International Cancer Conference Journal (2024) 13:22–25
https://doi.org/10.1007/s13691-023-00631-9

CASE REPORT - COMPLICATION

Tumor lysis syndrome followed by tumor regression after COVID-19 in a patient with chronic lymphocytic leukemia

Masato Yasumi[1] · Yudai Yamamoto[2] · Kimimori Kamijo[1] · Tsuyoshi Kamae[1] · Masaya Yamato[2] · Takahiro Karasuno[1]

Received: 16 June 2023 / Accepted: 10 August 2023 / Published online: 23 August 2023

Abstract

Coronavirus disease 2019 (COVID-19) can become lethal in patients with hematological malignancies; however, several cases of tumor regression after COVID-19 have been described, and the precise mechanism behind this paradoxical effect is unknown. Herein, we describe a case of Tumor lysis syndrome (TLS) followed by tumor regression after COVID-19. A 72-year-old woman with untreated chronic lymphocytic leukemia was admitted to our hospital with SARS-CoV-2 antigen-positive pneumonia. On admission, her anti-SARS-CoV-2 spike antibody was negative despite receiving two prior vaccinations. Immediately after admission, she developed confusion and ventricular tachycardia. Laboratory data showed acidosis, hyperkalemia, and a rapid decrease of tumor cells in peripheral blood, and she was diagnosed with clinical TLS. She was transferred to the intensive care unit and received continuous hemodialysis therapy. Although hyperferritinemia and bicytopenia, which suggest a cytokine storm followed, she recovered without steroids and additional COVID-19 treatment in 8 days. 2 months later, CT revealed a marked shrinking of lymphadenopathy, which was compatible with tumor regression after COVID-19. Considering the impaired humoral immunity and abrupt response, direct oncolysis caused by SARS-CoV-2 and cytokine storm-induced cell-mediated immune reaction may have been responsible for this paradoxical effect.

Keywords Tumor lysis syndrome · Tumor regression · COVID-19 · Chronic lymphocytic leukemia

Introduction

COVID-19 deleteriously impacts immunocompromised patients with hematological malignancies [1]. Mortality in COVID-19 patients has been linked to a cytokine storm induced by hyperactivity of the immune reaction in response to the virus. Excessive production of pro-inflammatory cytokines leads to acute respiratory distress syndrome aggravation, multi-organ failure, and death [2].

Tumor lysis syndrome (TLS) is a severe metabolic disorder that occurs when tumor cells undergo rapid disruption and release their intracellular contents into the systemic circulation during treatment initiation. TLS is commonly observed in rapidly growing hematological malignancies, such as Burkitt lymphoma and acute leukemia, but rarely in slow-growing chronic lymphocytic leukemia (CLL) patients without recent administration of targeted therapy, such as venetoclax therapy [3].

Although COVID-19 can be fatal in patients with hematological malignancies, several cases of paradoxical tumor regression after COVID-19 have been reported [4]. However, the precise effect of SARS-CoV-2 on the tumor microenvironment and immune responses that lead to tumor regression is not fully understood.

Herein, we describe a CLL patient who experienced unexpected TLS and tumor regression after COVID-19. This case may provide new insight into the antitumor effect of SARS-CoV-2.

Case report

A 72-year-old woman was referred to our hospital with leukocytosis and lymphadenopathy. Laboratory findings were: white blood cell (WBC) count of 24.0 × 109/L with 79.5% of mature lymphocytes, hemoglobin level of 12.0 g/dL, platelet count of 98 × 109/L, lactate dehydrogenase (LDH)

✉ Masato Yasumi
m-yasumi@rgmc.izumisano.osaka.jp

[1] Department of Hematology, Rinku General Medical Center, 2-3 Ourai-Kita, Rinku, Izumisano, Osaka 598-8577, Japan

[2] Department of General Internal Medicine and Infectious Diseases, Rinku General Medical Center, Osaka, Japan

level of 358 IU/L, and soluble interleukin-2 receptor (sIL-2R) level of 1890 IU/L. Peripheral blood flow cytometry was performed to assess the proliferation of monotypic B lymphocytes. The results showed positive for CD5, CD19, CD20, and CD23, and negative for CD10. Cytogenetic analysis revealed a normal karyotype, and fluorescence in situ hybridization revealed no deletion in 17q13. Computed tomography (CT) showed cervical, axillary, mediastinal, and inguinal lymph node enlargement up to 12 mm in diameter with mild splenomegaly. The patient was diagnosed with chronic lymphocytic leukemia (Rai stage IV). She preferred a watchful waiting policy, and careful observation was started.

