Successful treatment of severe splenic lymphoma-associated hemophagocytic syndrome by splenectomy and subsequent chemotherapy: A case report

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Abstract. Hemophagocytic lymphohistiocytosis (HLH) represents a fatal immunopathology derived from excessive inflammatory reactions. In particular, lymphoma-associated hemophagocytic syndrome (LAHS) is associated with a dismal prognosis. The current study presented a challenging case of splenic LAHS. A 71-year-old man presented with fatigue and anorexia. Laboratory test results revealed anemia, thrombocytopenia, lactate dehydrogenase elevation and markedly elevated levels of ferritin (6,210 ng/ml) and soluble interleukin 2 receptor (sIL-2R; 11,328 U/ml). Abdominal computed tomography revealed marked splenomegaly, while fluorodeoxyglucose positron emission tomography revealed increased tracer uptake in the spleen. An elective splenectomy was performed, which led to the diagnosis of B-cell splenic lymphoma with transformation from indolent to aggressive lymphoma. Prior to the splenectomy, thrombocytopenia and hepatic dysfunction with rapidly progressing jaundice appeared, accompanying further elevation of ferritin (25,197 ng/ml) and sIL-2R levels (30,420 U/ml). On postoperative day 5, the patient was transferred to a tertiary care institution and corticosteroid pulse therapy was immediately initiated after establishing the diagnosis of LAHS. Liver dysfunction gradually recovered and subsequent chemotherapy resulted in complete remission with improved performance status. At eight months after the onset, the patient remains alive without any signs of residual lymphoma. Although splenic lymphoma typically manifests with low-grade lymphoma, it can transform into high-grade lymphoma associated with severe complications, such as HLH and multiple organ failure. In this case, splenectomy assisted in not only establishing the diagnosis but also in tumor cytoreduction before commencing chemotherapy. Through interdisciplinary collaboration, the patient was successfully treated by performing a timely splenectomy, followed by steroid pulse therapy and chemotherapy.

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Abbreviations: HLH, hemophagocytic lymphohistiocytosis; MOF, multiple organ failure; LAHS, lymphoma-associated hemophagocytic syndrome; Hb, hemoglobin; Plt, platelet count; LDH, lactate dehydrogenase; sIL-2R, soluble interleukin 2 receptor; CT, computed tomography; FDG-PET, ^{18}F-fluorodeoxyglucose-positron emission tomography; HE, Hematoxylin and Eosin; POD, postoperative day; AST, aspartate aminotransferase; T-Bil, total bilirubin; D-Bil, direct bilirubin; CRP, C-reactive protein; ICU, intensive care unit; R-EPOCH, Rituximab, Etoposide, Prednisone, Oncovin, Cyclophosphamide and Hydroxydaunorubicin; SUV, standardized uptake value; mPSL, methylprednisolone

Key words: hemophagocytic lymphohistiocytosis, hemophagocytic syndrome, lymphoma-associated hemophagocytic syndrome, splenomegaly, splenectomy

Introduction

Hemophagocytic lymphohistiocytosis (HLH), also termed 'hemophagocytic syndrome' or 'macrophage activation syndrome', is a life-threatening condition characterized by pathological inflammatory responses (1). Clinical manifestations of HLH include recurrent fever, cytopenia, splenomegaly and sepsis-like syndrome, potentially culminating in multiple organ failure (MOF). HLH is classified into primary and secondary forms. Primary HLH is a hereditary condition predominantly observed in pediatric populations. Secondary HLH stems from malignancies, autoimmune diseases or idiopathic causes (2). Although numerous malignancies can accompany HLH, lymphoma-associated hemophagocytic syndrome (LAHS) is particularly prevalent. Malignant lymphoma is categorized into

low-grade and high-grade lymphoma. It is worth noting that LAHS can manifest as a symptom of high-grade lymphoma rather than low-grade lymphoma (3,4) and is associated with poor prognosis (5). Although LAHS is usually treated with corticosteroid therapy and cytotoxic chemotherapy for lymphoma (6), the significance of surgical intervention remains unclear, as no surgical cases have been reported to date.

