

## Case Report

# IgG4-related lung disease manifested as pneumonia in puerperium: a case report

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**Abstract:** IgG4-related lung disease (IgG4-RLD) is recently emerging entity. Several reports concerned with the clinicopathologic feature have been described, but this disease in puerperium has not been reported previously. Here, we report a 24-year-old woman diagnosed as IgG4-RLD in puerperium, who developed dry cough, low fever and exertional dyspnea following the delivery. The inflammatory markers and pulmonary lesions of the patient suggested pneumonia. However, there was no improvement after antibiotic treatment. The infiltration of IgG4-positive lymphoplasmacytes was found in lung biopsy by video-assisted thoracic surgery (VATS). And the serum IgG4 level was high. The patient was effectively treated with corticosteroids. This unique case highlights the occurrence of IgG4-RLD in puerperium and underscores it should be taken into consideration as a possible differential diagnosis when dense lymphoplasmacytic infiltration was found in pulmonary consolidation in complex puerperal respiratory cases.

**Keywords:** IgG4-related lung disease, pulmonary nodule, lymphoplasmacyte, puerperium

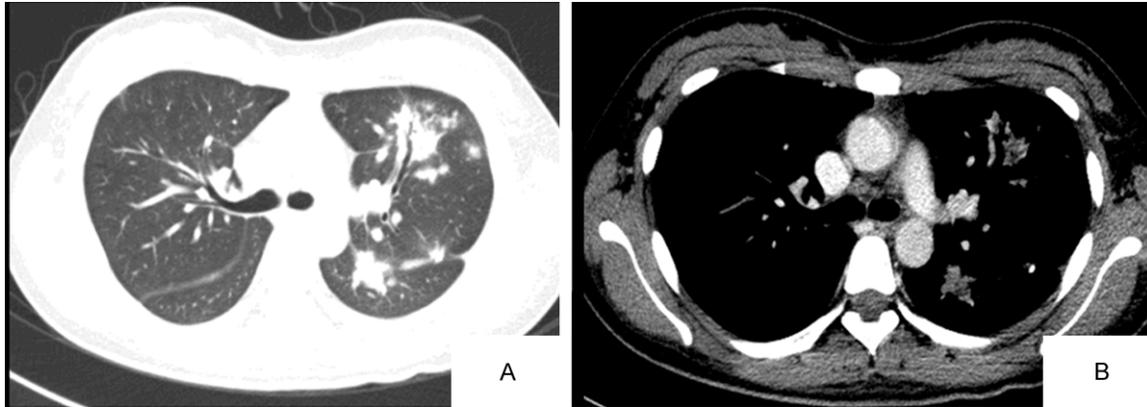
## Introduction

IgG4-related lung disease (IgG4-RLD), a condition characterized by IgG4-positive lymphoplasmacytic cells infiltration in lung and elevated serum IgG4 concentration in most patients, is a recently emerging entity [1]. Reports indicated IgG4-RLD has multiple forms of lung lesions, which is more than previously thought [2-9], but the full spectrum of clinicopathologic feature has not been well described, it appears to be rather nonspecific, so, it is easy to be misdiagnosed as pneumonia with pulmonary consolidations. In addition, the disease always occurs in adults, male predominance [3]. To date, no description of IgG4-RLD in puerperium has been published to our knowledge. Herein, we describe a case of IgG4-RLD in puerperium, who manifested inflammatory conditions and was misdiagnosed to pneumonia.

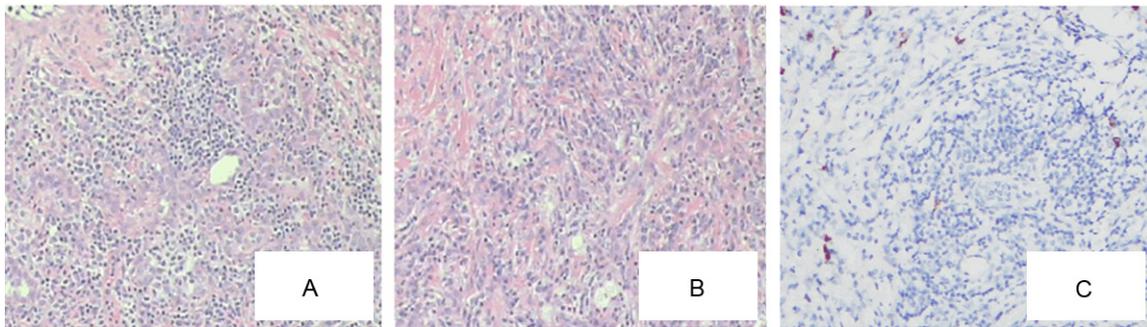
## Case report

A 24-year-old woman was administrated for management of delivery at 38 weeks of gestation at six weeks ago (gravida 1, para 1), who

