of COP (Fig. 4A and B). Oral prednisone (30 mg/day) was administered. After 2 weeks of treatment, the symptoms of coughing and chest tightness were relieved. The chest CT was reexamined. The absorption of the bilateral lung lesions was not obvious (Fig. 4C and D). Given the well-recognized phenomenon of imaging lag (radiological response typically lags behind clinical improvement), a plan was made to taper prednisone by 5 mg per week to 10 mg/day for long-term maintenance. A chest CT was planned as a follow-up to evaluate the therapeutic effect. The follow-up interval was 3-6 months. If the patient's imaging performance had not improved by this time, the combined use of macrolides would be considered. The patient is still under follow-up.

Comparison of three episodes and explanation of laboratory examinations. A systematic comparison of clinical manifestations, laboratory parameters, imaging features, treatment regimens and outcomes across the three episodes is presented in Table II.

Glucocorticoid dose modification rationale. The detailed glucocorticoid regimens, rationale for each dose adjustment, maintenance duration and corresponding outcomes across all episodes are summarized in Table III.

Discussion

The recurrence rate of COP is ~50%, but cases with three or more recurrences are rarely reported in the existing literature (12,14). Based on the present case and a review of the literature, multiple recurrences of COP exhibit the following characteristics: i) Onset mode: Mostly a subacute onset; symptoms are mainly a cough, chest tightness and shortness of breath after activity; these symptoms are non-specific, similar

Table II. Comparison of parameters across the three episodes of COP.

Parameters	First episode	Second episode	Third episode
Chief symptoms	Recurrent dry cough for >1 month, fatigue after activity	Chest tightness for 1 week, aggravated after activity	Recurrent cough for 2 weeks, mild chest tightness
White blood cell count	$7.79x10^9$/l (normal)	$6.52x10^9$/l (normal)	Not performed
C-reactive protein	76.8 mg/l (elevated)	8 mg/l (normal)	Not performed
Blood gas analysis	Mild hypoxemia	Not performed	Not performed
Autoantibody profile	All negative	All negative	Not performed
Tumor markers	All normal	Not performed	Not performed
BAL fluid examination	Not performed	Lymphocytes 10%, no pathogenic bacteria, no malignant cells	Not performed
Pulmonary function	Restrictive ventilatory disorder, decreased DLCO	Not performed	Not performed
Imaging findings	Multiple patchy consolidations in bilateral lower lung periphery, with air bronchograms	New migratory patchy consolidations in bilateral lung periphery	New patchy ground-glass opacity and consolidation around bilateral lower lobes
Pathological biopsy	CT-guided percutaneous lung biopsy, consistent with COP	Not performed (clinical-imaging diagnosis)	Not performed (clinical-imaging diagnosis)
Initial treatment	Methylprednisolone (40 mg/day) + piperacillin-tazobactam (4.5 g, every 8 h)	Methylprednisolone (40 mg/day) + moxifloxacin (0.4 g/day)	Oral prednisone (30 mg/day)
Maintenance regimen	Oral prednisone tapering, 2.5 mg/day for final maintenance; total course, 2 months	Oral methylprednisolone tapering, 4 mg/day long-term maintenance	Plan to taper to 10 mg/day for long-term maintenance
Outcome	Lesions completely absorbed; recurrence 18 months after withdrawal	Lesions completely absorbed; recurrence after 16 months during low-dose maintenance	Symptoms improved; imaging showed minimal absorption after 2 weeks; currently under follow-up

For the second and third episodes, full-panel laboratory examinations were not repeated. The diagnosis of recurrent COP was definitively confirmed by typical clinical manifestations and consistent, migratory imaging features. In consideration of the patient's family financial situation and the definitive clinical diagnosis, comprehensive laboratory testing was not repeated. Only necessary examinations to exclude secondary etiologies were performed for the second episode. COP, cryptogenic organizing pneumonia; CT, computed tomography; BAL, bronchoalveolar lavage; DLCO, diffusing capacity of the lungs for carbon monoxide.

to the symptoms of the first onset, without an obvious aggravation trend (5,12). ii) Imaging features: The lesions during recurrence are mostly migratory, that is, the distribution of lesions in each recurrence is different from the previous one. Imaging presents mainly peripheral consolidation shadows and ground-glass opacity in both lungs, accompanied by air bronchograms, consistent with the imaging manifestations of the first onset (7,8,15,16). iii) Laboratory indicators: C-reactive protein is often elevated during recurrence, the blood routine can be normal or slightly elevated in white blood cells, and tests for autoantibodies and tumor markers are mostly negative, indicating that recurrence is not related to infection, autoimmune activity or a tumor (9,14). iv) Glucocorticoid sensitivity: Glucocorticoid therapy (oral or intravenous) can quickly relieve symptoms and absorb lesions after each recurrence, indicating that glucocorticoids are still effective for recurrent lesions, but recurrences frequently occur following glucocorticoid dose tapering or discontinuation (5,13).