The present study described a challenging case of lymphoma-associated splenomegaly, which led to severe HLH following splenectomy. It was possible to save the patient through timely splenectomy to reduce the tumor burden, enabling safe and effective steroid pulse therapy and chemotherapy.

Case report

A 71-year-old man with a medical history of hypertension and hyperuricemia presented to the primary hospital, Japan Baptist Hospital's Department of Internal Medicine (Kyoto, Japan), with fatigue and anorexia in February 2023. Laboratory test results revealed anemia [hemoglobin (Hb), 10 g/dl; normal range, 12-16 g/dl], thrombocytopenia [platelet count (Plt), $100 \times 10^3/\mu l$; normal range, $150-450 \times 10^3/\mu l$], elevated lactate dehydrogenase levels (LDH, 627 U/l; normal range, 140-271 U/l) and a markedly elevated ferritin level (6,210 ng/ml; normal range, 15-500 ng/ml). In addition, the patient's soluble interleukin 2 receptor (sIL-2R) level was significantly increased at 11,328 U/ml (normal range, 122-496 U/ml). Abdominal computed tomography (CT) revealed splenomegaly, without enlarged lymph nodes (Fig. 1). ^{18}F-fluorodeoxyglucose-positron emission tomography (FDG-PET)/CT showed the most pronounced increased uptake of FDG in the spleen, followed by the right atrium and the bone marrow (Fig. 2). The bone marrow biopsy identified an increase in small lymphocytes with occasional large cells on Hematoxylin and Eosin (HE) staining (7) (Fig. 3A and B). Clonality was confirmed through cytogenetic examination of T cell receptor γ chain Jγ rearrangement (8,9) using Southern blot analysis (10) with restriction enzymes EcoRI, BamHI and HindIII (Takara Bio, Inc.) (Fig. 3C).In addition, clonality was supported by flow cytometric analysis with CD45 gating (11) (Fig. 3D). Flow cytometry utilized a panel of pre-diluted antibodies from BD Biosciences, including CD45 (PerCP) (cat. no. 347464), CD2 (FITC) (cat. no. 347593), CD19 (BV421) (cat. no. 562440), CD3 (PE) (cat. no. 347347), CD8 (BV510) (cat. no. 563919), CD4 (APC-H7) (cat. no. 641398), CD25 (BV421) (cat. no. 562442), CD5 (FITC) (cat. no. 347303), CD23 (BV421) (cat. no. 562707), CD10 (PE) (cat. no. 340921), CD20 (APC-H7) (cat. no. 641396), CD11c (BV510) (cat. no. 563026), CD16 (BV510) (cat. no. 563830), CD56 (APC) (cat. no. 341025), CD30 (FITC) (cat. no. 341644), CD7 (APC) (cat. no. 561604), kappa light chains (PE) (cat. no. 346601), and lambda light chains (APC-H7) (cat. no. 656648), all used according to the manufacturer's protocol; however, a definitive diagnosis of the histological subtype could not be established.