2 years later, she was admitted to our hospital with fever and dyspnea. An antigen test for SARS-CoV-2 was positive, and CT revealed bilateral multifocal ground-glass opacities suggestive of COVID-19. On admission, her oxygen level was 92% in room air, and her consciousness was clear; therefore, she was diagnosed with moderate COVID-19 according to World Health Organization guidelines [5]. Her clinical course is shown in Fig. 1. Before COVID-19, chronic lymphocytic leukemia tumor burden had increased and she had WBC count of 50.7 × 109/L with 92.0% of mature lymphocytes, LDH level of 458 IU/L, and sIL-2R levels of 3560 IU/L. On admission, her WBC count dropped to 22.9 × 109/L with 75.0% of mature lymphocytes. Blood chemistry tests showed increases in uric acid of 10.5 mg/dL, potassium of 5.9 mEq/L, phosphorus of 4.8 mg/dL, creatinine of 2.01 mg/dL, and IL-6 level of 20 pg/mL. Although she had received her second COVID-19 vaccination (BNT162b2, Pfizer-BioNTech) 2 months before, anti-SARS-CoV-2 spike antibody was negative. A few hours after receiving the first dose of remdesivir, she became confused and developed ventricular tachycardia. Laboratory data showed acidosis of pH 7.29, hyperkalemia of 7.4 mEq/L, and a decrease in ionized calcium of 1.03 mmol/L. These findings suggested that she had developed clinical tumor lysis syndrome after COVID-19. She was transferred to the intensive care unit and received continuous hemodialysis (CHD). Her ferritin increased to 9041 mg/dL, platelet count decreased to 52 × 109/L, Hb level decreased to 8.8 g/dL, and calculated *H*-score was 182, which fulfilled the hemophagocytic lymphohistiocytosis syndrome criteria [6]. She promptly regained clear consciousness, and acidosis and renal failure improved rapidly. She was withdrawn from CHD and the administration of oxygen on the following day.

