



Case report

A case of acute progressive diffuse interstitial lung disease preceding idiopathic multicentric Castleman disease

Daijiro Nabeya^{a,b,*}, Yuki Yoshimatsu^c, Hiroshi Fujiwara^d

^a Department of Respiratory Medicine, Okinawa Chubu Hospital, Okinawa, Japan

^b Department of Infectious Diseases, Respiratory, and Digestive Medicine, Graduate School of Medicine, University of the Ryukyus, Okinawa, Japan

^c Department of Respiratory Medicine, Iizuka Hospital, Iizuka, Japan

^d Department of Respiratory Medicine, Yodogawa Christian Hospital, Osaka, Japan

ARTICLE INFO

Keywords:

Multicentric castleman disease
 Interstitial lung disease
 Lymphocytic interstitial pneumonia
 Non-specific interstitial pneumonia

ABSTRACT

It has been considered that idiopathic multicentric Castleman disease often involves pulmonary complications recognized as lymphocytic interstitial pneumonia. On the other hand, recent reports show that the computed tomography often show diffuse interstitial lung disease inconsistency with lymphocytic interstitial pneumonia. Pulmonary diseases with idiopathic multicentric Castleman disease are still rare and poorly understood. Here, we report a case of acute progressive diffuse interstitial lung disease, diagnosed as non-specific interstitial pneumonia, preceding idiopathic multicentric Castleman disease.

A 65-year-old male visited our outpatient clinic for dyspnea on exertion. Imaging tests revealed interstitial lung disease showing non-specific interstitial pneumonia pattern, pulmonary function test proved the decline of vital capacity and laboratory tests showed increased fibrosis biomarkers; therefore, initially, he had been diagnosed as non-specific interstitial pneumonia. However, imaging tests also showed mediastinum lymphadenopathy, and laboratory tests revealed increased interleukin-6. Idiopathic multicentric Castleman disease was suspected. The lung and mediastinum lymph node biopsies were performed, and pathological findings of the lymph nodes were compatible with multicentric Castleman disease. Pathological findings of the lung showed that the fibrous thickening of interstitium and the collapse of alveoli. We diagnosed this case as idiopathic multicentric Castleman disease preceded by diffuse interstitial lung disease. Treatment with prednisolone improved the dyspnea, and the pulmonary lesions disappeared.

The presented case suggests that interstitial lung disease could precede idiopathic multicentric Castleman disease. Chest physicians should be aware that idiopathic multicentric Castleman disease is one of the causative diseases of diffuse interstitial lung disease like non-specific interstitial pneumonia on the chest images.

1. Introduction

Multicentric Castleman disease (MCD) is a systemic inflammatory disorder caused by interleukin-6 resulting in systemic inflammatory symptoms, lymphadenopathy and multi-organ involvement, and human herpesvirus-8-negative MCD is referred to as idiopathic MCD (iMCD) [1, 2]. iMCD often involves pulmonary complications, and typical computed tomography (CT) findings are classified as lymphocytic interstitial pneumonia (LIP) [3,4]. On the other hand, recent reports show that diffuse interstitial lung disease, inconsistency with the typical LIP pattern on chest CT, is often seen in lung involvement of iMCD [5,6].

It is considered that these pulmonary involvements are caused secondary with iMCD and slowly progressive to fibrosis if inadequately treated for iMCD [2]. However, pulmonary involvements with iMCD are still rare, and clinical features are poorly understood.

Here, we report a case of iMCD preceded by acute diffuse interstitial lung disease diagnosed as non-specific interstitial lung pneumonia (NSIP). This is a rare and valuable case.

2. Case presentation

The case was a 65-year-old Japanese male with no

Abbreviations: MCD, multicentric Castleman disease; iMCD, idiopathic multicentric Castleman disease; CT, computed tomography; LIP, lymphoid interstitial pneumonia; NSIP, nonspecific interstitial pneumonia.

* Corresponding author. 281 Miyazato, Uruma, Okinawa, 904-2293, Japan.

E-mail address: nabeya_daijiro@hosp.pref.okinawa.jp (D. Nabeya).