Despite the abnormal laboratory data, the patient's activities of daily living were relatively preserved. After comprehensive assessment under outpatient conditions, elective surgery was planned to obtain a histological diagnosis two weeks after the initial presentation. On admission, 2 days preoperatively, the patient exhibited a spike fever of 39°C and progressive cytopenia (Hb, 8.6 g/dl; and Plt, $62 \times 10^3/\mu l$) was observed. The next day (the day before surgery), 20 units of platelet concentrate were transfused, but the Plt count had dropped to $55 \times 10^3/\mu l$ on the operative day. Due to the patient's significant splenomegaly, laparotomy was selected instead of laparoscopy. Splenectomy was eventually performed via a left subcostal incision (Fig. 4A). The procedure involved the separate ligation of the splenic artery and vein, and the spleen was extracted by stapling the tail of the pancreas at the splenic hilum (Fig. 4B). The operation lasted for 100 min, with an estimated blood loss of 600 ml. The excised specimen weighed 1,100 g (Fig. 4C). Subsequent histological examination confirmed the diagnosis of low-grade B-cell lymphoma with focal transformation to high-grade lymphoma with severe hemophagocytosis on HE staining (7) (Fig. 5). To confirm red-pulp, but not white-pulp, involvement of the lymphoma, immunohistochemistry was performed using an anti-CD8 antibody (cat. no. M7103; DAKO) at a dilution of 1:100, and Bentana ultraView DAB universal kit (Roche Diagnostics) for identification of sinus endothelial cells according to the manufacturers' standard protocols. The lymphoma predominantly involved the red pulp with some remaining atrophic white pulp, and the histological diagnosis was immunohistochemically confirmed using a CD68 probe (cat. no. NCL-CD68-KP1; Novocastra) at a dilution of 1:400 (Fig. 5). Thus, splenic marginal-zone lymphoma (commonly seen in this organ) could not be included in the histologic differential diagnosis; the lymphoma was finally characterized as unclassifiable. The patient was diagnosed with stage IVB disease according to the Ann Arbor Classification System (12).

Despite having undergone surgery, the pre-existing symptoms of intermittent fever and fatigue did not improve postoperatively. The patient exhibited low blood pressure and required temporary dopamine administration. On postoperative day (POD) 3, a rapid decrease in the Plt count ($62 \times 10^3/\mu l$) and elevation in LDH (1,948 U/l), aspartate aminotransferase (AST) (234 U/l; normal range, 8-48 U/l), total bilirubin (T-Bil) (6.6 mg/dl; normal range, 0.3-1.2 mg/dl), direct bilirubin (D-Bil) (4.5 mg/dl; normal range, 0.0-0.3 mg/dl) and C-reactive protein (CRP) levels (18.56 mg/dl; normal range, <0.5 mg/dl) were observed (Fig. 6). CT scanning did not detect any postoperative complications, such as pancreatic leakage. To exclude the possibility of drug-induced liver damage or potential embolism, medication adjustments were made and heparin was administered. However, the patient's condition further deteriorated.

Consequently, the patient was transferred to a tertiary care institution on POD 5, where he was admitted to the intensive care unit (ICU). Laboratory reassessment revealed the following abnormalities: Decrease in Hb (8.3 g/dl) and Plt ($47 \times 10^3/\mu l$); and significant elevations in LDH (3,616 U/l), AST (691 U/l), alanine aminotransferase (112 U/l; normal range, 7-55 U/l), T-Bil (21 mg/dl), D-Bil (17 mg/dl), creatinine (1.77 mg/dl; normal range, 0.5-1.2 mg/dl), CRP (23.44 mg/dl), ferritin (25,197 ng/ml) and sIL-2R (30,420 U/ml). The patient also exhibited hypoglycemia, with a blood glucose level of 25 mg/dl (normal range: 70-99 mg/dl), indicative of hepatic failure. However, since coagulation markers, such as prothrombin time and activated partial thromboplastin clotting time, were normal, plasma exchange therapy was deemed unnecessary (13).

Figure 1. Preoperative abdominal CT. Dynamic contrast-enhanced CT in the (A) axial and (B) coronal planes revealed pronounced splenomegaly. No prominent lymphadenopathy was observed. CT, computed tomography.
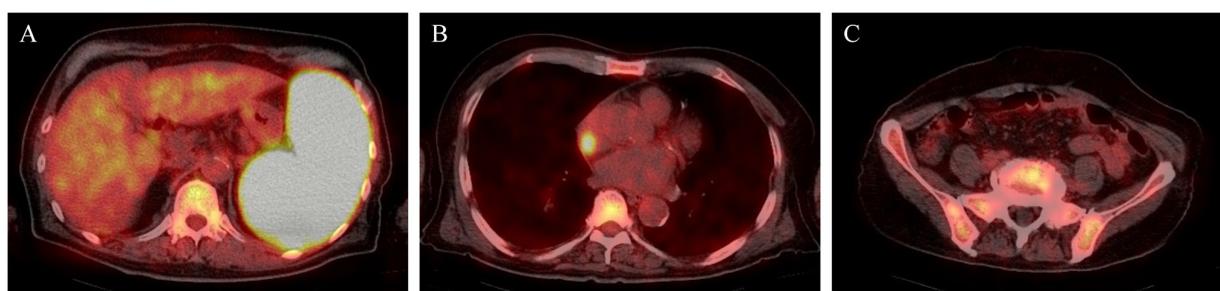