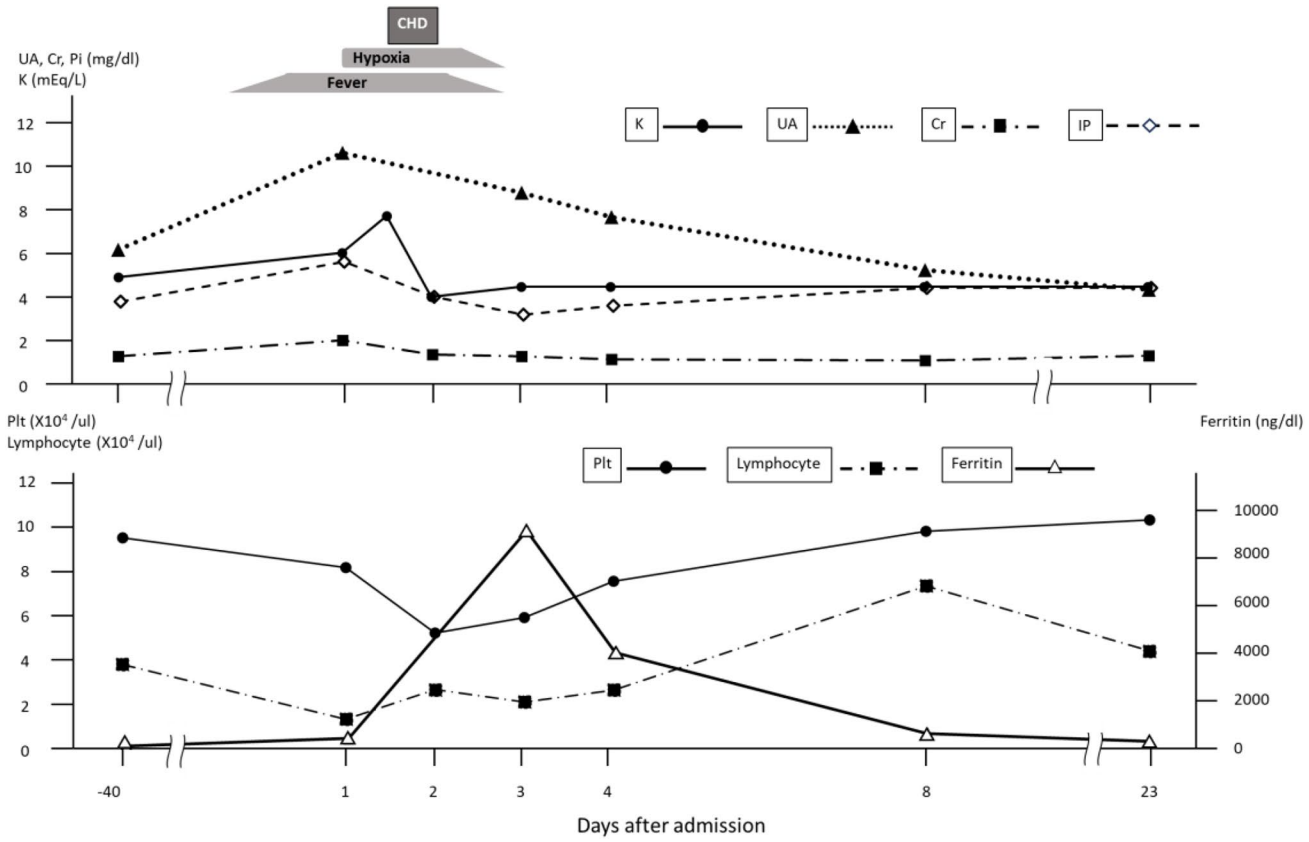

Fig. 1 Clinical course of the patient after COVID-19 and transition of TLS markers (potassium, uric acid, phosphorus, and creatinine), hematological parameters (lymphocyte count and platelet count), and inflammation marker (ferritin)

Laboratory data abnormalities were resolved without additional antiviral therapy and steroids. Her coronavirus antigen levels became negative, and she was discharged on 8 days of hospitalization. 2 months later, CT revealed marked regression of lymphadenopathy of axillae and mediastinum (Fig. 2).

Discussion

We experienced unexpected TLS followed by tumor regression after COVID-19. During the COVID-19 pandemic, several cases of tumor regression after SARS-CoV-2 infection in patients with hematological malignancies were described (Table 1) [7–19]. Some cases included tumor regression that unexpectedly occurred following prior weak chemotherapy. To the best of our knowledge, this is the first report of TLS followed by tumor regression after COVID-19 without administering a cytotoxic agent. Although the majority of tumor regressions were lymphoid malignancies, a response was also observed in myeloid malignancies. A response has also been recognized in slow-growing tumors, including CLL, multiple myeloma, and chronic myeloid leukemia. The severity of COVID-19 also varied from asymptomatic to critical disease. These heterogeneities of disease and the severity of COVID-19 suggest that several mechanisms may cause tumor regression after COVID-19.

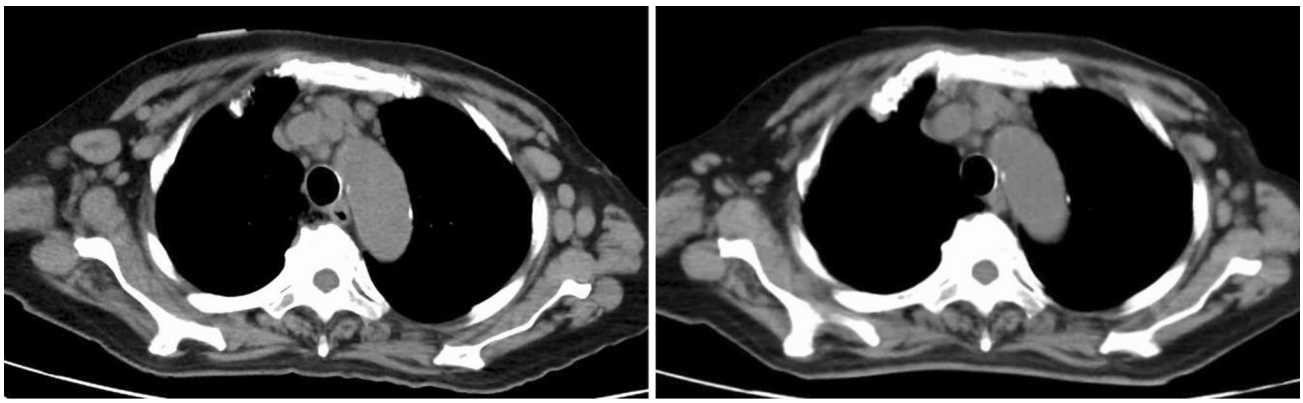

Fig. 2 Comparison of CT at admission (left panel) and CT after COVID-19 (right panel)

