

World Journal of *Clinical Cases*

World J Clin Cases 2021 February 16; 9(5): 999-1246



Contents

Thrice Monthly Volume 9 Number 5 February 16, 2021

MINIREVIEWS

- 999 Remote nursing training model combined with proceduralization in the intensive care unit dealing with patients with COVID-19

Wang H, Kang K, Gao Y, Yang B, Li J, Wang L, Bi Y, Yu KJ, Dai QQ, Zhao MY

ORIGINAL ARTICLE

Case Control Study

- 1005 Metabolic syndrome, ApoE genotype, and cognitive dysfunction in an elderly population: A single-center, case-control study

Wang JY, Zhang L, Liu J, Yang W, Ma LN

- 1016 Serum neuron-specific enolase: A promising biomarker of silicosis

Huang HB, Huang JL, Xu XT, Huang KB, Lin YJ, Lin JB, Zhuang XB

Retrospective Study

- 1026 Biochemical recurrence of pathological T2+ localized prostate cancer after robotic-assisted radical prostatectomy: A 10-year surveillance

Yang CH, Lin YS, Ou YC, Weng WC, Huang LH, Lu CH, Hsu CY, Tung MC

Observational Study

- 1037 Clinical characteristics of perineal endometriosis: A case series

Liang Y, Zhang D, Jiang L, Liu Y, Zhang J

- 1048 Safety of gastrointestinal endoscopy in patients with acute coronary syndrome and concomitant gastrointestinal bleeding

Elkafrawy AA, Ahmed M, Alomari M, Elkaryoni A, Kennedy KF, Clarkston WK, Campbell DR

SYSTEMATIC REVIEWS

- 1058 Clinical features of SARS-CoV-2-associated encephalitis and meningitis amid COVID-19 pandemic

Huo L, Xu KL, Wang H

CASE REPORT

- 1079 Neuropathy and chloracne induced by 3,5,6-trichloropyridin-2-ol sodium: Report of three cases

Ma Y, Cao X, Zhang L, Zhang JY, Qiao ZS, Feng WL

- 1087 Effect of rifampicin on anticoagulation of warfarin: A case report

Hu YN, Zhou BT, Yang HR, Peng QL, Gu XR, Sun SS

- 1096 Severe lumbar spinal stenosis combined with Guillain-Barré syndrome: A case report

Xu DF, Wu B, Wang JX, Yu J, Xie JX

- 1103** Treatment of pediatric intracranial dissecting aneurysm with clipping and angioplasty, and next-generation sequencing analysis: A case report and literature review
Sun N, Yang XY, Zhao Y, Zhang QJ, Ma X, Wei ZN, Li MQ
- 1111** Imaging characteristics of a rare case of monostotic fibrous dysplasia of the sacrum: A case report
Liu XX, Xin X, Yan YH, Ma XW
- 1119** Primary aldosteronism due to bilateral micronodular hyperplasia and concomitant subclinical Cushing's syndrome: A case report
Teragawa H, Oshita C, Orita Y, Hashimoto K, Nakayama H, Yamazaki Y, Sasano H
- 1127** Management of corneal ulceration with a moisture chamber due to temporary lagophthalmos in a brain injury patient: A case report
Yu XY, Xue LY, Zhou Y, Shen J, Yin L
- 1132** Bronchoscopy for diagnosis of COVID-19 with respiratory failure: A case report
Chen QY, He YS, Liu K, Cao J, Chen YX
- 1139** Pembrolizumab as a novel therapeutic option for patients with refractory thymic epithelial tumor: A case report
Wong-Chong J, Bernadach M, Ginzac A, Veyssière H, Durando X
- 1148** Successful bailout stenting strategy against rare spontaneous retrograde dissection of partially absorbed magnesium-based resorbable scaffold: A case report
Liao ZY, Liou JY, Lin SC, Hung HF, Chang CM, Chen LC, Chua SK, Lo HM, Hung CF
- 1156** Chronic myelomonocytic leukemia-associated pulmonary alveolar proteinosis: A case report and review of literature
Chen C, Huang XL, Gao DQ, Li YW, Qian SX
- 1168** Obturator nerve impingement caused by an osteophyte in the sacroiliac joint: A case report
Cai MD, Zhang HF, Fan YG, Su XJ, Xia L
- 1175** Venetoclax in combination with chidamide and dexamethasone in relapsed/refractory primary plasma cell leukemia without t(11;14): A case report
Yang Y, Fu LJ, Chen CM, Hu MW
- 1184** Heterochronic triple primary malignancies with Epstein-Barr virus infection and tumor protein 53 gene mutation: A case report and review of literature
Peng WX, Liu X, Wang QF, Zhou XY, Luo ZG, Hu XC
- 1196** Negative conversion of autoantibody profile in chronic hepatitis B: A case report
Zhang X, Xie QX, Zhao DM
- 1204** Dumbbell-shaped solitary fibrous tumor in the parapharyngeal space: A case report
Li YN, Li CL, Liu ZH
- 1210** Spontaneous small bowel perforation secondary to *Vibrio parahaemolyticus* infection: A case report
Chien SC, Chang CC, Chien SC

- 1215** Management protocol for Fournier's gangrene in sanitary regime caused by SARS-CoV-2 pandemic: A case report
Grabińska A, Michalczyk Ł, Banaczyk B, Syryło T, Ząbkowski T
- 1221** Infective bicuspid aortic valve endocarditis causing acute severe regurgitation and heart failure: A case report
Hou C, Wang WC, Chen H, Zhang YY, Wang WM
- 1228** Endoscopic repair of delayed stomach perforation caused by penetrating trauma: A case report
Yoon JH, Jun CH, Han JP, Yeom JW, Kang SK, Kook HY, Choi SK
- 1237** Bilateral musculocutaneous neuropathy: A case report
Jung JW, Park YC, Lee JY, Park JH, Jang SH

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Dr. Antonio Corvino is a PhD in the Motor Science and Wellness Department at University of Naples "Parthenope". In 2008, he obtained his MD degree from the School of Medicine, Second University of Naples. Then, he completed a residency in Radiology in 2014 at University Federico II of Naples. In 2015, he undertook post-graduate training at Catholic University of Rome, obtaining the 2nd level Master's degree in "Internal Ultrasound Diagnostic and Echo-Guided Therapies". In 2016-2018, he served on the directive board of Young Directive of Italian Society of Ultrasound in Medicine and Biology. His ongoing research interests involve ultrasound and ultrasound contrast media in abdominal and non-abdominal applications, etc. (L-Editor: Filipodia)

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The WJCC is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2020 Edition of Journal Citation Reports® cites the 2019 impact factor (IF) for WJCC as 1.013; IF without journal self cites: 0.991; Ranking: 120 among 165 journals in medicine, general and internal; and Quartile category: Q3. The WJCC's CiteScore for 2019 is 0.3 and Scopus CiteScore rank 2019: General Medicine is 394/529.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Jia-Hui Li; Production Department Director: Yu-Jie Ma; Editorial Office Director: Jin-Lai Wang.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Dennis A Bloomfield, Sandro Vento, Bao-gan Peng

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

February 16, 2021

COPYRIGHT

© 2021 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Chronic myelomonocytic leukemia-associated pulmonary alveolar proteinosis: A case report and review of literature

Can Chen, Xi-Lian Huang, Da-Quan Gao, Yi-Wei Li, Shen-Xian Qian

ORCID number: Can Chen 0000-0001-9268-5323; Xi-Lian Huang 0000-0002-7076-9312; Da-Quan Gao 0000-0002-8780-2123; Yi-Wei Li 0000-0003-4871-1031; Shen-Xian Qian 0000-0002-6844-7277.