<https://doi.org/10.1016/j.rmcr.2020.101216>

Received 6 May 2020; Received in revised form 8 August 2020; Accepted 7 September 2020

Available online 11 September 2020

2213-0071/© 2020 Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

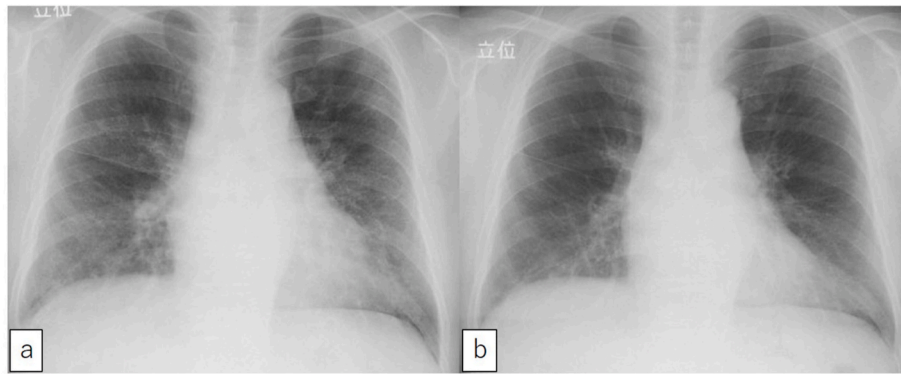


Fig. 1. (a) One month before admission. The chest X-ray showed diffuse ground-glass opacity and reticular shadows in the lower area of both lungs. (b) Four weeks after starting steroid therapy. Lung lesions have improved.

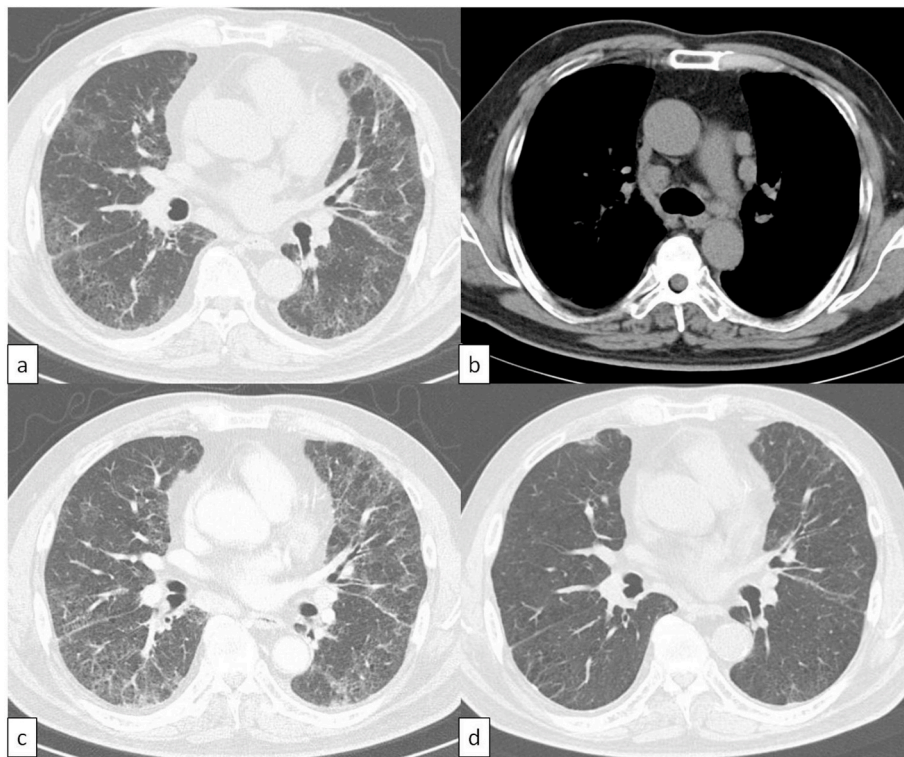


Fig. 2. (a) One month before admission. The chest CT scan showed diffuse ground-glass opacity and interlobular septal thickening in the inferior lobe, presenting a nonspecific interstitial pneumonia pattern. (b) Mediastinum lymphadenopathy can also be seen. (c) On admission. Lung lesions have advanced. (d) Four weeks after starting steroid therapy. Lung lesions have improved.