In the present case, the intervals between the three onsets of the patient were 18 and 16 months, respectively. There were no clear causes (such as infection or drug exposure) during recurrence, and the lesions were migratory, which was highly consistent with the aforementioned characteristics, further supporting the clinical particularity of multiple recurrent COP.

The diagnosis of COP should follow the principle of exclusion of secondary causes combined with clinical-radiological-pathological correlation (1,8). The diagnostic difficulty of patients with multiple recurrences lies in distinguishing recurrence from new diseases, and the following points should be noted: i) Excluding secondary organizing pneumonia: At each recurrence, the causes of secondary organizing pneumonia need to be re-examined, including infection (sputum culture and BAL fluid etiological detection), drugs (recent medication history), connective tissue diseases (autoantibody profile and joint ultrasound) and tumors (tumor markers and positron emission tomography-CT) (1,12). The three onsets of the present case excluded the aforementioned causes, which was consistent with the cryptogenic definition of a COP diagnosis. ii) Consistency between imaging and pathology: If the CT manifestation during recurrence is consistent with

Table III. Comparison of glucocorticoid treatment regimens across the three episodes.

Parameters	First episode	Second episode	Third episode
Initial induction	Methylprednisolone, 40 mg/day for 7 days	Methylprednisolone, 40 mg/day for 10 days	Oral prednisone, 30 mg/day
Tapering regimen	Tapered by 5 mg weekly, gradually down to 5 mg/day, then further reduced to 2.5 mg/day	Gradually tapered to 4 mg/day	Plan to taper by 5 mg weekly down to 10 mg/day
Maintenance dose	2.5 mg/day	4 mg/day	Planned long-term maintenance at 10 mg/day
Total course/maintenance duration	Total course: 2 months	Maintenance: 16 months	Under follow-up
Key rationale for dose adjustment	Calculated as 0.75 mg/kg/day; reduced to 40 mg/day to minimize the risk of glucocorticoid-related adverse effects	Extended low-dose maintenance after the first relapse to reduce recurrence risk	Recurrence occurred during low-dose maintenance in both prior episodes; maintenance dose increased accordingly
Outcome	Complete lesion resolution; recurrence 18 months after drug discontinuation	Complete lesion resolution; recurrence after 16 months of maintenance therapy	Symptom improvement; minimal radiographic absorption; under follow-up

the first onset (such as peripheral consolidation shadows), and BAL fluid excludes the possibility of infection/tumor, tentative glucocorticoid treatment can be administered. If the imaging manifestation is atypical (such as a solitary mass or diffuse fibrosis), a lung biopsy should be performed again to confirm the diagnosis to avoid misdiagnosis (10,11). During the second and third recurrences of the present case, the CT findings were similar to those observed at the time of the initial onset. Consequently, no repeat biopsy was performed, and treatment with glucocorticoid and other therapies was administered. Following treatment, the lesions gradually resolved. iii) Value of lung biopsy: Lung biopsy is the key to diagnosis during the first onset, while repeated biopsy is not needed during recurrence if clinical imaging is highly consistent with COP and secondary factors are excluded (7,11,17). This case was diagnosed by percutaneous lung biopsy at the first instance, and no repeated biopsy was performed for subsequent recurrences, which not only reduced the risk of invasive operation but also conformed to clinical diagnosis and treatment norms. At present, there is no treatment guideline for multiple recurrent COP. The existing schemes are based on case reports and observational studies, and the main controversies focus on glucocorticoid maintenance dose, course of treatment and combined treatment (5,9).

The conventional glucocorticoid scheme for COP is initially 0.5-1 mg/kg/day, with a gradual dose reduction after 8-12 weeks, and a total course of 6-12 months (5); however, patients with multiple recurrences need to extend the course of treatment or adopt low-dose maintenance. In the present study, the initial treatment regimen lasted only 2 months, which may have led to an early relapse due to its brevity. Following the second treatment, maintenance therapy with 4 mg/day methylprednisolone extended the remission period to 16 months but ultimately resulted in relapse. This suggests that further optimization of the maintenance dose or prolongation of the maintenance period is warranted (13,18). Notably, the patient experienced three sequential relapses after tapering glucocorticoid to ultra-low maintenance doses (2.5 and 4 mg/day), both below the widely accepted minimal maintenance dose of 5 mg/day recommended in current guidelines (8). Standard glucocorticoid protocols for COP recommend prolonged maintenance treatment and caution against rapid reduction to doses of <5 mg prednisone daily, given the elevated risk of disease recurrence.