Author contributions: Huang XL proposed the research idea; Chen C, Gao DQ and Qian SX were involved in the case management; Chen C, Gao DQ and Li YW performed the literature search and selection; Huang XL, Chen C and Li YW drafted the manuscript; Huang XL and Qian SX critically reviewed the manuscript; All authors approved the final version of the manuscript.

Supported by The Medical and Health Technology Project of Zhejiang Province, No. 2018KY567; and the Hangzhou Municipal Science and Technology Development Program, No. 20142013A61.

Informed consent statement: Informed written consent was obtained from the patient for publication of this report and any accompanying images.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

CARE Checklist (2016) statement: The authors have read the CARE

Can Chen, Xi-Lian Huang, Da-Quan Gao, Shen-Xian Qian, Department of Hematology, Affiliated Hangzhou First People's Hospital, Zhejiang University School of Medicine, Hangzhou 310006, Zhejiang Province, China

Yi-Wei Li, Department of Intensive Care Unit, Affiliated Hangzhou First People's Hospital, Zhejiang University School of Medicine, Hangzhou 310006, Zhejiang Province, China

Corresponding author: Xi-Lian Huang, MD, PhD, Doctor, Department of Hematology, Affiliated Hangzhou First People's Hospital, Zhejiang University School of Medicine, No. 216 Huansha Road, Hangzhou 310006, Zhejiang Province, China. syxluang@163.com

Abstract

BACKGROUND

Pulmonary alveolar proteinosis (PAP) is a rare condition that can cause progressive symptoms including dyspnea, cough and respiratory insufficiency. Secondary PAP is generally associated with hematological malignancies including chronic myelomonocytic leukemia (CMML). To the best of our knowledge, this is the first reported case of PAP occurring secondary to CMML.

CASE SUMMARY

We report the case of a 63-year-old male who presented with a recurrent cough and gradually progressive dyspnea in the absence of fever. Based upon clinical symptoms, computed tomography findings, bone marrow aspiration, flow cytometry studies and cytogenetic analyses, the patient was diagnosed with PAP secondary to CMML. He underwent whole lung lavage in March 2016 to alleviate his dyspnea, after which he began combined chemotherapeutic treatment with decitabine and cytarabine. The patient died in January 2020 as a consequence of severe pulmonary infection.

CONCLUSION

This case offers insight regarding the mechanistic basis for PAP secondary to CMML and highlights potential risk factors.

Key Words: Pulmonary alveolar proteinosis; Chronic myelomonocytic leukemia; Diagnosis; Treatment; Prognosis; Case report

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Specialty type: Medicine, research and experimental

Country/Territory of origin: China

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

Received: October 16, 2020

Peer-review started: October 16, 2020

First decision: November 24, 2020

Revised: December 6, 2020

Accepted: December 16, 2020

Article in press: December 16, 2020

Published online: February 16, 2021

P-Reviewer: Kontos CK

S-Editor: Zhang L

L-Editor: Filipodia

P-Editor: Ma YJ



Core Tip: Pulmonary alveolar proteinosis secondary to chronic myelomonocytic leukemia is a rare disease that has been insufficiently studied to date. Herein, we report a case of pulmonary alveolar proteinosis secondary to chronic myelomonocytic leukemia and perform a comprehensive literature review. We also provide a framework for understanding the mechanistic basis of this disease. It is likely that pulmonary alveolar proteinosis symptoms can be alleviated by achieving primary disease control. Together, these findings may contribute to improvements in clinical practice.

Citation: Chen C, Huang XL, Gao DQ, Li YW, Qian SX. Chronic myelomonocytic leukemia-associated pulmonary alveolar proteinosis: A case report and review of literature. *World J Clin Cases* 2021; 9(5): 1156-1167

URL: <https://www.wjgnet.com/2307-8960/full/v9/i5/1156.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v9.i5.1156>

INTRODUCTION

Pulmonary alveolar proteinosis (PAP) is a rare condition wherein patients exhibit excessive surfactant accumulation within the pulmonary alveoli, resulting in progressive symptoms including dyspnea, cough and respiratory insufficiency. The overall incidence of PAP is 8.7 per million^[1]. It is classified into three categories: Idiopathic PAP (90% of total cases), secondary PAP (sPAP, less than 10% of total cases), and congenital PAP (2% of total cases). Cases of sPAP are most commonly associated with myelodysplastic syndrome (MDS), acute myelogenous leukemia (AML) and other hematological malignancies^[2,3], affecting an estimated 5.3% of individuals with such malignancies^[4]. The median age of MDS/sPAP onset is 51 years, and the most common symptoms include fever (45%), dyspnea on exertion (42%) and cough (42%)^[5]. The estimated 2-year survival rate for patients with sPAP complicating hematological disorders is 46%^[5].

Some evidence suggests that interactions between aspergillosis antigens may interact with lung surfactant to induce PAP. Granulocyte-macrophage colony-stimulating factor (GM-CSF) knockout mice or interleukin-3/GM-CSF/interleukin-5βc chain knockout mice also develop pulmonary involvement similar to that observed in the context of human PAP^[6]. This suggests that PAP may arise due to insufficient phospholipid clearance by pulmonary macrophages. In contrast to idiopathic PAP, congenital PAP may be due to a lack of macrophage-mediated surfactant clearance as a consequence of the deletion of the GM-CSF gene^[5]. However, sPAP is primarily due to conditions that alter alveolar macrophage numbers or functionality.

Chronic myelomonocytic leukemia (CMML) is an age-related disease characterized by impaired hematopoiesis and myeloid cell dysplasia owing to myeloid cell progenitors being hypersensitive to GM-CSF stimulation^[7]. It demonstrates a propensity to transform into AML and has long been considered a form of MDS. A variety of mechanisms may cause PAP in patients with hematologic malignancies including CMML. For example, prior work suggests that changes in cytokines capable of inhibiting GM-CSF synthesis such as IL-10 may cause PAP^[8]. Moreover, macrophages develop from monocyte precursors, consistent with the etiology of CMML and sPAP being associated with mononuclear cell abnormalities. There are very few reports to date of patients presenting with both sPAP and CMML. Herein, we describe a case of a patient suffering from both of these conditions, providing further evidence for the relationship between sPAP incidence and mononuclear cell abnormalities.

CASE PRESENTATION

Chief complaints

A 63-year-old male was admitted to our hospital in December 2015 for recurrent cough and gradually progressive dyspnea over the past 3 mo. The condition had become aggravated during the 2 wk prior to admission.

