Respiratory Medicine Case Reports 37 (2022) 101625

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

A case of lung intravascular large B cell lymphoma developed with respiratory failure rescued by corticosteroid prior to definite diagnosis

Mayoko Tsuji [a], Mitsuko Kondo [a,*], Fumi Onizawa [a], Osamu Shishime [a], Soshi Muramatsu [a], Yuka Matsuo [b], Shuji Sakai [b], Junji Tanaka [c], Etsuko Tagaya [a]

[a] Department of Respiratory Medicine, Tokyo Women's Medical University, Tokyo, 162-8666, Japan
[b] Department of Diagnostic Imaging and Nuclear Medicine, Tokyo Women's Medical University, Tokyo, 162-8666, Japan
[c] Department of Hematology, Tokyo Women's Medical University, Tokyo, 162-8666, Japan

ARTICLE INFO

Keywords:
Lung intravascular large B cell Lymphoma
Corticosteroid
^{18}FDG-PET
Lung perfusion scintigraphy

ABSTRACT

A 56-year-old man complained progressive dyspnea, fatigue and fever for one month. His chest CT exhibited faint ground-glass opacities, and the levels of serum LDH and soluble interleukin 2 receptor were markedly elevated. Positron emission tomography (PET) showed high uptake of 18-fluoro deoxy glucose (^{18}FDG) only on both lungs. We performed transbronchial lung biopsies (TBLB) for the diagnosis. After bronchoscopy, he had prolonged hypoxemia. Because defects of 99m-Technetium macroaggregated albumin (^{99m}Tc-MAA) in pulmonary blood flow scintigraphy were consistent with the distribution of ^{18}FDG uptake in PET, we speculated that the presence of intravascular lymphoma (IVL) cells in the capillaries might have behaved like tumor embolism. We started rescue by prednisolone based on treatment of lymphoma. As a result, his hypoxemia was gradually improved. Histological findings in TBLB specimen showed that $CD20^{+}CD79^{+}Bcl\text{-}2^{+}c\text{-}myc^{+}$ lymphoma cells were localized to small vessel lumina in alveoli and bronchioles, and he was definitely diagnosed with lung intravascular large B cell lymphoma (IVLBCL). He was treated with complete cyclophosphamide, doxorubicin, vincristine, and prednisolone with rituximab (R–CHOP) in combination with intrathecal methotrexate injection. After eight cycles of R–CHOP and three times of intrathecal methotrexate, ^{18}FDG uptake of PET on both lungs completely disappeared, achieving complete metabolic remission. We experienced a rare case of lung IVLBCL developed with respiratory failure successfully rescued by prednisolone prior to definite diagnosis.

