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Cryptogenic organizing pneumonia associated with pregnancy: A case report

Young Joo Lee, Young Sun Kim

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Abstract

BACKGROUND

Cryptogenic organizing pneumonia (COP), formerly known as bronchiolitis obliterans organizing pneumonia, is an extremely rare disease in pregnancy. In this case, we report on COP diagnosed in recurrent pneumonia that does not respond to antibiotics in pregnant woman.

CASE SUMMARY

A 35-year-old woman with no prior lung disease presented with concerns of chest pain with cough, sputum, dyspnea, and mild fever at 11 wk' gestation. She was diagnosed with community-acquired pneumonia and treated with antibiotics; her symptoms improved temporarily. Four weeks after discharge, she was re-admitted with aggravated symptoms. Chest computed tomography demonstrated multifocal patchy airspace consolidation and ground-glass opacities at the basal segments of the right lower lobe, at the lateral basal segment of the lower lobe, and at the lingular segment of the left upper lobe. Bronchoalveolar lavage revealed an increased lymphocyte count and a decreased CD4/CD8 ratio. Prednisolone (0.5 mg/kg/d) was administered for 10 d after the second admission. Dyspnea improved after 3 d of steroid treatment and other symptoms improved on the 5th day of steroid administration. Post-delivery transbronchial lung biopsy further revealed the presence of granulation tissue with fibroblasts in small-bronchiole lumens.

CONCLUSION

This case suggests that it is important to differentiate COP from atypical pneumonia in the deteriorated condition despite antibiotic treatment.

Key Words: Antibiotics; Bronchiolitis obliterans organizing pneumonia; Corticosteroid; Cryptogenic organizing pneumonia; Pregnancy; Case report

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Core Tip: Cryptogenic organizing pneumonia (COP) is a diffuse infiltrating lung disease, wherein granulation tissue proliferates in the small bronchiolar epithelium. The COP is an extremely rare in pregnancy. We present the fourth case of COP during pregnancy. This case highlights that it is important to differentiate COP from other types of pneumonia that does not respond and aggravated despite of empirical antibiotics in pregnant woman. The corticosteroid administration is effective in the treatment of COP during pregnancy.

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INTRODUCTION

Cryptogenic organizing pneumonia (COP) is a diffuse infiltrating lung disease, wherein granulation tissue proliferates in the small bronchiolar epithelium damaged owing to various causes and consequently obstructs alveolar ducts and alveoli[1,2]. The occurrence of COP in pregnancy is extremely rare and pregnancy-related physiological changes may worsen respiratory complications in COP. Previously reported cases had pre-onset underlying diseases such as asthma, fungal infection and Crohn's disease that can cause inflammatory condition (Table 1). Here, we report the fourth case of COP in a pregnant woman without underlying medical history initially diagnosed with community-acquired pneumonia that did not improve with antibiotic treatment.

CASE PRESENTATION

Chief complaints

A 35-year-old woman, gravida 2, para 1, presented with concerns of chest wall pain with cough, sputum, dyspnea, and mild fever of 37.7 °C at 11 wk of gestation.

History of present illness

The mild cough was started ten days ago with gradually aggravated feature.

History of past illness

Her obstetric history included spontaneous vaginal delivery at 40 wk of gestation, with no special medical history. In particular, there was no history of previous pulmonary diseases.

Personal and family history

A 7.5 pack-year history of smoking was noted before the first pregnancy by an antenatal evaluation.

Physical examination

On admission, the patient's blood pressure was 120/80 mmHg, body temperature was 37.7 °C, pulse rate was 108/min, oxygen saturation was 96%, and respiratory rate was 28/min with a rale in the right lower lung area.

Laboratory examinations

Laboratory tests indicated a white blood cell count of $7.59 \times 10^3/\mu\text{L}$ (74.9% neutrophils, 10.8% lymphocytes, and 3.5% monocytes) with an absolute neutrophil count of 5680 cells/ μL , a hemoglobin level of 12.1 g/dL, a platelet count of $284 \times 10^3/\mu\text{L}$, and an elevated C-reactive protein level of 4.77 mg/dL.