Figure 2. PET-CT scanning. PET-CT images reveal increased FDG uptake most prominently in (A) the spleen with a SUV-max of 16.7, followed by (B) a part of the right atrium (SUV-max of 6.8) and (C) the bone marrow (SUV-max of 4.2), with no significant FDG uptake in the liver. PET-CT, positron emission tomography-computed tomography; SUV-max, maximum standardized uptake value; FDG, ^{18}F-fluorodeoxyglucose.

The diagnosis of concurrent HLH was made and treatment with immunosuppressive therapy, steroid pulse therapy at 1,000 mg/day for 3 days, was immediately initiated under mechanical ventilation and continuous hemodiafiltration. Following this intervention, liver dysfunction was gradually ameliorated; the steroid dosage was tapered down (Fig. 6). The patient was extubated on POD 12 and subsequent chemotherapy for lymphoma with the R-EPOCH regimen (Rituximab, Etoposide, Prednisone, Oncovin, Cyclophosphamide and Hydroxydaunorubicin) was initiated on POD 14. Considering the hepatic dysfunction and tumor load, the initial dose of the regimen was reduced to 50%, and the administration of rituximab was delayed until POD 26. Bradycardia with a heart rate of 40 beats/min was transiently observed, presumably due to the infiltration of lymphoma into the sinoatrial node (Fig. 2B). However, there was no need for the placement of a pacemaker. After chemotherapy initiation, this bradycardia gradually improved, and further improvements in liver function were observed. The patient was discharged from the ICU on POD 23 and hemodialysis was discontinued on POD 30.

After experiencing gastric ulcer bleeding on POD 19 and acute pancreatitis on POD 27 as complications of steroid treatment, which were successfully managed with hemostasis and endoscopic drainage, a second course of R-EPOCH therapy was initiated on POD 77. After the patient's condition stabilized, he was transferred back to our primary hospital on POD 93 and was discharged home on POD 168. At eight months after the onset, the patient remains alive with improved performance status and his treatment is ongoing, specifically continuing with consolidation therapy for lymphoma. He is undergoing outpatient consultations with a frequency of approximately once every two weeks.