However, individualized dose adjustment remains challenging in clinical practice. Awareness of potential cumulative glucocorticoid toxicities, including osteoporosis, glucose intolerance and weight gain, often prompts clinicians to pursue further dose reduction. The present case highlights that premature tapering <5 mg/day substantially increases relapse susceptibility in patients with relapse-prone COP. For subjects with multiple recurrent COP, we suggest maintaining prednisone at a minimum of 5 mg daily for an extended period before further slow tapering, unless intolerable adverse events develop. Prospective studies are required to establish personalized maintenance strategies for patients with frequently relapsing COP.

Macrolide drugs (such as clarithromycin) have been used as adjuvant therapy for patients with COP and glucocorticoid intolerance or recurrence due to their anti-inflammatory and immunomodulatory effects. An observational study by Radzikowska *et al* (13) showed that clarithromycin (500 mg, twice a day for 3 months) had a complete remission rate of 63% in the treatment of COP. However, a separate study reported that the recurrence rate after macrolide monotherapy remained as high as 80% (19); Pathak *et al* (20) reported that clarithromycin combined with low-dose glucocorticoids could

reduce the recurrence rate to 30%. For multiple recurrent COP, clarithromycin (500 mg, once a day) can be considered during glucocorticoid dose reduction to reduce glucocorticoid dosage and recurrence risk, but attention should be paid to adverse reactions such as gastrointestinal reactions and QT interval prolongation.

For patients with COP and glucocorticoid dependence or multiple recurrences, there are literature reports indicating that immunosuppressants such as azathioprine and cyclophosphamide combined with glucocorticoid treatment can reduce recurrence, but there is a lack of randomized controlled study evidence (12,14). At present, this treatment is only recommended for patients with glucocorticoid intolerance or those undergoing ineffective macrolide treatment (5,21). The present case was sensitive to glucocorticoids, so immunosuppressants were not administered.

The present study has several inherent limitations. First, this is a single-case report, and the conclusions have limited generalizability; the recurrence pattern, glucocorticoid response and optimal maintenance dose may vary among different patients. Second, a repeated lung biopsy and full-panel laboratory examinations were not performed during the second and third episodes; the diagnosis was mainly based on the consistency of clinical and imaging features, which may carry a small risk of diagnostic bias. Third, the follow-up time of the third episode is limited, and the long-term treatment outcome and prognosis remain to be further observed. Fourth, the glucocorticoid regimen adjustment in this case was based on clinical experience, lacking high-level evidence-based medical support, and the optimal maintenance dose and treatment course for multiple recurrent COP still need to be verified by large-sample prospective clinical studies.

In conclusion, the present case validates the core clinical features of relapsing disease: Migratory bilateral pulmonary lesions, sustained glucocorticoid sensitivity and heightened relapse risk upon dose tapering or withdrawal. Pathological biopsy is the gold standard for initial diagnosis; for recurrent episodes with consistent clinical-radiological findings and excluded secondary etiologies, a repeat invasive lung biopsy is unnecessary.

Inadequate glucocorticoid maintenance may have been a major driver of the multiple relapses in the present patient. Premature tapering of prednisone to <5 mg/day confers substantial recurrence risks in relapse-prone COP. While standard guideline regimens provide generalized treatment frameworks, clinical management requires individualized balancing of relapse risk against patients' intolerance to long-term glucocorticoid administration and clinicians' concerns about glucocorticoid-related adverse effects, including hyperglycemia, osteoporosis and metabolic disturbances. Currently, no universal consensus exists on the optimal minimal maintenance dose for repeatedly relapsing COP. For patients with multiple recurrences, prolonged maintenance therapy with prednisone at ≥5 mg/day should be prioritized unless marked glucocorticoid-related complications emerge. Adjuvant macrolide therapy may be considered for suboptimal imaging response or glucocorticoid intolerance, with immunosuppressants reserved for refractory cases.

The present case offers practical insights for the individualized management of recurrent COP. Further prospective clinical studies are needed to define personalized minimal effective maintenance doses and establish standardized treatment protocols for multiple recurrent disease.

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Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Authors' contributions

Conception and design of the case report was performed by SX and QW. Acquisition of clinical and imaging data was the responsibility of SX and BL. Analysis and interpretation of patient data was performed by YL and JS. SX, JS and QW drafted and critically revised the manuscript for important intellectual content. Final approval of the version to be published was given by SX, BL, YL, JS and QW. All authors take public responsibility for their respective portions of the work and agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. SX and QW confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

All clinical procedures were performed in accordance with the principles of the Declaration of Helsinki.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying clinical images.

Competing interests

The authors declare that they have no competing interests.

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