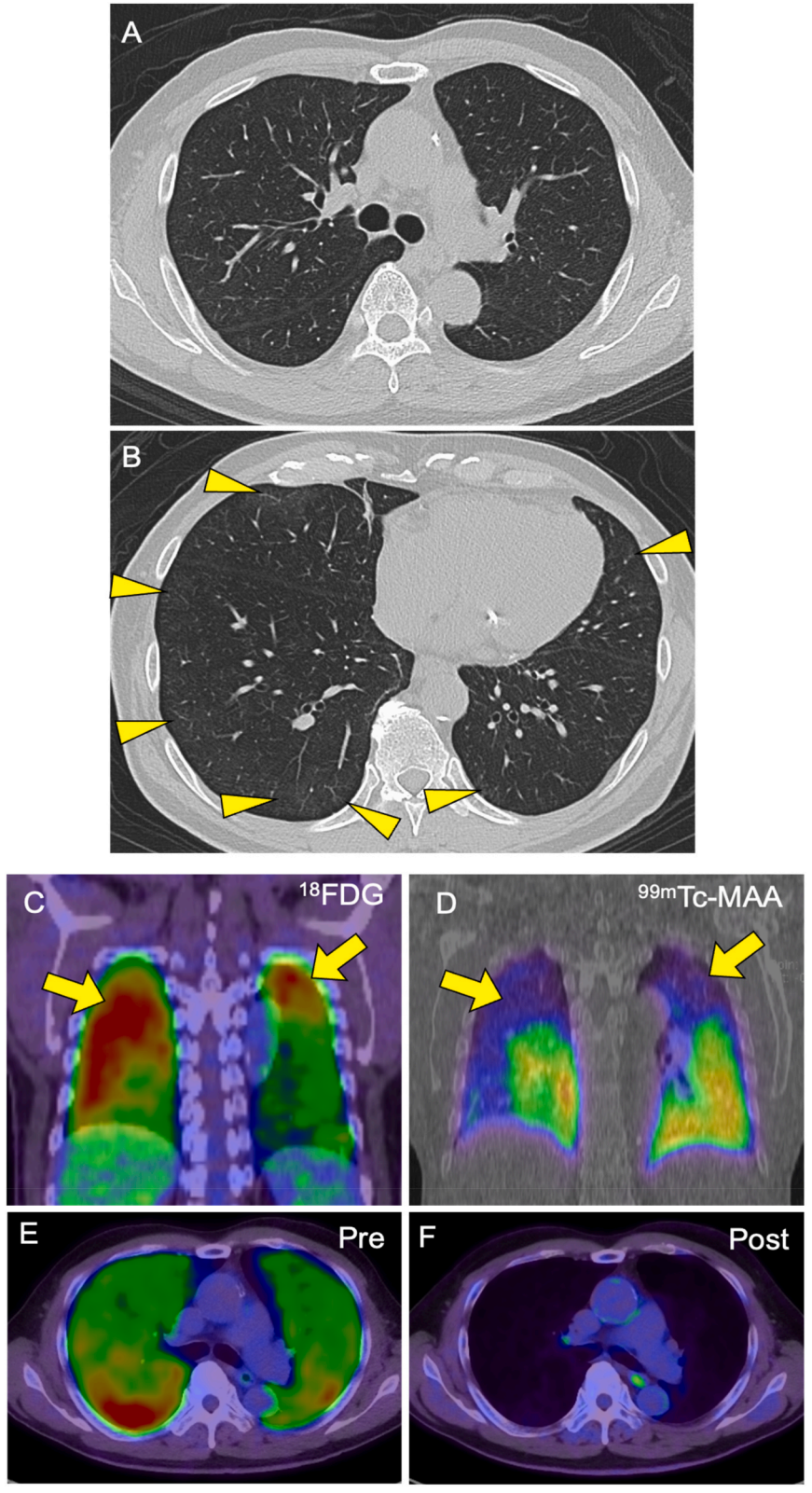
1. Introduction

Intravascular large B-cell lymphoma (IVLBCL) is a rare subtype of B cell lymphoma characterized by the selective growth of lymphoma cells in particularly capillaries in organs [1]. Approximately 30% of IVLBCL patients exhibit lung involvement. However,

Abbreviations: DLco, diffusion lung capacity for carbon monoxide; HRCT, high resolution computed tomography; IVL, intravascular lymphoma; IVLBCL, intravascular large B cell lymphoma; LDH, lactate dehydrogenase; PET, positron emission tomography; R–CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone with rituximab; sIL-2R, soluble interleukin 2 receptor; SpO_2, percutaneous oxygen saturation; TBLB, transbronchial lung biopsy; ^{18}FDG, 18-fluoro deoxy glucose; ^{99m}Tc-MAA, 99m-Technetium macroaggregated albumin.