History of present illness

The patient first presented 5 years ago with a cough and dyspnea with exercise that improved with rest. He returned to the clinic for follow-up care at regular intervals. He was admitted to the emergency department due to the gradual aggravation of these symptoms 2 wk ago. Chest computed tomography (CT) scans revealed a pattern of acute bilateral interstitial pneumonia, and as such the patient required hospitalization.

History of past illness

The patient had a 20-year history of hypertension and had been taking amlodipine regularly.

Personal and family history

The patient was free of any known congenital disease.

Physical examination

Vital signs were within normal limits at the time of admission, with a heart rate of 106 bpm, blood pressure of 178/71 mmHg, a respiratory rate of 20 breaths/min and a temperature of 37.1 °C. His height was 175 cm, and his weight was 76 kg. Physical examination revealed audible bilateral crackling in the lungs.

Laboratory examinations

Hematological examination revealed a white blood cell count of $11.1 \times 10^9/L$, a hemoglobin level of 9.5 g/dL, a platelet count of $769 \times 10^9/L$, an absolute monocyte count of $3.8 \times 10^9/L$ and an absolute eosinophil count of $0.3 \times 10^9/L$.

Bronchoalveolar lavage fluid (BALF) appeared light and milky, and differential BALF cell counts revealed the presence of 82% lymphocytes, 11% monocytes and 7% neutrophils. Arterial blood gas analyses under ambient air were performed in an effort to identify the causes of cough and dyspnea, revealing both hypoxemia and hypocapnia. Histological analyses exhibited the thickening of the alveolar septum with fiber hyperplasia, vasodilation, congestion and the infiltration of histiocytes and inflammatory cells. Samples were positive for periodic acid-Schiff staining, and flow cytometry analyses were performed as previously described^[9], revealing an elevated frequency of monocytes in the BALF samples (12.4%) with CD33+ CD14+ CD300e+ mature monocytes accounting for 4% of nucleated cells and CD33+ CD14- CD300e+ partially immature monocytes accounting for 8.4% of nucleated cells (Figure 1A).

To better understand the complete blood count abnormalities observed in this patient, we additionally conducted bone marrow aspiration and biopsy. Marked monocytic (30%) hyperplasia was detected with 7.4% monocytic blasts, while myeloid blasts were within the normal range (0.5%). Flow cytometry analyses of bone marrow samples additionally revealed elevated frequencies of monocytes (44% of nucleated cells) and of CD33^{bright} CD14- CD300e+ immature monocytes (7.4% of nucleated cells) (Figure 1B). Samples were negative for BCR/ABL, PDGFRA or PDGFRB cytogenetic aberrations but were positive for JAK2-V617F. CMML molecular studies revealed the presence of synonymous ASXL and SRSF mutations without any corresponding TET2 mutations. These examinations were performed as previously described^[9]. Karyotyping revealed the inversion of chromosome 6.

Imaging examinations

Ultrasonographic analyses revealed mild splenomegaly. High creatinine levels were also detected. CT scans identified bilateral regions of ground-glass opacity (GGO) in the lungs of this patient (Figure 2A). Lung function tests revealed moderate reductions in the diffusing capacity of the lungs for carbon monoxide.

FINAL DIAGNOSIS

The patient was diagnosed with CMML-1 without eosinophilia, and his revised International Prognostic Scoring System score was 3 points.

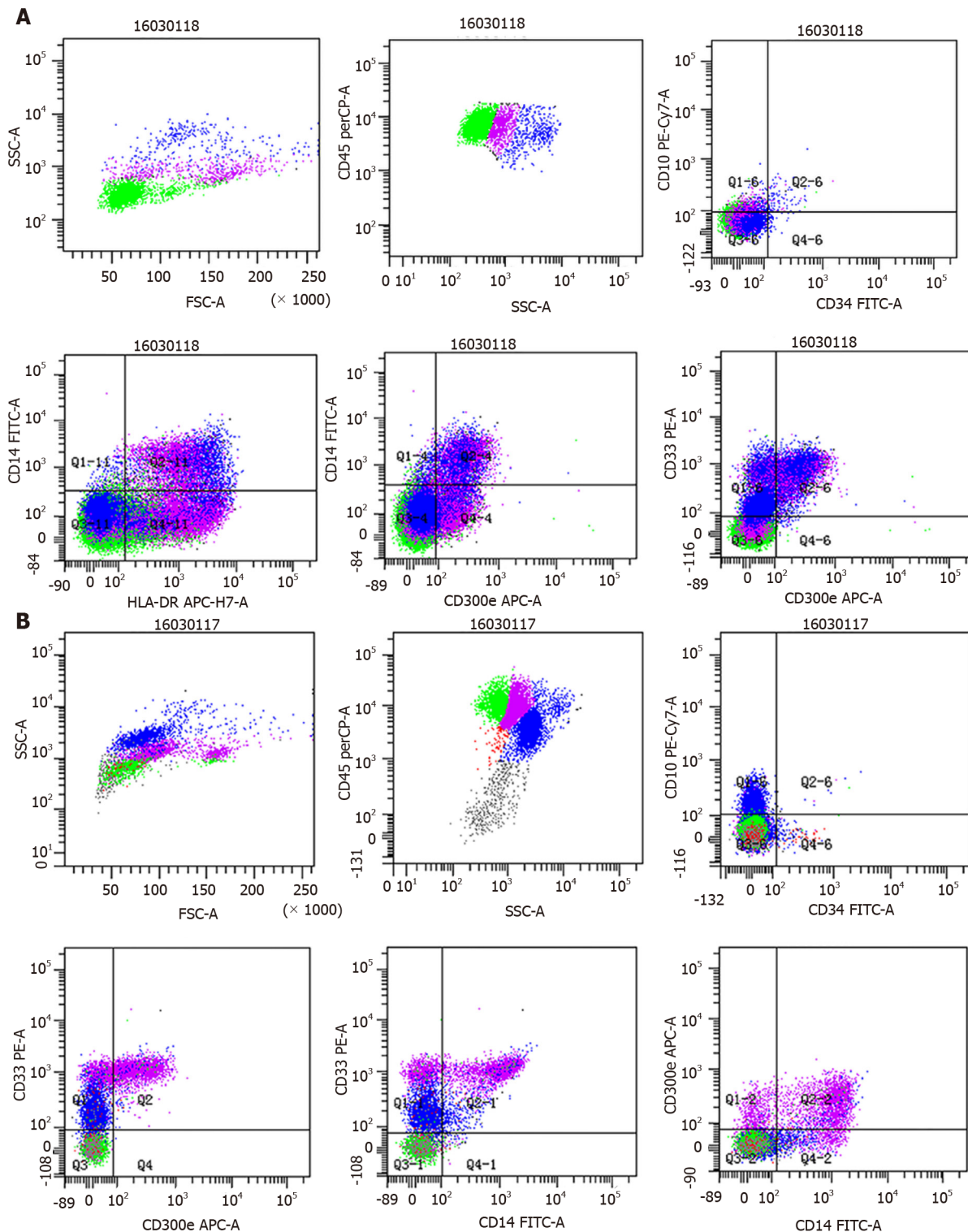


Figure 1 Flow cytometry analyses of patient bronchoalveolar lavage and bone marrow. A: Bronchoalveolar lavage fluid samples were analyzed via flow cytometry, revealed an increased proportion of monocytes (12.4%, purple), CD33+ CD14+ CD300e+ mature monocytes accounted for approximately 4% of nucleated cells, and CD33+ CD14- CD300e+ partially immature monocyte accounted for 8.4% of nucleated cells; B: Flow cytometry studies of bone marrow samples revealed an increased proportion of monocytes (purple) that accounted for 44% of nucleated cells, and CD33^{bright} CD14- CD300e+ immature monocytes accounted for approximately 7.4% of nucleated cells.