Imaging examinations

Chest radiography showed increased patchy opacities in the right lower lobe (Figure 1), and computed tomography (CT) revealed some patchy lobular consolidation and peripheral ground-glass opacities (GGOs) in the posterior and lateral basal segments of the right lower lobe (Figure 2). The pulmonary function test showed a forced vital capacity (FVC) of 2.87 L (77% of predicted), forced expiratory volume in one second (FEV1) of 2.35 L (74% of predicted), FEV1/FVC ratio of 82%, and peak expiratory flow of 6.19 L/s. The tidal flow-volume curve revealed minimal obstructive lung disease. An ultrasound examination showed that appropriate fetal growth for the gestational age, a normal amount of amniotic

Table 1 Characteristics of cryptogenic organizing pneumonia with pregnancy: Previous published case report

Case No.	1	2	3	4
Ref.	Ghidini <i>et al</i> [1], 1999	Futagami <i>et al</i> [10], 2003	Holder <i>et al</i> [5], 2011	Present
Age (yr)	27	33	16	35
Underlying disease	HIV	ITP, asthma	COP, pulmonary hypertension, asthma, partial right lower-lobe resection	None
Gestational age (wk) at diagnosis	26 + 5	38	20	16 + 1
Gestational age (wk) at delivery	34	38	28	39+4
Symptoms	Cough, dyspnea, chest pain	Cough, fever	Dyspnea, chest pain, fatigue	Chest pain, cough, dyspnea, sputum
Radiologic Findings	Diffuse bilateral parenchymal infiltrates (left lower lobe) in chest X-ray	Diffuse bilateral parenchymal infiltrates in chest X-ray	Patchy ground glass infiltrates in chest CT	Multifocal patchy airspace consolidation and GGO
Initial diagnosis	Asthmatic bronchitis or interstitial; Pneumonia	Asthmatic bronchitis or mycoplasmic pneumonia	Pre-existing COP	CAP
Definite diagnosis method	Open lung biopsy	BAL, TBLB	NA	BAL, TBLB
Initial treatment	Trimethoprim (300 mg) + sulfamethoxazole (1500 mg) IV every 6 h + ceftriaxone (2 g) IV daily, methylprednisolone, 60 mg IV every 8 h	Cefmetazole 1 g every 12 h + gabexatemesilate 2 g IV continuously	NA	Ceftriaxone (2 g daily) IV + amoxicillin (250 mg every 8 h), cefpodoxime (100 mg every 12 h) orally
Final treatment	Dexamethasone, 5 mg IV every 12 h for 72 h, followed by methylprednisolone, 60 mg IV daily for 48 h, then 30 mg IV every 8 h for 4 d; and prednisone 40 mg/d orally	Minocycline 100 mg + methylprednisolone 125 mg every 12 h and every 8 h, for 5 d, followed 40 mg per day orally for 11 d	Nebulizer of a beta-2 agonist and corticosteroids	Prednisolone (0.5 mg/kg/d) for 10 d

BAL: Bronchoalveolar lavage; CAP: Community acquired pneumonia; COP: Cryptogenic organizing pneumonia; GGO: Ground glass opacity; HIV: Human immunodeficiency virus; ITP: Immune thrombocytopenia; IV: Intravenous; NA: Not available; TBLB: Transbronchial lung biopsy; CT: Computed tomography.