Discussion

HLH comprises a spectrum of conditions driven by uncontrolled inflammatory reactions. Among secondary HLH, malignancy-related HLH is predominantly associated with non-Hodgkin lymphomas. Of note, LAHS demonstrates a dismal prognosis with an average survival of only 37 days after
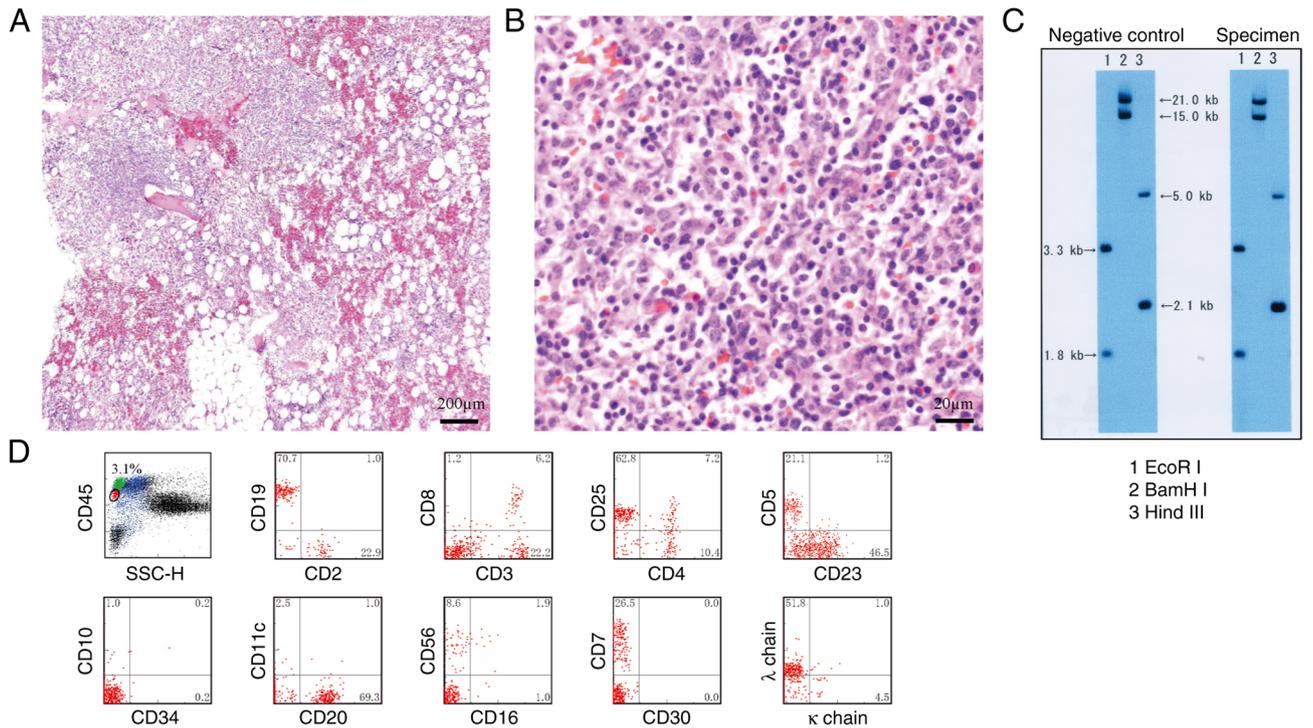
Figure 3. Histopathological features of bone marrow biopsy. (A) HE staining shows the bone marrow is hypercellular, demonstrating a vaguely nodular appearance (scale bar, 200 μm). (B) Higher magnification shows an increase in small lymphoid cells interspersed with large cells (scale bar, 20 μm). (C) Clonality was confirmed through cytogenetic examination of T cell receptor γ chain Jγ rearrangement. (D) Gating on CD45-dimly positive cells in flow cytometry dot plots; the highlighted area represents a cell population where ~70% of the cells are CD19-positive, CD20-positive and CD10-negative. These cells exhibit unequivocal light chain restriction, also suggesting the presence of a clonal cell population. However, even with immunohistochemistry and flow cytometry, the findings are not sufficient to characterize the transition to large-cell lymphoma. HE, hematoxylin and eosin.
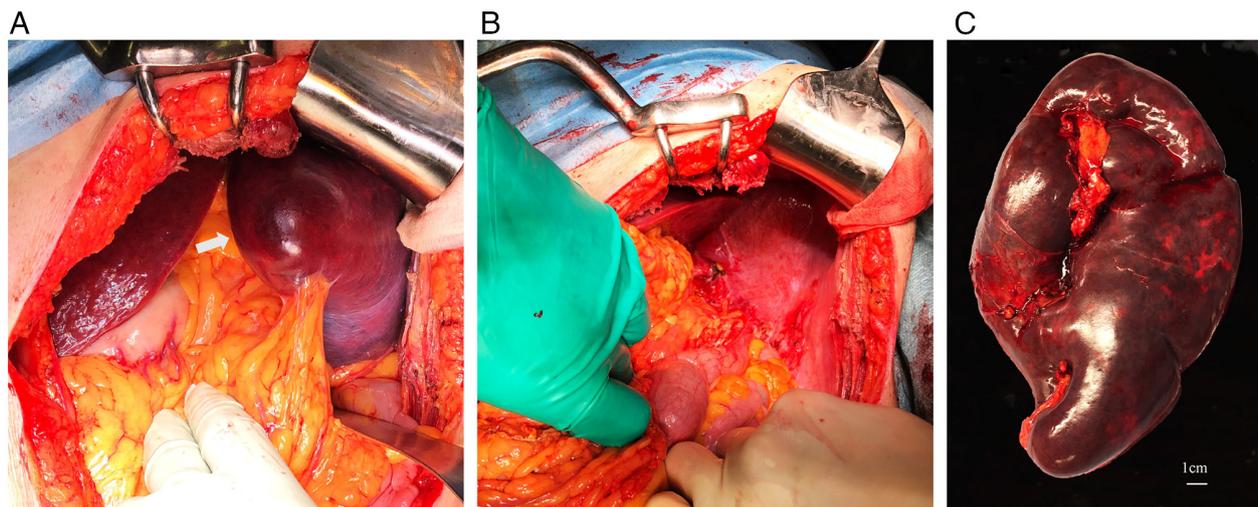