TREATMENT

The patient underwent whole lung lavage in March 2016 to alleviate his dyspnea, after which he began combined chemotherapeutic treatment with decitabine (30 mg qd for 5 d) and cytarabine (30 mg qd for 14 d). His white blood cell counts rapidly declined, and bronchoalveolar lavage was no longer required after one cycle of chemotherapy. This therapeutic regimen was maintained, and the patient underwent six total cycles of

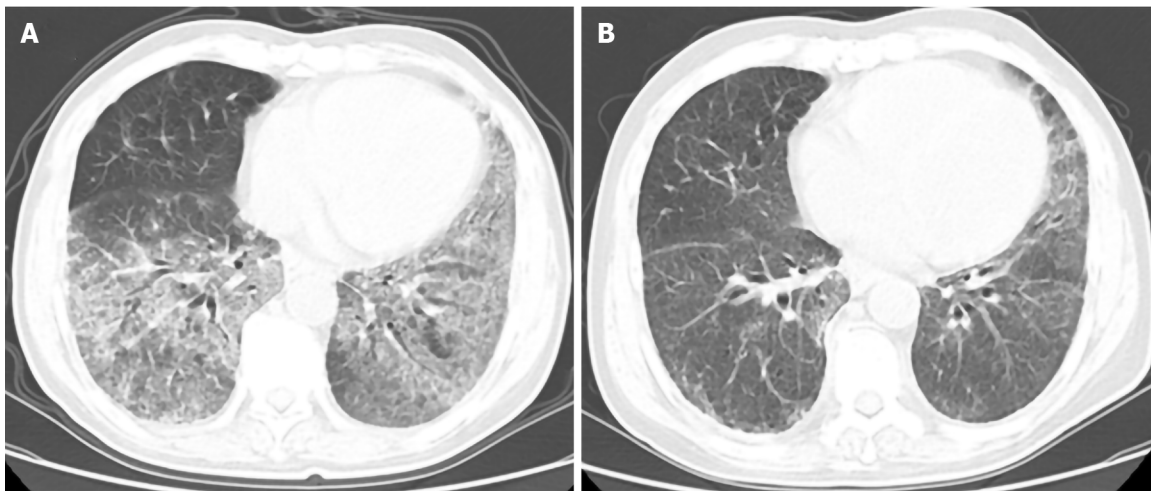


Figure 2 Lung computed tomography findings before and after treatment. A: Computed tomography scans revealed bilateral regions of ground-glass opacity in the lungs before treatment; B: Computed tomography scans revealed good responses to treatment.

monthly chemotherapy. During cycles 2-4 of treatment, the patient developed anemia that progressed from moderate to severe, while his platelet counts rose to $(700-1000) \times 10^9/L$. Subsequent bone marrow biopsy was indicative of myelofibrosis. The patient was then treated for 2 mo with ruxolitinib without any response.

OUTCOME AND FOLLOW-UP

After five cycles of chemotherapy, a lung CT scan was performed to assess sPAP status in this patient, revealing marked improvements in analyzed lung abnormalities (Figure 2B). The patient required transfusion therapy 1-2 times per month followed by maintenance iron removal therapy.

From January 2018 through April 2019, the patient accepted an additional eight cycles of combined azacitidine and cytarabine treatment. At 2 mo following the final round of chemotherapy, the disease had progressed to CMML-2 with 16% blasts in the peripheral blood. Treatment with a Bcl-2 inhibitor was recommended, but the patient was unable to accept this treatment for financial reasons. The patient died in January 2020 as a consequence of severe pulmonary infection.

DISCUSSION

PAP is a rare pulmonary disorder wherein patients exhibit alveolar surfactant-derived lipoprotein accumulation that can cause symptoms ranging from mild shortness of breath to severe respiratory distress. Patients suffering from PAP may exhibit impaired phagocytosis, chemotaxis or phagolysosomal fusion with defective surfactant clearance being linked to impaired alveolar macrophage functionality^[10-12]. In mice, GM-CSF or GM-CSF/IL-3/IL-5-receptor common β chain defects result in the development of a PAP-like syndrome, and β c-chain defects impairing GM-CSF receptor expression on circulating mononuclear cells have been detected in those with congenital PAP^[13]. Patients with idiopathic PAP have also been found to exhibit serum and BALF neutralizing antibodies specific for GM-CSF, whereas these are not evident in those with sPAP^[14]. This indicates that idiopathic PAP is a form of autoimmune disease and that measuring anti-GM-CSF titers can differentiate between sPAP and idiopathic PAP^[15].

PAP is reported to affect approximately 8.7 per million persons, with sPAP secondary to MDS affecting fewer than 1 per million persons^[16]. Hematologic malignancies are the most common underlying cause of sPAP^[17], with PAP secondary to hematologic malignancy being associated with a range of conditions among which hematological malignancies of myeloid origin are the most common^[17-19]. In prior studies, MDS was identified as the underlying disease most often associated with PAP secondary to hematologic malignancy, accounting for 16% of such cases^[10]. As sPAP secondary to MDS is very rare, only a limited number of case reports and small case

series have been published to date. In total, 65 such cases have been reported to date as noted in Table 1^[9,20-30] with ages ranging from 18-75-years-old and with a male/female ratio of 27/38. Of the eleven cases of PAP diagnosed prior to MDS, only four, including the present case, were diagnosed as PAP coinciding with MDS. For all secondary cases, PAP likely occurred as a consequence of disease progression.

Several factors are potentially associated with the development of PAP secondary to MDS. Monocytes can be separated into three primary subtypes *via* flow cytometry: classical (CD14⁺/CD16⁻, MO1), intermediate (CD14⁺/CD16⁺, MO2) and nonclassical (CD14^{dim}/CD16⁺, MO3). Normally, classical monocytes account for 94% of total circulating monocytes, and an MO1 frequency $\geq 94\%$ can be used to differentiate between CMML and reactive monocytosis with over 90% sensitivity and specificity^[31]. Circulating nonclassical monocyte frequencies are elevated in the context of a range of conditions including sepsis, human immunodeficiency virus infection or cancer. Yoshioka *et al.*^[23] reported a case of MDS and sPAP in a patient exhibiting elevated CD14^{dim}CD16⁺ monocyte counts, suggesting that these nonclassical monocytes may influence the development of pulmonary lesions in PAP patients. However, further studies of additional patients will be required to fully resolve the role of these nonclassical monocytes in PAP secondary to MDS.