Table 1 Case reports of tumor regression after COVID-19 in patients with hematological malignancies

References	Age	Sex	Primary disease	Prior chemotherapy	Severity of COVID-19
Challenor et al. [7]	61	M	Hodgkin lymphoma	No	Moderate
Sollini et al. [8]	61	N/A	Follicular lymphoma	RB	Asymptomatic
Yilmaz et al. [9]	81	F	High-grade B cell lymphoma	R-CHOP	Mild
Kandeel et al. [10]	63	F	AML	No	Moderate
Kandeel et al. [10]	28	M	T-ALL	No	Moderate
Barnabei [11]	64	M	CLL	No	Moderate
Antwi-Amoabeng et al. [12]	76	F	Multiple myeloma	CyBorD	Mild
Barkhordar et al. [13]	57	F	AML	No	Critical
Kurlapski et al. [14]	58	F	Hodgkin lymphoma	No	Asymptomatic
Baptista et al. [15]	79	F	Follicular lymphoma	No	N/A
Bülbül et al. [16]	67	M	CLL	No	Moderate
Snowden et al. [17]	66	F	Sezary syndrome	No	Critical
Ohadi et al. [18]	64	M	Mycosis fungoides	No	Moderate
Waseem Hajjar et al. [19]	45	M	CML	Hydroxyurea	Mild

A PubMed search was performed in December 2022 using the following search terms: SARS-CoV-2 and remission and "lymphoma or hematological malignancies or tumor". In addition, cases reviewed in the literature are also included

AML acute myeloid leukemia, *ALL* acute lymphocytic leukemia, *CLL* chronic lymphocytic leukemia, *CML* chronic myeloid leukemia, *RB* rituximab and bendamustine, *R-CHOP* rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone, *CyBorD* cyclophosphamide, bortezomib, and dexamethasone

The proposed mechanism for the antitumor effect of SARS-CoV-2 infection includes two distinct mechanisms: direct oncolysis and systemic antitumor immunity, such as innate immunity, adaptive immunity, and epitope spreading [4]. In the present case, impaired humoral immunity was presumed by the inadequate response to COVID-19 vaccination, and the rapid disruption of tumor cells is thought to be the essence of the TLS. Therefore, direct oncolysis might be the underlying mechanism. Computational analysis indicated that the SARS-CoV-2 spike proteins bind tumor cells via the surface markers CD27, CD45, and CD152 [20], which are commonly expressed on CLL [21, 22].

Our findings do not exclude the possibility of systemic immune activation by SARS-CoV-2. The patient experienced hyperferritinemia and a platelet decrease following TLS, suggesting a cytokine storm [2]. Inflammatory cytokines activate pathogen-specific T cells with tumor antigens and natural killer cells, which may lead to the killing of tumor cells [4]. This hypercytokinemia-induced cell-mediated immunity may contribute to further tumor regression.

In conclusion, we experienced a case of unexpected TLS followed by tumor regression after COVID-19, which raises the possibility that direct oncolysis may be involved in this tumor regression. Further investigations are needed to elucidate the mechanism of the antitumor effect of SARS-CoV-2 and develop oncolytic virus therapy.

Declarations

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

Informed consent Witten informed consent was obtained from the patient to write this manuscript.