* Corresponding author. Department of Respiratory Medicine, Tokyo Women's Medical University 8-1 Kawada-cho, Shinjuku-ku, Tokyo, 162-8666, Japan.
E-mail address: kondo.mitsuko@twmu.ac.jp (M. Kondo).

https://doi.org/10.1016/j.rmcr.2022.101625
Received 13 December 2021; Received in revised form 2 February 2022; Accepted 7 March 2022
Available online 11 March 2022



(caption on next page)

Fig. 1. A, B) Upper (A) and lower (B) chest computed tomography (CT) axial image before hospitalization. A few diffuse ground glass opacities (yellow arrow heads) in the both lungs. C) Coronal ^{18}FDG-PET-CT image before hospitalization. D) Coronal ^{99m}Tc-MAA lung perfusion scintigraphy before steroid therapy. ^{18}FDG accumulation area and ^{99m}Tc-MAA defects area were matched (yellow arrows). E, F) Axial ^{18}FDG-PET-CT before (E) and after (F) R–CHOP with methotrexate intrathecally. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

lung primary or predominant form of IVLBCL is extremely rare with poor prognosis. Although the diagnosis of lung IVLBCL is often determined by transbronchial lung biopsies (TBLB), we must pay attention to hypoxemia because of the presence of tumor in the pulmonary capillaries. There had been no appropriate therapeutic guideline for IVLBCL because prospective trials are absent due to rarity of IVLBCL. The cyclophosphamide, doxorubicin, vincristine, and prednisolone with rituximab (R–CHOP) regimens had been weakly recommended for IVLBCL based on several case reports [2,3]. Recently, R–CHOP regimens combined with methotrexate intrathecally, phase 2 trial, has been reported [4].

Here, we report a rare case of lung IVLBCL developed with respiratory failure successfully rescued by prednisolone prior to definite diagnosis. Further, to the best of our knowledge, this is the first report showing the defects of 99m-Technetium macroaggregated albumin (^{99m}Tc-MAA) in lung perfusion scintigraphy were consistent with the distribution of high uptake of 18-fluoro deoxy glucose (^{18}FDG)-positron emission tomography (PET) on both lungs in IVLBCL. This suggest that the hypoxemia might have been caused by the tumor embolism.

2. Case presentation

A 56-year-old man complained dyspnea, fatigue and fever for one month, and was referred to our hospital. Although he had the past history of mild asthma, his dyspnea was not improved by asthma therapy. He had normal physical findings including breath sounds and no murmurs. Percutaneous oxygen saturation (SpO_2) was 94% (room air), and body temperature was 37.2 °C on admission. Blood test showed slight leukopenia (white blood cell count 3580 cells/μL) and thrombocytopenia (100,000 cells/μL). No atypical cells were detected in the peripheral blood. The levels of serum LDH (1416 U/L) and soluble interleukin 2 receptor (sIL-2R; 1744 U/mL) were remarkably elevated. His renal function, total protein, and coagulation were normal. Arterial blood gases revealed hypoxemia (PaO_2 63.2 mmHg) and hypocapnia (PCO_2 31.7 mmHg) at room air. Lung functions by spirometry showed normal, but diffusion lung capacity for carbon monoxide (DLco: 12.67 ml/min/mmHg, %DLco: 54.4%) was decreased. HRCT showed only faint ground-glass opacities in the middle and lower lung fields without lymph node swelling (Fig. 1A and B). PET-CT showed diffuse and remarkably high ^{18}FDG uptake on both upper lungs (Fig. 1C) without uptake of lymph nodes or other organs.

On the 2nd day after admission, he underwent the bronchoscopy for TBLB. After the lung biopsies, severe hypoxemia with stridor suddenly occurred. There was no pneumothorax, no active bleeding and no skin rash. Because he had a past history of asthma, we considered that rapid hypoxemia was caused by bronchospasm and/or laryngospasm then. We immediately added intravenous hydrocortisone 200 mg, antihistamine and high dose of oxygen, and finished the examination. However, since hypoxemia prolonged after the bronchoscopy, oxygen therapy of 5L/min with a nasal canula was continued, and we speculated the possibility of hypoxemia due to tumor embolism or pulmonary thromboembolism. On the 3rd day, he underwent lung perfusion scintigraphy. ^{99m}Tc-MAA defects were consistent with ^{18}FDG accumulation in both upper lobes (Fig. 1C and D) but not wedge-shaped defect. These data suggested that his desaturation was caused by IVL cell embolism. Judging from hypoxemia and the disease characteristics, we had decided rescue treatment. Considering that sufficient lung tissues had already been obtained by TBLB, we started prednisolone 50 mg per day based on therapeutic dose of lymphoma. After the treatment for ~10 days, the desaturation of oxygen and his dyspnea were gradually improved,