gave birth by spontaneous delivery and had uneventful antenatal follow-up period. The female newborn had a birth of 3,203 grams and Apgar scores of 8. No obvious deficits were noted during delivery. Three weeks following the delivery, she was admitted to our hospital because of dry cough, coexisting with fever and exertional dyspnea. She had a history of allergic rhinitis. Her body temperature was 38 degree centigrade, and there were no any signs in chest physical examination. Laboratory findings showed erythrocyte sedimentation rate (ESR) was 105 mm/1 H (normal range, 0-20 mm/1 H) and C reaction protein (CRP) was 28.74 mg/L (normal range,  $\leq 10$  mg/L). The total count and classification of white blood cells were  $11.47 \times 10^9/L$  (normal range,  $4.0-10.0 \times 10^9/L$ ) and 70.1%. Serum IgG (1860 mg/dl, normal range, 700-1600 mg/dl) and IgM (290 mg/dl, normal range, 50-270 mg/dl) were mildly increased. Other laboratory tests including IgA, IgE, interleukin-6 (IL-6), carcino-embryonic antigen (CEA), carbohydrate antigen-125 (CA-125), CA-153, CA-199, Antinuclear antibodies (ANA), rheumatoid factors (RF), anti-neutrophil cytoplasmic antibody (ANCA) were normal.



**Figure 1.** Multiple pulmonary consolidations revealed by Chest CT of the patient with IgG4-RLD prior to treatment (May 22, 2013).

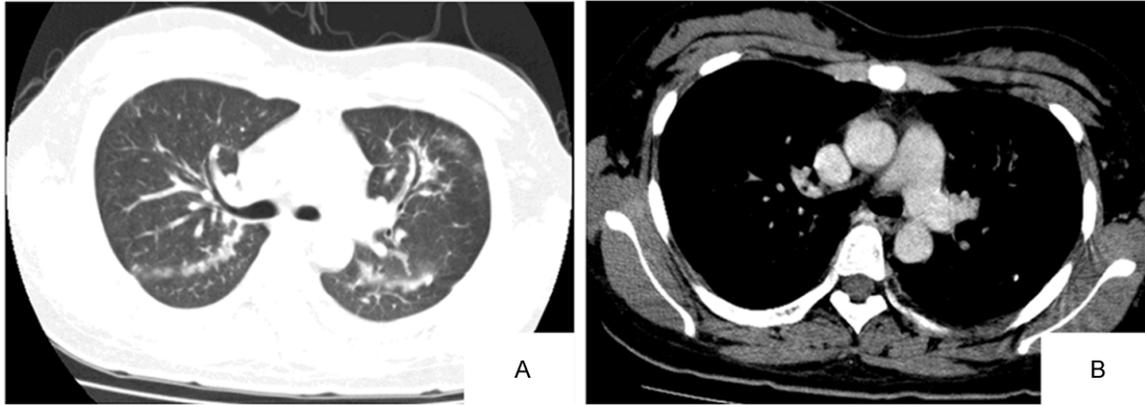


**Figure 2.** Pathological section of the nodules. A. Dense lymphoplasmacytes infiltrated in the alveolar septa and bronchovascular bundle (H&E staining; magnification  $\times 10$ ). B. Fibrosis was found in a storiform pattern (H&E staining; magnification  $\times 10$ ). C. IgG4 immuno-staining revealed predominant IgG4<sup>+</sup> plasma cells, the percentage of IgG4<sup>+</sup>/IgG<sup>+</sup> was 60% (magnification,  $\times 10$ ).

A chest X-ray and computed tomography (CT) revealed multiple pulmonary consolidations in bilateral lungs (**Figure 1A, 1B**). “Pneumonia” was considered, but there was no obvious improvement after using azithromycin and piperacilli/tazobactam for ten days. CT scan images found that there were no obvious changes compared with the previous one, then a bronchoscopy and transbronchial lung biopsy (TBLB) were performed and the histopathology of TBLB samples showed fibrosis and infiltration of plasma cells and lymphocytes in alveolar septa. Bronchoalveolar lavage fluid (BALF) revealed macrophage 46%, lymphocytes 35%, neutrophils 8%, eosinophils 11%, CD4/CD8 ratio 0.234. The bacterial examination was negative. It can't be ruled out the possibility of fungal infection, treatment strategy was changed to use moxifloxacin and voriconazole, but there was still no obvious improvement. To obtain a definitive diagnosis and an appropri-

ate treatment, VATS lung biopsy was performed and the final pathological slice found dense lymphoplasmacytic infiltration, fibrosis in a storiform pattern, IgG4 immuno-staining revealed predominant IgG4 positive plasma cells, the percentage of IgG4 positive versus IgG positive plasma cells (IgG4<sup>+</sup>/IgG<sup>+</sup>) was 60% (**Figure 2A-C**). To further investigate the available TBLB-samples, IgG4 immuno-staining was performed and unexpected found that the percentage of IgG4<sup>+</sup>/IgG<sup>+</sup> was 51%. To determine the involvement of other organs, a total-body CT scan examination showed no other abnormality, including the pancreas, salivary gland, bile duct. A diagnosis of isolated IgG4-RLD was made considering the elevation of serum IgG4 concentration (378 mg/dl) and no other organ involvement.