Figure 4. Intra- and postoperative images from the open splenectomy. (A) Intraoperative view showing the spleen during the open procedure. Note the marked enlargement of the spleen (arrow). (B) Post-splenectomy operative view. (C) Gross appearance of the resected spleen (scale, 1 cm). The weight of the spleen was 1,100 g.

treatment initiation (5), and this condition has been extensively studied (14,15). LAHS is itself a fatal condition, which often results in death despite intensive treatment with corticosteroid pulse therapy and cytotoxic chemotherapy (4,16-20).

Splenomegaly, or an increased standardized uptake value on FDG-PET, is a frequent manifestation of numerous hematological disorders, including malignant lymphomas (21). An enlarged spleen may act as a reservoir for malignant cells,

potentially accelerating disease progression. Splenectomy can alleviate related symptoms, such as abdominal discomfort and cytopenia, while allowing for diagnosis based on histopathological examination. This procedure may also offer therapeutic benefits, particularly in cases of B-cell splenic lymphoma (22-24). There is a distinct subset of HLH cases of unknown etiology that poses a clinical challenge. In such cases, splenectomy has been shown to serve as an effective
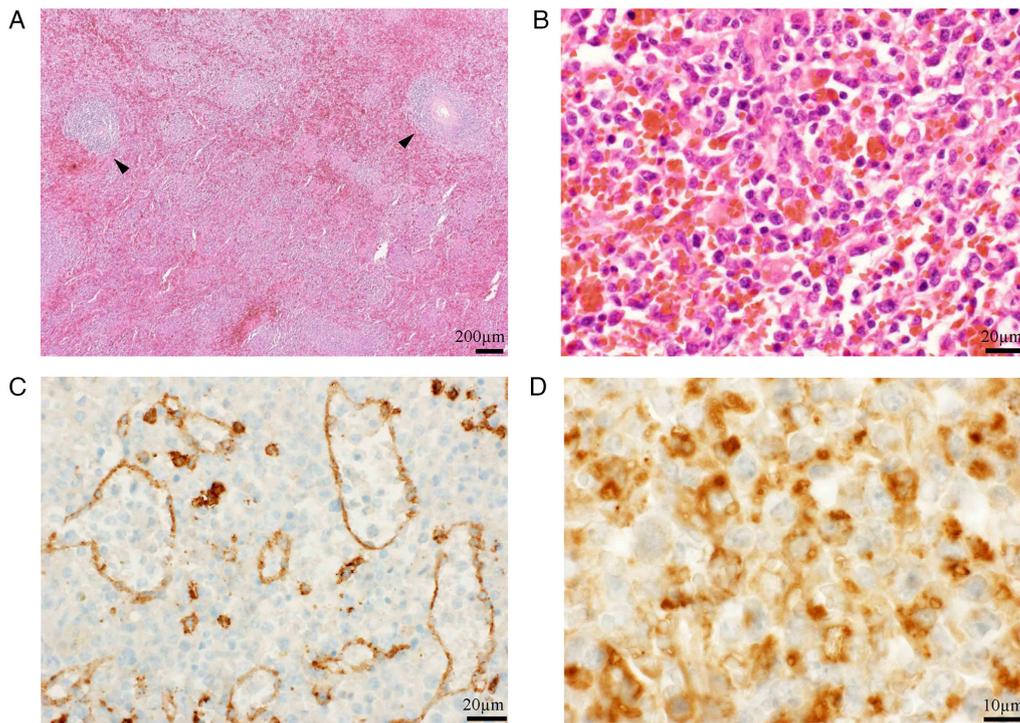
Figure 5. Histopathological and immunohistochemical features of the excised spleen. (A) The normal architecture is effaced by diffuse processes with atrophic white pulp on HE staining (arrowheads; scale bar, 200 μm). (B) A higher magnification on HE staining shows diffuse proliferation of predominantly small, with occasional large cells. Aggregations of erythrocytes due to phagocytosis by macrophages can be observed (scale bar, 20 μm); cell classification was confirmed by immunohistochemical probing for CD68. (C) Sinusoidal and Billroth cord involvement is evident by CD8-positive (brown) sinus endothelial cells (scale bar, 20 μm), which were counterstained with Hematoxylin (Blue). (D) Immunohistochemical staining for CD68. The tissue section was strongly stained, highlighting the presence of macrophages (scale bar, 10 μm). HE, hematoxylin and eosin.
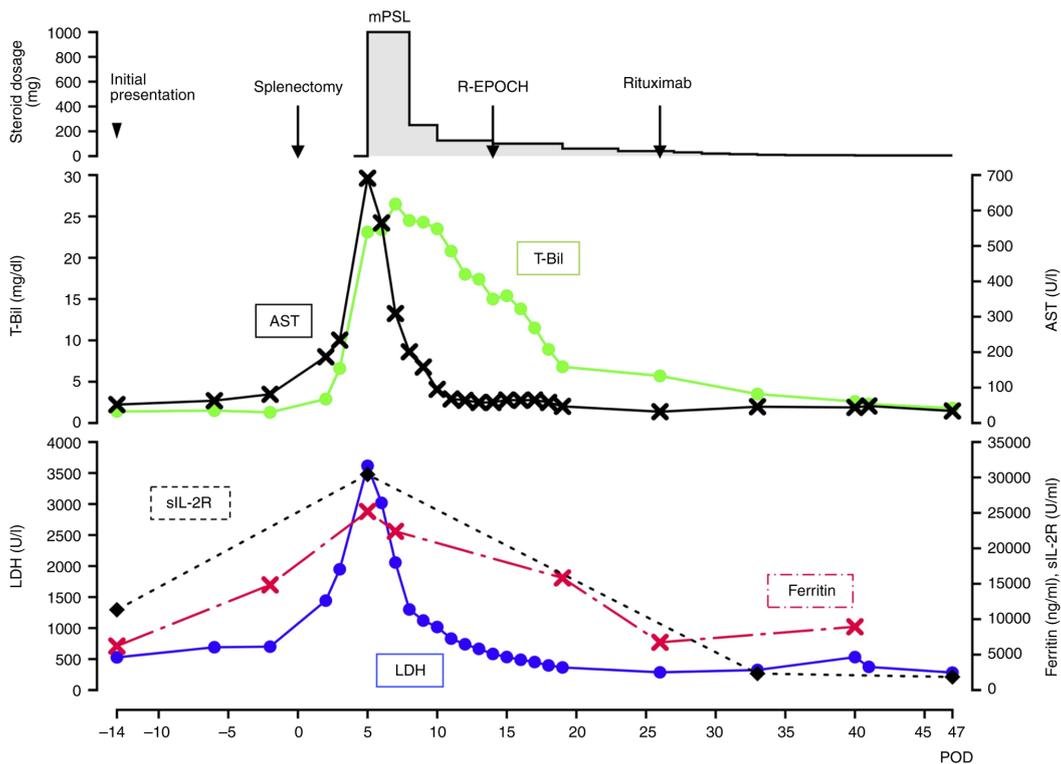