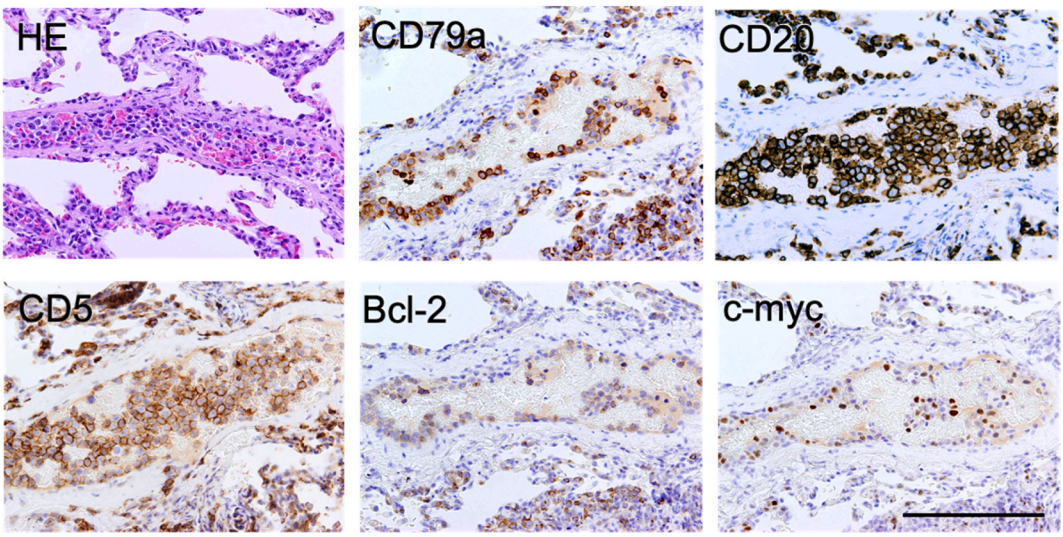


Fig. 2. Hematoxylin and eosin staining and immunohistochemistry staining against CD79a, CD20, CD5, Bcl-2, and c-myc of lung biopsy. Scale bar: 200μm.

and the levels of LDH and sIL-2R were slightly decreased (Supplemental table). Later, histology of biopsy specimens stained with hematoxylin and eosin revealed that atypical large cells were clearly shown in the lumina of lung capillaries but not extra capillaries. Immunohistochemical examination showed that these atypical large cells were positive to CD79a, CD20, CD5, Bcl-2, and c-myc (Fig. 2). On the 11th day, he was definitely diagnosed with lung IVLBCL, because there were weak findings of lymphoma cells in bone marrow and random skin biopsies. On the 14th day, he started R–CHOP combination with intrathecal methotrexate therapy. After eight cycles of R–CHOP combination with three times of intrathecal methotrexate, sIL-2R and LDH levels were normalized, and lung ^{18}FDG accumulation in PET-CT completely disappeared (Fig. 1E and F), achieving complete metabolic remission.

3. Discussion

IVLBCL is described as intravascular large B-cell lymphoma, and is a subtype of extra nodal diffuse large B-cell lymphoma. World Health Organization (WHO) classification defined IVLBCL is a rare type of cutaneous B cell lymphoma characterized by the selective growth of lymphoma cells particularly in the capillaries of organs [5]. IVLBCL provokes fever of unknown origin, sweats, fatigue, and weight loss. Approximately 30% of IVLBCL patients involve lung lesion. Here, we have experienced a case of lung IVLBCL with hypoxemia which was diagnosed as tumor embolization by distribution of ^{18}FDG and ^{99m}Tc-MAA. Furthermore, we successfully rescued the hypoxemia by corticosteroid prior to definite diagnosis.