Several chromosomal abnormalities have been linked to PAP secondary to MDS, with trisomy 8 being the most common karyotypic finding in these patients^[27]. Four of the seven reported cases of trisomy 8 in patients with sPAP and MDS were associated with Behçet's disease (BD), while two of these seven patients were diagnosed with inflammatory bowel disease. One prior meta-analysis detected high frequencies of intestinal lesions (66%) and trisomy 8 (80%) in patients with MDS complicated by confirmed or suspected BD^[28]. Immunosuppressive treatment of BD has the potential to cause sPAP and/or MDS, although such drugs were not used in the majority (2/3) of previously reported cases. BD and inflammatory bowel disease are both autoimmune diseases, and as such sPAP and MDS may also arise as a consequence of autoimmune diseases not secondary to immunosuppressive drug use. As trisomy 8 only affects 10%-15% of patients with MDS, this condition may be linked to a high risk of autoimmune diseases or PAP.

A karyotype analysis of the patient in the present case report revealed the inversion of chromosome 6, which is associated with myeloid neoplasms but has not been previously reported in the context of MDS complicated by sPAP. No gene abnormalities were found to be associated with CMML in this patient. GATA2 deficiency has recently been described as a condition resulting from heterozygous mutations and consequent GATA2 haploinsufficiency, resulting in a range of clinical manifestations including virus infections, CMML, MDS or AML^[29]. Spinner *et al.*^[29] conducted a systematic review of 57 patients with GATA2 deficiency and found that 84%, 14% and 8% suffered from MDS, AML and CMML, respectively. The 10 patients with biopsy-confirmed PAP in their study did not exhibit autoantibodies specific for GM-CSF, and GATA2 mutation status was not assessed for this patient owing to laboratory limitations. GATA2 is a zinc finger transcription factor that serves as a key regulator of hematopoietic cell gene expression^[32] while also regulating alveolar macrophage phagocytosis^[33]. Patients with a GATA2 deficiency are more susceptible to both MDS and PAP. As there were no reductions in alveolar macrophage counts in the BALF of these patients, this may suggest that there is a functional defect in these alveolar macrophages thus explaining the link between PAP and hematologic malignancies^[32].

Unlike other forms of lung disease, PAP has been studied only rarely and is often only diagnosed upon postmortem examination^[10]. In the present case, the patient presented with dyspnea. Owing to the detection of leukocytosis, pulmonary infection was first considered as a possible diagnosis. Following a systematic evaluation, the diagnosis of PAP was confirmed after BALF examination. While dry cough and dyspnea were consistent with PAP, they were nonspecific findings. PAP can be difficult to differentiate from infections *via* chest X-ray, and even following chest CT-mediated detection of GGO regions it was difficult to exclude leukemic infiltration or noncardiogenic edema.

In general, leukemia infiltration is more likely to present with smooth or nodular thickening of the bronchovascular bundles^[34]. Nodular disease can also present with prelymphatic, GGO, centrilobular or random radiological patterns^[35]. As sensitive or specific biomarkers of this condition are lacking, invasive approaches such as lung biopsy, BAL or bronchoscopy are necessary in order to definitively diagnose PAP. Most patients suffering from hematologic malignancies exhibit severe thrombocytopenia, potentially precluding the implementation of these invasive procedures. Given that our patient presented with GGO findings upon chest CT scan

Table 1 Clinical characteristics of published cases of secondary pulmonary alveolar proteinosis associated with myelodysplastic syndrome in adults

Order	Diagnosis	Case number	Age/Gender	Duration from MDS to PAP	Treatment	Anti-GM-CSF Ab	Concomitant disease	Chromosomal abnormality	Genetic abnormality	Survival time after PAP	Outcome	Survival time after MDS	Ref.
1	MDS	1	39/M	1 yr after MDS	NA	NA	Pulmonary fungus	NA	NA	Shortly	Died	1 yr	[21]
2	MDS	1	65/F	Coincidence	Methylprednisolone and GM-CSF	NA	None	NA	NA	Shortly	Died	Shortly	[21]
3	RA deteriorated into AL after 2 yr	1	27/M	1 yr after AL	Antibiotics and anti-tuberculosis agents	NA	None	NA	NA	4 mo	Died	3 yr	[10]
4	RA deteriorated into AL after 1 yr	1	65/F	1 mo after AL	Fluconazole and miconazole	NA	Pulmonary fungus	NA	NA	1 mo	Died	1 yr	[10]
5	RAEB-T	1	52/F	2 yr after RAEB-T	Amphotericin B	NA	Pulmonary fungus	NA	NA	4 mo	Died	1 yr	[10]
6	RA deteriorated into AL within 1 yr	1	70/M	1 yr after AL	Chemotherapy	NA	Malignant melanoma	NA	NA	4 mo	Died	2 yr	[10]
7	RA deteriorated into RAEB after 12 yr	1	50/M	Coincidence with RAEB	Prednisolone	Negative	Hypereosinophil	46, XY, -1,-14,+2mar ^[1] and 46, XY ^[3] at first diagnosis and 47, XY, add (1)(p11), +add(1), t(1;19)(q11;q11), -14, +mar at disease progression	NA	2 yr	Alive	14 yr	[22]
8	MDS	1	66/M	12.5 yr	Prednisolone and amobroxol	Negative	NA	47, XY, add(1)(p11), +add(1),t(1;19)(p10; q10), -14, +mar1[20/20]	NA	NA	NA	NA	[23]
9	MDS	1	47/M	2 yr	NA	Negative	NA	NA	NA	Shortly	Died	2 yr	[24]
10	MDS-RA deteriorated into RAEB after 9 yr	1	36/M	1 yr after RAEB	Cord blood transplantation and GM-CSF	Negative	None	NA	NA	1 yr	Alive	11 yr	[25]
11	MDS	1	39/F	NA	BAL	NA	NA	NA	NA	NA	Alive	NA	[8]
12	MDS-RA deteriorated into RAEB after 1 yr	1	48/M	1 yr with RAEB	WLL	Negative	None	47, XY, +8	NA	2 r	Alive	3 yr	[26]
13	RCMD	1	41/F	3 yr	Prednisolone and antibiotics	NA	None	46, XX, -20; der (20)del (20)(q11q13) idic(20) (p11), or idic(20q-)	NA	7 mo	Died	4 yr	[4]
14	MDS-RA	1	34/M	1 yr	Unrelated bone marrow	Negative	IBD	47, XY, +8	NA	1 yr	Alive	3 yr	[27]