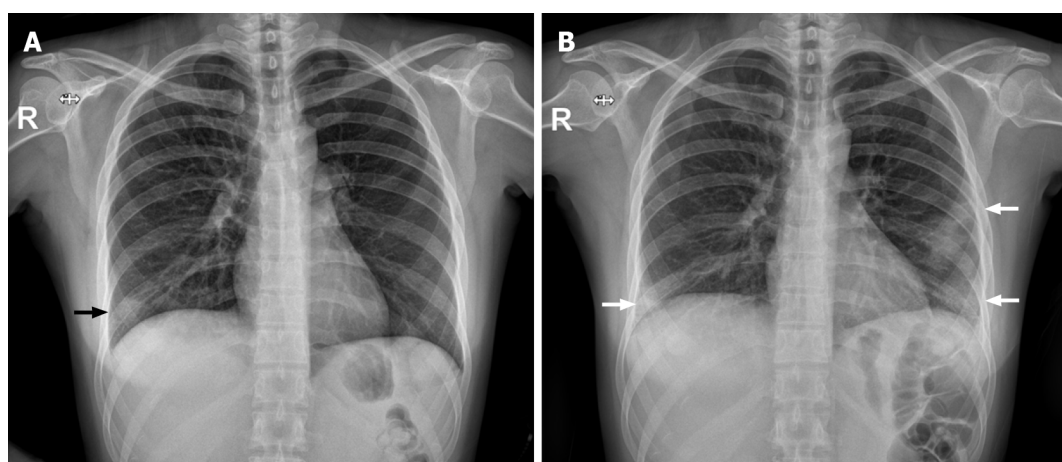


Figure 1 Chest radiography findings. A: Ill-defined increased opacities in the right lower lobe at first onset (black arrow); B: Increased bilateral patchy opacities in both lower lobes with a subpleural portion at second onset (white arrow).

fluid, and no specific abnormal findings.

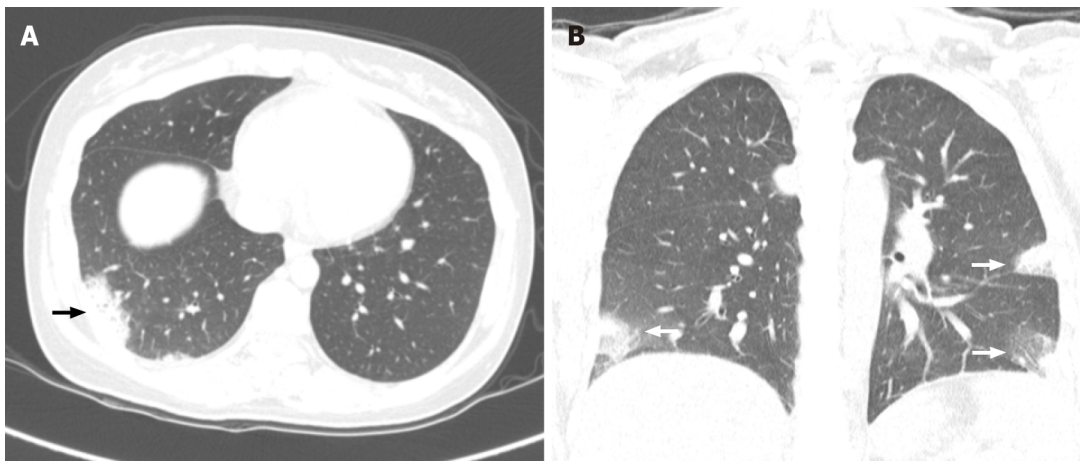


Figure 2 Computed tomography findings. A: Focal patchy consolidation and peripheral ground-glass opacities (GGOs) of posterior and lateral basal segments of the right lower lobe at first onset (black arrow); B: Interval developed multifocal patchy consolidation and GGOs at anterior and lateral basal segments of the right lower lobe, lateral basal segment of the left lower lobe, and lingular segment of the left upper lobe at second onset of coronal section (white arrow).

FINAL DIAGNOSIS

The increased lymphocyte count (40%) and a decrease in the CD4/CD8 ratio (0.6) with the presence of macrophages (25%) and neutrophils (8%) in BAL suggested a diagnosis of COP.

TREATMENT

We began steroid treatment with prednisolone (0.5 mg/kg/d), and progressive improvement of radiological findings was noted. Dyspnea improved after 3 d of steroid treatment, and other symptoms were reduced on the 5th day of steroid administration.