In our case, defect of ^{99m}Tc-MAA area was not wedge-shaped but concordant with ^{18}FDG accumulation (Fig. 1C and D). These findings suggested that the cause of hypoxemia was not pulmonary thromboembolism but tumor occlusion in pulmonary blood vessels. Although diffuse deficiency by ^{99m}Tc-MAA lung perfusion scintigraphy is previously reported in cases of IVL [6,7], our case suggested that combination of ^{18}FDG-PET and ^{99m}Tc-MAA lung perfusion scintigraphy was useful to diagnose the cause of hypoxemia in IVL patient. Furthermore, as ^{18}FDG accumulation on lungs (Fig. 1E) were completely disappeared after chemotherapy (Fig. 1F), ^{8}FDG-PET was very useful to evaluate the therapeutic effect.

It is known to be useful to diagnose lung IVL by transbronchial lung biopsy [3,8–10], but others reported that TBLB could not be performed because of hypoxemia during examination [11]. Since lung primary or predominant form of IVLBCL has poor prognosis [12, 13], early diagnosis is needed. Since random skin biopsies and bone marrow biopsies are safer and more non-invasive, these approaches are firstly recommended. Meanwhile, TBLB is useful for a definite diagnosis of lung IVLBCL. In our case, as ^{18}FDG accumulation was localized to only lungs on PET-CT, we selected TBLB for histological diagnosis. As a result, lymphoma cells were clearly seen in vessels collected from lungs (Fig. 2), whereas there were few histological findings in the biopsies from skin and bone marrow. However, we need pay attention to the risk of hypoxemia when performing bronchoscopy.

Approximately 80% of IVLBCL cases receive systemic chemotherapy including corticosteroids such as CHOP or R–CHOP [2] after definite diagnosis. Recently, combination with intrathecal methotrexate injection has been reported [4]. Prednisolone is known to induce lymphocyte apoptosis and inhibit lymphocyte mobilization [14, 15]. Although there is no evidence of corticosteroid rescue for desaturation of oxygen due to IVLBCL, corticosteroid was effective in our case, and the patient was able to receive complete chemotherapies.

In conclusion, we experienced a rare case of lung IVLBCL developed with hypoxemia diagnosed by combination of ^{18}FDG-PET CT and ^{99m}Tc-MAA perfusion scintigraphy, and succeeded in rescuing him by administrating corticosteroids empirically prior to definite diagnosis.

Declaration of competing interest

The authors declare that no conflicts of interest related to the publication.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2022.101625.

References

[1] S. Sh, C. E, H. Nl, J. Es, P. Sa, S. H, T. J, in: fourth ed.WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues, Revised, vol. 2, IARC, Lyon, France, 2017, pp. 317–318.
[2] T. Takeshige, N. Harada, Y. Sekimoto, R. Kanemaru, T. Tsutsumi, K. Matsuno, S. Shiota, A. Masuda, A. Gotoh, M. Asahina, T. Uekusa, K. Takahashi, Pulmonary intravascular large B-cell lymphoma (IVLBCL) disguised as an asthma exacerbation in a patient with asthma, Intern. Med. 56 (14) (2017) 1885–1891.
[3] M. Ponzoni, E. Campo, S. Nakamura, Intravascular large B-cell lymphoma: a chameleon with multiple faces and many masks, Blood 132 (15) (2018) 1561–1567.
[4] K. Shimada, M. Yamaguchi, Y. Atsuta, K. Matsue, K. Sato, S. Kusumoto, H. Nagai, J. Takizawa, N. Fukuhara, K. Nagafuji, K. Miyazaki, E. Ohtsuka, M. Okamoto, Y. Sugita, T. Uchida, S. Kayukawa, A. Wake, D. Ennishi, Y. Kondo, T. Izumi, Y. Kin, K. Tsukasaki, D. Hashimoto, M. Yuge, A. Yanagisawa, Y. Kuwatsuka, S. Shimada, Y. Masaki, N. Niitsu, H. Kiyoi, R. Suzuki, T. Tokunaga, S. Nakamura, T. Kinoshita, Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone combined with high-dose methotrexate plus intrathecal chemotherapy for newly diagnosed intravascular large B-cell lymphoma (PRIMEUR-IVL): a multicentre, single-arm, phase 2 trial, Lancet Oncol 21 (4) (2020) 593–602.
[5] R. Willemze, L. Cerroni, W. Kempf, E. Berti, F. Facchetti, S.H. Swerdlow, E.S. Jaffe, The 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas, Blood 133 (16) (2019) 1703–1714.
[6] M. Martusewicz-Boros, E. Wiatr, E. Radzikowska, K. Roszkowski-Sliz, R. Langfort, Pulmonary intravascular large B-cell lymphoma as a cause of severe hypoxemia, J. Clin. Oncol. 25 (15) (2007) 2137–2139.
[7] C. Colavolpe, M. Ebbo, D. Trousse, H. Khibri, J. Franques, B. Chetaille, D. Coso, M.J. Ouvrier, L. Gastaud, E. Guedj, N. Schleinitz, FDG-PET/CT is a pivotal imaging modality to diagnose rare intravascular large B-cell lymphoma: case report and review of literature, Hematol. Oncol. 33 (2) (2015) 99–109.