					transplantation								
15	MDS-RAEB	1	42/F	4 mo before RAEB	Unrelated cord blood transplantation.	Negative	IBD	47, XX, +8	NA	4 mo	Died	Shortly	[27]
16	MDS-RAEB	1	52/F	8 yr before RAEB	Unrelated bone marrow transplantation	Negative	BD and IBD	47, XX, +8	NA	10 yr	Alive	2 yr	[27]
17	MDS	1	34/M	2 yr before MDS	BAL	NA	NA	NA	NA	NA	NA	NA	[17]
18	MDS-MLD	1	38/M	NA	NA	Negative	NA	NA	NA	NA	Died	< 2 yr	[15]
19	MDS-SLD	1	26/M	NA	NA	Negative	NA	NA	NA	NA	Died	< 2 yr	[15]
20	MDS-U	1	37/M	NA	NA	Negative	NA	NA	NA	NA	Died	< 2 yr	[15]
21	MDS-EB	1	33/M	NA	NA	Negative	NA	NA	NA	NA	Died	< 2 yr	[15]
22	Very low + low MDS	13	Age: 45 (30-67); Gender: 7 M/6 F	MDS to sPAP: 0 to 168 mo 2 case before	NA	Negative	NA	Good: 2; Intermediate: 11	NA	13 mo	7 Died; 6 Alive	NA	[5]
34	Inter-high + very high	18	Age: 50 (27-57); Gender: 12 M/6 F	MDS to sPAP: 0 to 228 mo 6 cases before	NA	Negative	NA	Intermediate: 13; Poor: 5	NA	15 mo	10 Died; 8 Alive	NA	[5]
51	MDS-U deteriorated into RCMD after 11 mo and deteriorated into RAEB-1 after 13 mo	1	75/F	Coincidence with RAEB1	Prednisolone	Negative	Organizing pneumonia	Normal karyotype	NA	6 mo	Died	19 mo	[16]
52	MDS-RA	1	46/F	3 yr	Steroid pulse, cyclosporine A and infliximab	NA	BD and myelofibrosis	Trisomy 8	NA	30 mo	Died	66 mo	[28]
53	MDS-RA	1	31/M	2 yr	Steroid	NA	BD	Trisomy 8	NA	2 mo	Died	2 yr	[28]
54	MDS-RAEB2	1	50/F	Coincidence with RAEB	WLL	NA	BD	Trisomy 8	NA	2 yr	Alive	2 yr	[28]
55	MDS	1	40/M	NA	Stem cell transplantation	NA	NA	NA	NA	NA	Alive	NA	[19]
56	MDS	1	51/F	NA	NA	Negative	LGL, metastatic melanoma, DVT	Normal karyotype	GATA2	NA	Died	12 yr	[29]
57	MDS/AML	1	33/M	Less than 1 yr	NA	Negative	None	-7	GATA2	< 1 yr	Died	< 1 yr	[29]
58	MDS	1	26/F	Less than 1 yr	NA	Negative	Hypothyroidism	Normal karyotype	GATA2	< 1 yr	Died	< 1 yr	[29]
59	MDS	1	26/F	NA	NA	Negative	LGL, breast cancer,	Normal karyotype	GATA2	NA	Died	27 yr	[29]

miscarriage													
60	MDS/AML	1	19/F	NA	NA	Negative	LGL/DVT	Normal karyotype	GATA2	NA	Died	25 yr	[29]
61	MDS	1	28/M	NA	NA	Negative	None	Trisomy 8	GATA2	NA	Alive	6 yr	[29]
62	MDS	1	18/F	NA	NA	Negative	LGL, miscarriage	Normal karyotype	GATA2	NA	Died	31 yr	[29]
63	CMML	1	48/F	NA	NA	Negative	LGL, HT, Pancreatic cancer	Normal karyotype	GATA2	NA	Died	11 yr	[29]
64	MDS	1	59/F	Very soon	NA	Negative	NA	NA	GATA2	Shortly	Died	Shortly	[30]
65	CMML	1	63/M	Coincidence with CMML-1	Chemotherapy	NA	None	inv(6)	JAK2-V617F	5 yr	Died	5 yr	Current study

AL: Acute leukemia; AML: Acute myelogenous leukemia; BAL: Bronchoalveolar lavage; BD: Behçet's disease; CMML: Chronic myelomonocytic leukemia; DVT: Deep venous thrombosis; EB: Excess blasts; GM-CSF: Granulocyte-macrophage colony stimulation factor; HT: Hereditary thrombocythemia; IBD: Inflammatory bowel disease; LGL: Large granular lymphocyte; MDS: Myelodysplastic syndrome; MLD: Multilineage dysplasia; NA: Not available; PAP: Pulmonary alveolar proteinosis; RA: Refractory anemia; RAEB: Refractory anemia with excess blasts; RAEB-T: Refractory anemia with excess blasts in transformation; RCMD: Refractory cytopenia with multilineage dysplasia; SLD: Single lineage dysplasia; sPAP: Secondary pulmonary alveolar proteinosis; U: Unclassifiable; WLL: Whole lung lavage.

and had been diagnosed with CMML, further classification of his lung disease would have been challenging in the absence of invasive diagnostic evaluation. Fortunately, this patient was able to tolerate BAL treatment. As the patient was found to be negative for leukemic infiltration and periodic acid-Schiff staining was positive, a diagnosis of PAP was confirmed. Flow cytometry analyses of BALF samples further provided strong evidence of a model wherein sPAP is primarily a result of abnormal alveolar macrophage numbers and functionality. In patients with hematologic malignancies, sPAP is thought to be underestimated as a driver of respiratory failure^[9]. PAP should therefore be considered in the differential diagnosis when evaluating patients suffering from hematologic malignancies accompanied with pulmonary symptoms or abnormal radiographic findings^[11].

CMML treatment is challenging and is largely influenced by patient age, with hypomethylating agents such as 5-azacitidine and decitabine often being used in this therapeutic context. The patient in this report was treated with a low dose combination of cytarabine and decitabine with whole lung lavage and exhibited a good response to this treatment. After one cycle of treatment, the patient's pulmonary lesions were significantly improved, and he was free of hypoxia. An analysis of prior cases of sPAP and MDS revealed that pulmonary function could only be restored when MDS was controlled, consistent with the present case. These findings suggest that the treatment of underlying disease is essential when attempting to alleviate PAP symptoms. Whole lung lavage can also effectively alleviate patient symptoms.

CONCLUSION

In summary, the present case offers evidence regarding the mechanistic basis for PAP secondary to CMML. As PAP is associated with a high mortality rate, early detection is essential. No predictive models are currently available to gauge the risk of PAP development, and genetic analyses of GATA2 may offer value as a means of more precisely diagnosing underlying hematological conditions in affected patients. When patients present with unexplained dyspnea and GGO findings upon chest CT while suffering from hematologic disorders, PAP should be considered as a possible diagnosis. Patients with GATA2 deficiencies or primary disease progression are also at a high risk of PAP development. Other factors including trisomy 8 and autoimmune diseases. High levels of CD14^{dim}CD16⁺ monocytes may also be indicative of an increased PAP risk. Future prospective or high-quality objective studies are needed to better evaluate risk factors associated with sPAP and to confirm related prior findings.