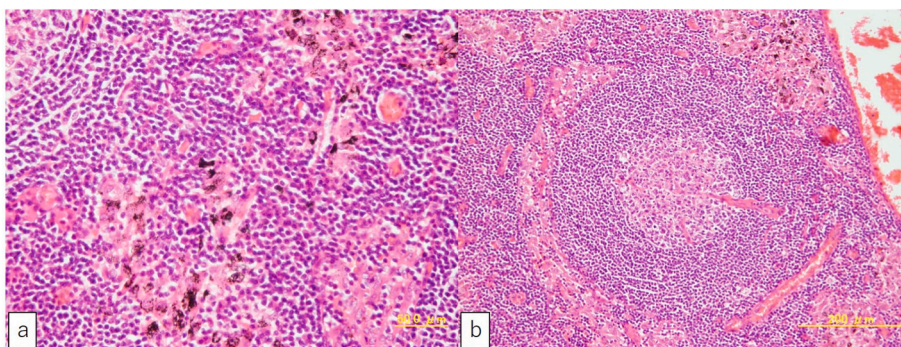


Fig. 3. Pathological findings of the mediastinum lymph node. (a) High magnification view. Atrophic germinal center with proliferating sclerotic blood vessels (hyaline vascular variant). (b) Plasma cells proliferate in interfollicle (plasma cell variant).

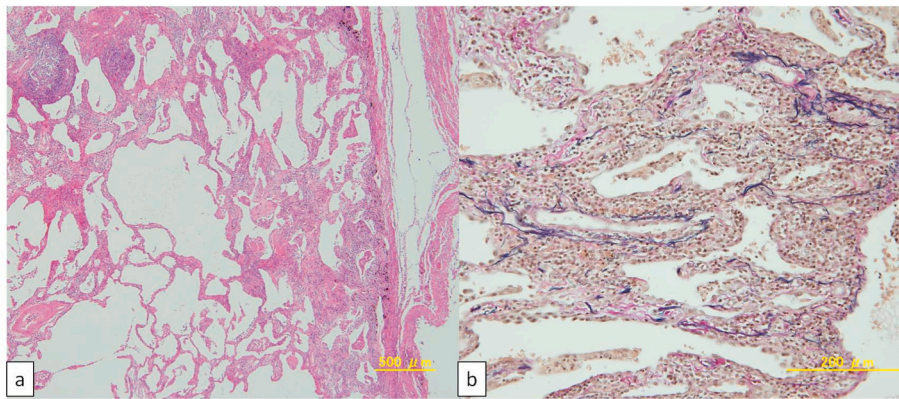


Fig. 4. (a) Pathological findings of the lung revealed plasma cell infiltration in the interlobular septa and interalveolar septum with a thickening. Lymphoid follicles were shown around the bronchiole. (b) Elastic van Gieson stain showing the fibrous thickening of the interstitium and collapse of alveoli.