[8] K. Wakamatsu, M. Komori, N. Nagata, H. Kumazoe, A. Kajiki, Y. Kitahara, [Two cases of intravascular lymphomatosis diagnosed by transbronchial lung biopsy], Nihon Kokyuki Gakkai Zasshi 47 (10) (2009) 875–880.
[9] K. Takamura, Y. Nasuhara, T. Mishina, T. Matsuda, M. Nishimura, Y. Kawakami, M. Fujita, C. Mikuni, K. Yamashiro, Intravascular lymphomatosis diagnosed by transbronchial lung biopsy, Eur. Respir. J. 10 (4) (1997) 955–957.
[10] Y. Taura, H. Yamazaki, T. Katou, [Two cases of intravascular lymphomatosis diagnosed antemortem by transbronchial lung biopsy], Nihon Kokyuki Gakkai Zasshi 38 (1) (2000) 34–38.
[11] H.J. Bae, G.R. Chon, D.J. Kim, S.H. Lee, J.Y. Ahn, A case of intravascular large B-cell lymphoma of lung presenting with progressive multiple nodules on chest computed tomography, Respir. Med. Case Rep. 21 (2017) 108–112.
[12] Z. Zhou, L.H. Sehn, A.W. Rademaker, L.I. Gordon, A.S. Lacasce, A. Crosby-Thompson, A. Vanderplas, A.D. Zelenetz, G.A. Abel, M.A. Rodriguez, A. Nademanee, M.S. Kaminski, M.S. Czuczman, M. Millenson, J. Niland, R.D. Gascoyne, J.M. Connors, J.W. Friedberg, J.N. Winter, An enhanced International Prognostic Index (NCCN-IPI) for patients with diffuse large B-cell lymphoma treated in the rituximab era, Blood 123 (6) (2014) 837–842.
[13] J.J. Castillo, E.S. Winer, A.J. Olszewski, Sites of extranodal involvement are prognostic in patients with diffuse large B-cell lymphoma in the rituximab era: an analysis of the Surveillance, Epidemiology and End Results database, Am. J. Hematol. 89 (3) (2014) 310–314.
[14] S. Greenstein, K. Ghias, N.L. Krett, S.T. Rosen, Mechanisms of glucocorticoid-mediated apoptosis in hematological malignancies, Clin. Cancer Res. 8 (6) (2002) 1681–1694.
[15] J.A. Burger, E. Montserrat, Coming full circle: 70 years of chronic lymphocytic leukemia cell redistribution, from glucocorticoids to inhibitors of B-cell receptor signaling, Blood 121 (9) (2013), 1501-9.