References

1. Vijenthira A, Gong IY, Fox TA et al (2020) Outcomes of patients with hematologic malignancies and COVID-19: a systematic review and meta-analysis of 3377 patients. Blood 136(25):2881–2892
2. Ragab D, Salah Eldin H, Taeimah M et al (2020) The COVID-19 cytokine storm; what we know so far. Front Immunol 11:1446
3. Sharman JP, Biondo JML, Boyer M et al (2022) A review of the incidence of tumor lysis syndrome in patients with chronic lymphocytic leukemia treated with venetoclax and debulking strategies. EJHaem 3(2):492–506
4. Shin DH, Gillard A, Van Wieren A et al (2022) Remission of liquid tumors and SARS-CoV-2 infection: a literature review. Mol Ther Oncolytics 26:135–140
5. Living guidance for clinical management of COVID-19: living guidance, 23 November 2021—World Health Organization (WHO). WHO/2019-nCoV/clinical/2021.2
6. Fardet L, Galicier L, Lambotte O et al (2014) Development and validation of the HScore, a score for the diagnosis of reactive hemophagocytic syndrome. Arthritis Rheumatol 66(9):2613–2620
7. Challenor S, Tucker D (2021) SARS-CoV-2-induced remission of Hodgkin lymphoma. Br J Haematol 192(3):415
8. Sollini M, Gelardi F, Carlo-Stella C et al (2021) Complete remission of follicular lymphoma after SARS-CoV-2 infection: from the "flare phenomenon" to the "abscopal effect." Eur J Nucl Med Mol Imaging 48(8):2652–2654
9. Yilmaz F, Yasar S, Tuncali MC et al (2021) Complete response in a frail patient with high-grade B-cell lymphoma to only one cycle of R-CHOP or prolonged COVID-19? Semin Oncol 48(4–6):279–282
10. Kandeel EZ, Refaat L, Abdel-Fatah R et al (2021) Could COVID-19 induce remission of acute leukemia? Hematology 26(1):870–873
11. Barnabei R, Di Michele G, Cellini A et al (2021) Transient disappearance of $CD19^{+}/CD5^{+}$ B-lymphocyte clone in peripheral blood in a patient with CLL during SARS-CoV-2-related mild disease. Clin Case Rep 9(6):e04238
12. Antwi-Amoabeng D, Ulanja MB, Beutler BD et al (2021) Multiple myeloma remission following COVID-19: an observation in search of a mechanism (a case report). Pan Afr Med J 39:117
13. Barkhordar M, Rostami FT, Yaghmaie M et al (2022) Spontaneous complete remission of acute myeloid leukemia in the absence of disease-modifying therapy following severe pulmonary involvement by coronavirus infectious disease-19. Case Rep Hematol 2022:2603607
14. Kurlapski M, Romanowicz G, Taszner M, Zaucha JM et al (2022) SARS-CoV-2-induced remission of advanced classical Hodgkin lymphoma. Pol Arch Intern Med 132(7–8):16266
15. Baptista RL, Moreira R, Rego E (2022) COVID-19 induced follicular lymphoma remission. Hematol Transfus Cell Ther 44(2):291–292
16. Bülbül H, Nazlı HE, Olgun A et al (2022) Spontaneous remission of chronic lymphocytic leukemia in a patient with SARS-CoV2. Leuk Res Rep 18:100336
17. Snowden C, Ng S, Choi J (2022) Partial remission of advanced untreated Sézary syndrome after COVID-19. JAAD Case Rep 21:165–168
18. Ohadi L, Hosseinzadeh F, Dadkhahfar S et al (2022) Oncolytic effect of SARS-CoV-2 in a patient with mycosis fungoides: a case report. Clin Case Rep 10(4):e05682
19. Waseem Hajjar AH, Abbarh S, Al-Mashdali A et al (2022) Tumor lysis syndrome in the chronic phase of chronic myeloid leukemia following COVID-19 infection: a case report. Cureus 14(4):e24386
20. Barh D, Tiwari S, Gabriel Rodrigues Gomes L, Weener ME et al (2021) Potential molecular mechanisms of rare anti-tumor immune response by SARS-CoV-2 in isolated cases of lymphomas. Viruses 13(10):1927
21. Damle RN, Ghiotto F, Valetto A et al (2002) B-cell chronic lymphocytic leukemia cells express a surface membrane phenotype of activated, antigen-experienced B lymphocytes. Blood 99(11):4087–4093
22. Kosmaczewska A, Ciszak L, Suwalska K et al (2005) CTLA-4 overexpression in CD19+/CD5+ cells correlates with the level of cell cycle regulators and disease progression in B-CLL patients. Leukemia 19(2):301–304