immunocompromising diseases or recent medical history. Cigarette smoking history was one pack/day for 25 years. An abnormality on chest X-ray was found three months before hospitalization at an annual health check-up, but he didn't follow recommendations for further testing. He first visited Yodogawa Christian Hospital one month ago because of progressive dyspnea on exertion. The chest X-ray showed diffuse ground-glass opacity (GGO) (Fig. 1a). The chest CT scan revealed diffuse interstitial lung disease consisting of GGO, patterned NSIP (Fig. 2a), and pulmonary function test proved the decline of vital capacity. Laboratory tests showed that increased Krebs von den Lungen-6 and Surfactant protein-D, and autoimmune antibodies were negative (Table). He was diagnosed as NSIP and followed at our outpatient clinic. However, in one month, his dyspnea had progressed further, and body weight had decreased by 3 kg, and he was admitted to our hospital. On admission, vital signs were normal, and oxygen saturation was 96%. Physical examination showed fine crackles on auscultation of the posterior lung fields. There was no superficial lymphadenopathy. The chest CT scan showed that ground-glass opacities had progressed in one month (Fig. 2c). Also, multiple mediastinal lymph nodes enlargements were found (Fig. 2b), and laboratory tests revealed increased interleukin-6 (Table). Therefore, MCD was suspected. Thoracoscopic lung and mediastinal lymph node biopsies were performed, and pathologic findings of the lymph node suggested Castleman disease of mixed hyaline vascular and plasma cell variant (Fig. 3). Pathological findings of the lung showed that the fibrous thickening of interstitium with plasma cells infiltration and the collapse of alveoli (Fig. 4). Human immunodeficiency virus antibody and human herpesvirus-8 antibody were negative, and two major criteria and two minor criteria (increased erythrocyte sedimentation rate and immunoglobulin G) were met for diagnosing iMCD [7]. Tuberculosis, lymphoma, and other mimicking iMCD diseases were excluded by clinical findings, pathological findings and laboratory tests. Then, we diagnosed this case as iMCD preceded by acute progressive diffuse interstitial lung disease. We started treatment with prednisolone 0.7 mg/kg (50 mg/day), and his dyspnea improved within two weeks. Chest images one month later showed improvement (Figs. 1b and 2d). Although prednisolone was tapered by 5–10mg every week and maintained at 15–20mg/body, he did not relapse.

3. Discussion and conclusion

Previous reports show chest CT findings of the lung involvement of iMCD are commonly consist of poorly defined centrilobular nodules, thin-walled cysts, thickening of the bronchovascular bundles, and interlobular septal thickening. These findings had been recognized as the typical LIP patterns in iMCD [3,4]. However, the presented case showed that diffuse interstitial lung disease patterned as NSIP on the chest CT. Recent reports show that diffuse GGO and consolidation are

often seen in CT findings of lung involvements of iMCD [5,6]. These CT findings are different from the typical LIP pattern in iMCD and probably diagnosed as diffuse interstitial lung disease such as NSIP.

In pathological findings of the lung involvements of iMCD, lymphoplasmacytic proliferating lesions mainly in the alveolar area adjacent to the perilymphatic stromal area and lymphoid follicles are often seen [8,9]. The pathological findings of the lung involvement of the presented case are compatible with these reports. Otherwise, the presented case showed the fibrous thickening of interstitium collapsing alveolar space. Generally, lung involvement of iMCD can progress to lung fibrosis if inadequately treated [2], therefore, lung fibrosis is considered as the end-stage of lung involvement of iMCD. However, the presented case showed acute progressive interstitial lung disease with pathological lung fibrosis. It is supposed that the presented case was in the acute progressive phase of lung fibrosis and the collapse of alveoli caused by fibrous thickening of interstitium was recognized as diffuse GGO on the chest CT.

The presented case suggests that diffuse interstitial lung disease precedes iMCD. Chest physicians should be aware that iMCD is one of the causative diseases of diffuse interstitial lung disease such as in the NSIP pattern on the chest images. If mediastinum lymphadenopathy is seen in an interstitial lung disease patterned NSIP on the CT, lymph node biopsy should be considered.

Funding details

This report did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics

There are no ethical issues regard to this manuscript. The medical record of the case was retrospectively reviewed, with identifying information removed.