ACKNOWLEDGEMENTS

The authors gratefully appreciate the staff of the Medical Records Room of Hangzhou First People's Hospital for the support of this study. The authors are also thankful to all the patients for their understanding and cooperation.

REFERENCES

- 1 **Trapnell BC**, Whitsett JA, Nakata K. Pulmonary alveolar proteinosis. *N Engl J Med* 2003; **349**: 2527-2539 [PMID: 14695413 DOI: 10.1056/NEJMra023226]
- 2 **Rosen SH**, Castleman B, Liebow AA. Pulmonary alveolar proteinosis. *N Engl J Med* 1958; **258**: 1123-1142 [PMID: 13552931 DOI: 10.1056/NEJM195806052582301]
- 3 **Cordonnier C**, Fleury-Feith J, Escudier E, Atassi K, Bernaudin JF. Secondary alveolar proteinosis is a reversible cause of respiratory failure in leukemic patients. *Am J Respir Crit Care Med* 1994; **149**: 788-794 [PMID: 8118651 DOI: 10.1164/ajrccm.149.3.8118651]
- 4 **Xue Y**, Han Y, Li T, Chen S, Zhang J, Pan J, Wu Y, Wang Y, Shen J. Pulmonary alveolar proteinosis as a terminal complication in a case of myelodysplastic syndrome with idic(20q-). *Acta Haematol* 2010; **123**: 55-58 [PMID: 19955712 DOI: 10.1159/000262292]
- 5 **Ishii H**, Seymour JF, Tazawa R, Inoue Y, Uchida N, Nishida A, Kogure Y, Saraya T, Tomii K, Takada T, Itoh Y, Hojo M, Ichihata T, Goto H, Nakata K. Secondary pulmonary alveolar proteinosis complicating myelodysplastic syndrome results in worsening of prognosis: a retrospective cohort study in Japan. *BMC Pulm Med* 2014; **14**: 37 [PMID: 24597668 DOI: 10.1186/1471-2466-14-37]
- 6 **Robb L**, Drinkwater CC, Metcalf D, Li R, Köntgen F, Nicola NA, Begley CG. Hematopoietic and lung abnormalities in mice with a null mutation of the common beta subunit of the receptors for granulocyte-macrophage colony-stimulating factor and interleukins 3 and 5. *Proc Natl Acad Sci USA* 1995; **92**: 9565-9569 [PMID: 7568173 DOI: 10.1073/pnas.92.21.9565]
- 7 **Solary E**, Itzykson R. How I treat chronic myelomonocytic leukemia. *Blood* 2017; **130**: 126-136 [PMID: 28572287 DOI: 10.1182/blood-2017-04-736421]
- 8 **Pollack SM**, Gutierrez G, Ascensao J. Pulmonary alveolar proteinosis with myeloproliferative syndrome with myelodysplasia: bronchoalveolar lavage reduces white blood cell count. *Am J Hematol* 2006; **81**: 634-638 [PMID: 16906593 DOI: 10.1002/ajh.20670]
- 9 **Can Chen**, Kuang Chen, Xilian Huang, Kaile Wang, Shenxian Qian. Concurrent eosinophilia and IgG4-related disease in a child: A case report and review of the literature. *Exp Ther Med* 2018; **2739**-2748 [PMID: 5795490 DOI: 10.3892/etm.2018.5743]
- 10 **Shoji N**, Ito Y, Kimura Y, Nishimaki J, Kuriyama Y, Tauchi T, Yaguchi M, Payzulla D, Ebihara Y, Ohyashiki K. Pulmonary alveolar proteinosis as a terminal complication in myelodysplastic syndromes: a report of four cases detected on autopsy. *Leuk Res* 2002; **26**: 591-595 [PMID: 12007507 DOI: 10.1016/s0145-2126(01)00178-3]
- 11 **Chaulagain CP**, Pilichowska M, Brinckerhoff L, Tappa M, Erban JK. Secondary pulmonary alveolar proteinosis in hematologic malignancies. *Hematol Oncol Stem Cell Ther* 2014; **7**: 127-135 [PMID: 25300566 DOI: 10.1016/j.hemonc.2014.09.003]
- 12 **Shah PL**, Hansell D, Lawson PR, Reid KB, Morgan C. Pulmonary alveolar proteinosis: clinical aspects and current concepts on pathogenesis. *Thorax* 2000; **55**: 67-77 [PMID: 10607805 DOI: 10.1136/thorax.55.1.67]
- 13 **Dirksen U**, Nishinakamura R, Gronbeck P, Hattenhorst U, Nöge L, Murray R, Burdach S. Human pulmonary alveolar proteinosis associated with a defect in GM-CSF/IL-3/IL-5 receptor common beta chain expression. *J Clin Invest* 1997; **100**: 2211-2217 [PMID: 9410898 DOI: 10.1172/JCI119758]
- 14 **Kitamura T**, Tanaka N, Watanabe J, Uchida, Kanegasaki S, Yamada Y, Nakata K. Idiopathic pulmonary alveolar proteinosis as an autoimmune disease with neutralizing antibody against