The patient received corticosteroids 1 mg/kg. d (60 mg) initially, the symptoms gradually



**Figure 3.** The following scan during steroid treatment in five months showed the consolidations disappeared almost (November 14, 2013).

improved and disappeared. One month later, the dose was reduced to 50 mg and tapered 10 mg per month until the discontinuation. Two months later, the IgG4 concentration decreased to 117 mg/dl, CT scan revealed the consolidations got smaller, and five months later almost disappeared (**Figure 3A, 3B**). In fifteen months of follow-up, the patient remained stable with no recurrence.

### Discussion

The first case of IgG4-related disease (IgG4-RD) was first described as autoimmune pancreatitis (AIP) with elevated serum IgG4 concentration in 2001 [10]. In 2008, Takato et al. [11] first presented a case of isolated IgG4-RLD which was without the complication of AIP, manifested as ground-glass opacities (GGO) and reticular shadows on chest CT. Some scholars considered that isolated IgG4-RLD need to be classified as a new separate entity among IgG4-RD [2, 11], but there is no consensus concerning whether it is an isolated forms of IgG4-RLD or forms with AIP.

IgG4-RLD shows a greater variety of clinico-pathologic features. The symptoms include dry cough, exertional dyspnea, bloody sputum etc, and there is no specificity of symptom [3]. Inoue D et al. [5] classified the pulmonary lesions of IgG4-RD into four subtypes, including solid nodular, bronchovascular, alveolar interstitial, and round-shaped GGO type, respectively. Most patients may show any combination of these patterns. A diagnosis of IgG4-RLD is finally established based on the histological findings

of the biopsy, the characteristics are infiltration of IgG4 positive plasma cells and fibrosis, IgG4 immuno-staining is the key to the diagnosis [12, 13]. In our case, the pulmonary lesions mainly presented as multiple consolidations, combined with respiratory and constitutional symptoms, inflammatory makers and lymphoplasmacytic infiltration, although the TBLB samples showed infiltration of lymphoplasmacytes, but the exact diagnosis was hard to be made as IgG4 immuno-staining was not been conventionally performed. In 2008, Yamashita K et al. [6] presented a patient, who was initially diagnosed as lymphoid interstitial pneumonia, a final diagnosis of IgG4-RLD was confirmed when the obtained samples were submitted to author's laboratory for further investigation. For the diagnosis of IgG4-RLD, there are many disorders that can mimic IgG4-RD, such as lymphoma, Castleman's disease, lung cancer, and granulomatosis with polyangiitis. Therefore, it is important for pathologists and clinicians to recognize this rare entity and its histological finding.

IgG4-RLD always affects individuals mean aged about 60 years, and men have a higher incidence of disease in most populations [3]. To our knowledge, this is the first case who diagnosed in puerperium. An exact determination of the cause of IgG4-RLD remains elusive. An elevated IgG4 level has been found in most patients, but it is unclear what role the IgG4 antibody properties have in, or even whether the antibodies are responsible for the pathogenesis of IgG4-RLD [14]. IgG4-RLD is characterized by Th2 predominance and an increase

in expression of the Th2 cytokines IL-4, IL-5, IL-10, and IL-13 [13]. As we know, during a pregnancy and puerperium, individuals connect with a preferential Th2-type response (IL-4, IL-10) caused by presence of fetal tissues. Specific, cell-mediated immunity (CMI) is suppressed and changed to Th2 by progesterone and prostaglandin E2 (PGE2). A higher sensitivity of lymphocytes to progesterone also was found. Th2 cytokines are expressed on deciduas and inhibit secretion of Th1 cytokines [15]. Systematic data on IgG4-RLD in pregnancy and puerperium is needed, and further studies addressing the change of immunity of IgG4-RLD in pregnancy and puerperium may shed further light the underlying pathophysiology.

IgG4-RLD is often effectively responsive to corticosteroid therapy, from therapeutic perspective, it is important to differentiate IgG4-RLD from others, such as Castleman's disease, lymphoma.

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### Disclosure of conflict of interest

None.

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