Author contribution

D.N. designed the case report and drafted the manuscript. Y.Y., H.F. contributed to review of this manuscript. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- [1] A.Y. Liu, C.S. Nabel, B.S. Finkelman, J.R. Ruth, R. Kurzrock, F. van Rhee, V. P. Krymskaya, D. Kelleher, A.H. Rubenstein, D.C. Fajgenbaum, Idiopathic multicentric Castleman's disease: a systematic literature review, *Lancet Haematol* 3 (4) (2016) e163–e175.
- [2] F. van Rhee, P. Voorhees, A. Dispenzieri, A. Fosså, G. Srkalovic, M. Ide, N. Munshi, S. Schey, M. Streetly, S.K. Pierson, H.L. Partridge, S. Mukherjee, D. Shilling, K. Stone, A. Greenway, J. Ruth, M.J. Lechowicz, S. Chandrakasan, R. Jayanthan, E. S. Jaffe, H. Leitch, N. Pemmaraju, A. Chadburn, M.S. Lim, K.S. Elenitoba-Johnson, V. Krymskaya, A. Goodman, C. Hoffmann, P.L. Zinzani, S. Ferrero, L. Terriou, Y. Sato, D. Simpson, R. Wong, J.F. Rossi, S. Nasta, K. Yoshizaki, R. Kurzrock, T. S. Uldrick, C. Casper, E. Oksenhendler, D.C. Fajgenbaum, International, evidence-based consensus treatment guidelines for idiopathic multicentric Castleman disease, *Blood* 132 (20) (2018) 2115–2124.
- [3] T. Johkoh, N.L. Müller, K. Ichikado, N. Nishimoto, K. Yoshizaki, O. Honda, N. Tomiyama, H. Naitoh, H. Nakamura, S. Yamamoto, Intrathoracic multicentric Castleman disease: CT findings in 12 patients, *Radiology* 209 (2) (1998) 477–481.
- [4] H. Kawabata, N. Kadowaki, M. Nishikori, T. Kitawaki, T. Kondo, T. Ishikawa, H. Yoshifuji, N. Yamakawa, Y. Imura, T. Mimori, Y. Matsumura, Y. Miyachi, T. Matsubara, M. Yanagita, H. Haga, A. Takaori-Kondo, Clinical features and treatment of multicentric castleman's disease : a retrospective study of 21 Japanese patients at a single institute, *J. Clin. Exp. Hematop.* 53 (1) (2013) 69–77.
- [5] H. Huang, R. Feng, J. Li, X. Song, S. Li, K. Xu, J. Cao, L. Zhang, Y. Bi, Z. Xu, Castleman disease-associated diffuse parenchymal lung disease: a STROBE-compliant retrospective observational analysis of 22 cases in a tertiary Chinese hospital, *Medicine (Baltim.)* 96 (39) (2017), e8173.
- [6] J.M. Luo, S. Li, H. Huang, J. Cao, K. Xu, Y.L. Bi, R.E. Feng, C. Huang, Y.Z. Qin, Z. J. Xu, Y. Xiao, Clinical spectrum of intrathoracic Castleman disease: a retrospective analysis of 48 cases in a single Chinese hospital, *BMC Pulm. Med.* 15 (2015) 34.
- [7] D.C. Fajgenbaum, T.S. Uldrick, A. Bagg, D. Frank, D. Wu, G. Srkalovic, D. Simpson, A.Y. Liu, D. Menke, S. Chandrakasan, M.J. Lechowicz, R.S. Wong, S. Pierson, M. Paessler, J.F. Rossi, M. Ide, J. Ruth, M. Croglio, A. Suarez, V. Krymskaya, A. Chadburn, G. Colleoni, S. Nasta, R. Jayanthan, C.S. Nabel, C. Casper, A. Dispenzieri, A. Fosså, D. Kelleher, R. Kurzrock, P. Voorhees, A. Dogan, K. Yoshizaki, F. van Rhee, E. Oksenhendler, E.S. Jaffe, K.S. Elenitoba-Johnson, M. S. Lim, International, evidence-based consensus diagnostic criteria for HHV-8-negative/idiopathic multicentric Castleman disease, *Blood* 129 (12) (2017) 1646–1657.
- [8] K. Otani, D. Inoue, K. Fujikura, T. Komori, S. Abe-Suzuki, T. Tajiri, T. Itoh, Y. Zen, Idiopathic multicentric Castleman's disease: a clinicopathologic study in comparison with IgG4-related disease, *Oncotarget* 9 (6) (2018) 6691–6706.
- [9] Y. Terasaki, S. Ikushima, S. Matsui, A. Hebisawa, Y. Ichimura, S. Izumi, M. Ujita, M. Arita, K. Tomii, Y. Komase, I. Owan, T. Kawamura, Y. Matsuzawa, M. Murakami, H. Ishimoto, H. Kimura, M. Bando, N. Nishimoto, Y. Kawabata, Y. Fukuda, T. Ogura, T.D.L.D.S. Group, Comparison of clinical and pathological features of lung lesions of systemic IgG4-related disease and idiopathic multicentric Castleman's disease, *Histopathology* 70 (7) (2017) 1114–1124.