OUTCOME AND FOLLOW-UP

Post-discharge, the patient did not express any special events during pregnancy and gave birth by vaginal delivery at 39+4 d of gestation (male, 3370 g; Apgar scores of 8 and 9 at 1 and 5 min, respectively). Transbronchial lung biopsy was conducted after delivery without any complications, and the proliferation of granulation tissue into the bronchioles and alveolar duct indicated COP (Figure 3).

DISCUSSION

The prevalence of COP is unknown and is mainly observed in individuals aged 50-60 years[3]. COP occurrence during pregnancy is extremely rare, but it could be more severe owing to physiologic changes in pregnant women, such as an elevated diaphragm, increased oxygen demand, decreased functional residual capacity, and decreased chest wall compliance[4]. Thus, previous reports have recommended close antenatal care and regular pulmonary function tests to reduce respiratory complications during pregnancy; further, elective preterm delivery can be an option in more severe cases[5].

The clinical features of COP in the case described above were not notably different from the general clinical features of COP. The respiratory symptoms began with a flu-like illness with cough, mild fever, malaise and progression of shortened breathing to dyspnea[2]. Although a quarter of patients with COP had no special physical findings[3], inhalation rales or crackling were observed in the physical examination in this case.

In general, imaging approaches are employed to diagnose COP. Chest radiography for COP has three characteristic features: multiple alveolar opacities (typical COP), solitary opacity (focal COP), and infiltrative opacities (infiltrative COP). Bilateral multiple opacities are more common than solitary patterns[6, 7]. In our patient, bilateral patchy opacities were observed in both lower lobes. Thin-section CT scans have a correct diagnosis rate of 79% with histologically proved COP[8]. CT findings for COP are patchy GGOs in the subpleural and/or peribronchovascular area (80%), airspace consolidation in bilateral lower lobes (71%), wall thickening and cylindrical dilatation of air bronchogram (71%), ill-defined small nodular opacities (50%), and pleural effusion (in a third of patients)[9]. The specific multifocal patchy

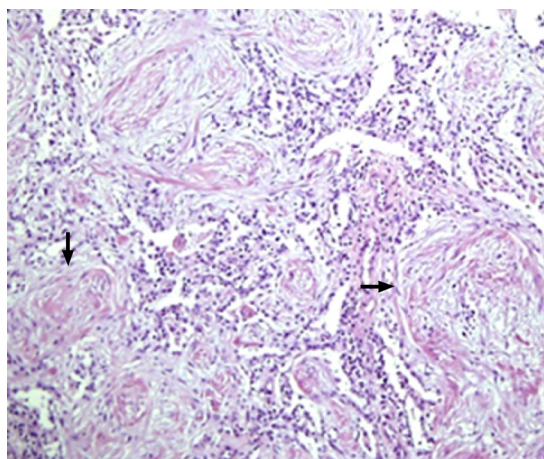


Figure 3 H&E (× 200) stain of TBLB specimen showed intraluminal proliferated granulation tissue with fibrosis in bronchioles (black arrow).

airspace consolidation, GGOs, and bilateral pleural effusion were observed.

Corticosteroids are administered as the initial treatment for COP and are effective for both typical and focal COP. The recommended treatment regimens include initial dosages of 0.75-1.5 mg/kg prednisolone for 3 mo with gradual reduction according to clinical symptom improvement[10]. In this case, we began with a low initial oral dose of prednisolone of 0.5 mg/kg/d after the patient's second admission because corticosteroid use in first trimester can be associated with the development of an orofacial cleft. Fortunately, symptoms improved after 5 d of the low-dose administration and maintenance therapy was continued for 5 more days. This rare case is about the COP diagnosed in pregnant women without underlying medical conditions. In addition, it suggests a diagnostic value of COP, which is less effective in conventional initial treatment. In this case, a pregnant woman was initially diagnosed with community-acquired pneumonia and treated with antibiotics; her symptoms seemed to improve temporarily but then recurred with greater severity.

CONCLUSION

COP has similar clinical features with other types of pneumonia and in particular, chest radiographic differentiation of COP could be difficult. The progressive condition indicates a specific clinical aspect of COP; thus, it is important to differentiate COP from other atypical pneumonia that recur despite initial antibiotic treatment.

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