- granulocyte/macrophage colony-stimulating factor. *J Exp Med* 1999; **190**: 875-880 [PMID: [10499925](#) DOI: [10.1084/jem.190.6.875](#)]
- 15 **Zhang D**, Tian X, Feng R, Guo X, Wang P, Situ Y, Xiao Y, Xu KF. Secondary pulmonary alveolar proteinosis: a single-center retrospective study (a case series and literature review). *BMC Pulm Med* 2018; **18**: 15 [PMID: [29368649](#) DOI: [10.1186/s12890-018-0590-z](#)]
 - 16 **Inoue D**, Marumo S, Ishii H, Fukui M. Secondary pulmonary alveolar proteinosis during corticosteroid therapy for organising pneumonia associated with myelodysplastic syndrome. *BMJ Case Rep* 2019; **12** [PMID: [31537595](#) DOI: [10.1136/bcr-2019-231055](#)]
 - 17 **Zhao Y**, Xiong W, Wu X. A case of secondary pulmonary alveolar proteinosis, but prior to myelodysplastic syndrome. *Respirol Case Rep* 2013; **1**: 58-61 [PMID: [25473545](#) DOI: [10.1002/rcr2.29](#)]
 - 18 **Gacouin A**, Le Tulzo Y, Suprin E, Briens E, Bernard M, Camus C, Thomas R. Acute respiratory failure caused by secondary alveolar proteinosis in a patient with acute myeloid leukemia: a case report. *Intensive Care Med* 1998; **24**: 265-267 [PMID: [9565812](#) DOI: [10.1007/s001340050563](#)]
 - 19 **Chung JH**, Pipavath SJ, Myerson DH, Godwin D. Secondary pulmonary alveolar proteinosis: a confusing and potentially serious complication of hematologic malignancy. *J Thorac Imaging* 2009; **24**: 115-118 [PMID: [19465834](#) DOI: [10.1097/RTI.0b013e3181930ed6](#)]
 - 20 **Ohmachi K**, Ogiya D, Morita F, Kojima M, Tsuboi K, Tazume K, Komatsu M, Hayama N, Kumaki N, Ogawa Y, Ando K. Secondary pulmonary alveolar proteinosis in a patient with chronic myeloid leukemia in the accelerated phase. *Tokai J Exp Clin Med* 2008; **33**: 146-149 [PMID: [21318986](#)]
 - 21 **Liu Y**, Chen LL, Qiu YY, Xiao YL, Cai HR. Clinical features of secondary pulmonary alveolar proteinosis associated with myelodysplastic syndrome: Two case reports. *Medicine (Baltimore)* 2017; **96**: e8481 [PMID: [29095306](#) DOI: [10.1097/MD.00000000000008481](#)]
 - 22 **Ando J**, Tamayose K, Sugimoto K, Oshimi K. Late appearance of t(1;19)(q11;q11) in myelodysplastic syndrome associated with dysplastic eosinophilia and pulmonary alveolar proteinosis. *Cancer Genet Cytogenet* 2002; **139**: 14-17 [PMID: [12547151](#) DOI: [10.1016/s0165-4608\(02\)00652-0](#)]
 - 23 **Yoshioka Y**, Ohwada A, Harada N, Satoh N, Sakuraba S, Dambara T, Fukuchi Y. Increased circulating CD16+ CD14dim monocytes in a patient with pulmonary alveolar proteinosis. *Respirology* 2002; **7**: 273-279 [PMID: [12153694](#) DOI: [10.1046/j.1440-1843.2002.00392.x](#)]
 - 24 **Sawada K**, Yamada G, Shijubo N, Takagi-Takahashi Y, Ohnishi T, Saitoh E, Takahashi H, Watanabe A, Satoh M, Abe S. Biphasic pulmonary blastoma presenting as endobronchial polyp with a long stalk. *Intern Med* 2005; **44**: 516-517 [PMID: [15942110](#) DOI: [10.2169/internalmedicine.44.516](#)]
 - 25 **Fukuno K**, Tomonari A, Tsukada N, Takahashi S, Ooi J, Konuma T, Uchiyama M, Fujii T, Endo T, Iwamoto A, Oyaizu N, Nakata K, Moriwaki H, Tojo A, Asano S. Successful cord blood transplantation for myelodysplastic syndrome resulting in resolution of pulmonary alveolar proteinosis. *Bone Marrow Transplant* 2006; **38**: 581-582 [PMID: [16953205](#) DOI: [10.1038/sj.bmt.1705491](#)]
 - 26 **Tabata S**, Shimoji S, Murase K, Takiuchi Y, Inoue D, Kimura T, Nagai Y, Mori M, Togami K, Kurata M, Ito K, Hashimoto H, Matsushita A, Nagai K, Takahashi T. Successful allogeneic bone marrow transplantation for myelodysplastic syndrome complicated by severe pulmonary alveolar proteinosis. *Int J Hematol* 2009; **90**: 407-412 [PMID: [19693450](#) DOI: [10.1007/s12185-009-0404-4](#)]
 - 27 **Nishida A**, Miyamoto A, Yamamoto H, Uchida N, Izutsu K, Wake A, Ohta Y, Fujii T, Araoka H, Taniguchi S, Kishi K. Possible association of trisomy 8 with secondary pulmonary alveolar proteinosis in myelodysplastic syndrome. *Am J Respir Crit Care Med* 2011; **184**: 279-280 [PMID: [21765036](#) DOI: [10.1164/ajrcm.184.2.279a](#)]
 - 28 **Handa T**, Nakatsue T, Baba M, Takada T, Nakata K, Ishii H. Clinical features of three cases with pulmonary alveolar proteinosis secondary to myelodysplastic syndrome developed during the course of Behçet's disease. *Respir Investig* 2014; **52**: 75-79 [PMID: [24388375](#) DOI: [10.1016/j.resinv.2013.05.005](#)]
 - 29 **Spinner MA**, Sanchez LA, Hsu AP, Shaw PA, Zerbe CS, Calvo KR, Arthur DC, Gu W, Gould CM, Brewer CC, Cowen EW, Freeman AF, Olivier KN, Uzel G, Zelazny AM, Daub JR, Spalding CD, Claypool RJ, Giri NK, Alter BP, Mace EM, Orange JS, Cuellar-Rodriguez J, Hickstein DD, Holland SM. GATA2 deficiency: a protean disorder of hematopoiesis, lymphatics, and immunity. *Blood* 2014; **123**: 809-821 [PMID: [24227816](#) DOI: [10.1182/blood-2013-07-515528](#)]
 - 30 **Griese M**, Zarbock R, Costabel U, Hildebrandt J, Theegarten D, Albert M, Thiel A, Schams A, Lange J, Krenke K, Wesselak T, Schön C, Kappler M, Blum H, Krebs S, Jung A, Kröner C, Klein C, Campo I, Luisetti M, Bonella F. GATA2 deficiency in children and adults with severe pulmonary alveolar proteinosis and hematologic disorders. *BMC Pulm Med* 2015; **15**: 87 [PMID: [26264606](#) DOI: [10.1186/s12890-015-0083-2](#)]
 - 31 **Itzykson R**, Fenaux P, Bowen D, Cross NCP, Cortes J, De Witte T, Germing U, Onida F, Padron E, Platzbecker U, Santini V, Sanz GF, Solary E, Van de Loosdrecht A, Malcovati L. Diagnosis and Treatment of Chronic Myelomonocytic Leukemias in Adults: Recommendations From the European Hematology Association and the European LeukemiaNet. *Hemasphere* 2018; **2**: e150 [PMID: [31723789](#) DOI: [10.1097/HS9.0000000000000150](#)]
 - 32 **Bresnick EH**, Katsumura KR, Lee HY, Johnson KD, Perkins AS. Master regulatory GATA transcription factors: mechanistic principles and emerging links to hematologic malignancies. *Nucleic Acids Res* 2012; **40**: 5819-5831 [PMID: [22492510](#) DOI: [10.1093/nar/gks281](#)]
 - 33 **Lasbury ME**, Tang X, Durant PJ, Lee CH. Effect of the transcription factor GATA-2 on phagocytic

- activity of alveolar macrophages from *Pneumocystis carinii*-infected hosts. *J Eukaryot Microbiol* 2001; **Suppl**: 158S-159S [PMID: 11906041 DOI: 10.1111/j.1550-7408.2001.tb00499.x]
- 34 **Tanaka N**, Matsumoto T, Miura G, Emoto T, Matsunaga N, Satoh Y, Oka Y. CT findings of leukemic pulmonary infiltration with pathologic correlation. *Eur Radiol* 2002; **12**: 166-174 [PMID: 11868094 DOI: 10.1007/s003300101013]
- 35 **Heyneman LE**, Johkoh T, Ward S, Honda O, Yoshida S, Müller NL. Pulmonary leukemic infiltrates: high-resolution CT findings in 10 patients. *AJR Am J Roentgenol* 2000; **174**: 517-521 [PMID: 10658733 DOI: 10.2214/ajr.174.2.1740517]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