Figure 6. Detailed treatment course of the patient. Line graph illustrating changes in key biochemical markers (T-Bil, AST, LDH, Ferritin and sIL-2R) over time, starting from the preoperative period. Note that a significant improvement is observed following steroid pulse therapy and subsequent chemotherapy for the lymphoma. The steroid administration was switched from intravenous injection of mPSL to oral intake of prednisolone on POD 14. T-Bil, total bilirubin (normal range, 0.3-1.2 mg/dl); AST, aspartate transaminase (normal range, 8-48 U/l); LDH, lactate dehydrogenase (normal range, 140-271 U/l); Ferritin (normal range, 15-500 ng/ml); sIL-2R, soluble interleukin 2 receptor (normal range, 122-496 U/ml); mPSL, methylprednisolone; POD, postoperative day; R-EPOCH, Rituximab, Etoposide, Prednisone, Oncovin, Cyclophosphamide and Hydroxydaunorubicin.

diagnostic and therapeutic strategy (25-27), while a clinical trial is currently underway to validate its efficacy (NCI02862054). It can be inferred from these observations that the role of splenectomy in the context of splenic lymphoma and secondary HLH of idiopathic etiology has been established.

Malignant HLH is associated with MOF, leading to high rates of morbidity and mortality. In the present case, the preoperative progressive decrease in Hb and Plt indicates that signs of MOF were already present. If only chemotherapy had been administered without surgical intervention, there would have been a potential risk of triggering a severe tumor lysis syndrome and exacerbating pre-existing HLH due to the high tumor burden (28). Therefore, without splenectomy, the patient may have experienced more disastrous outcomes, such as the progression of MOF, splenic rupture (29), and even death. Retrospectively, the splenectomy did have a role in reducing the tumor burden, which in turn facilitated safer and more effective chemotherapy.

However, a critical question remains in the present case: Despite the removal of a significant tumor mass, why did the patient still develop severe HLH? Based on the postoperative course of the case, it is evident that surgery alone failed to halt the development of HLH, with hypotension observed postoperatively, suggesting a concurrent cytokine storm. Initially, it was assumed that his splenic lymphoma was primarily indolent. However, highly elevated ferritin levels at the presentation suggested the presence of HLH preoperatively. Pathological findings of the spleen supported this, further revealing high-grade lymphoma transformation. There is a high likelihood that the acute transformation occurred immediately before surgery. On the other hand, the widespread progression of HLH may have resulted from several factors during the surgical procedure: The surgical stimulation could have activated the lymphoma cells to secrete large amounts of soluble factors, such as TNF-α (30), or the operative procedure may have dispersed cellular components into the systemic circulation (31).

The HLH-2004 diagnostic criteria are well-known (2). However, adult patients may exhibit symptoms that are difficult to distinguish from sepsis or MOF of other causes. Delayed diagnosis of LAHS may have fatal consequences (17,18). Currently, no standardized treatment strategy exists, and whether an HLH-directed or malignancy-directed approach should be adopted (32,33) remains unclear. In the case of the present study, upon his transfer to a tertiary hospital on POD 5, the patient met 6 of the 8 HLH-2004 diagnostic criteria, leading to the identification of his condition. Finally, immunosuppressive therapy preceded, stabilizing the patient's condition and allowing us to commence chemotherapy. At the time of conclusion of the present study, eight months postoperatively, the patient has achieved a longer survival than typical reported cases.

In conclusion, while splenic lymphoma typically manifests with low-grade lymphoma, it can transform into a high-grade lymphoma, which can accompany severe complications such as HLH and MOF. In the present case, splenectomy served not only in the diagnosis but also in tumor cytoreduction before chemotherapy. Furthermore, through interdisciplinary collaboration between the surgical and hematology teams, the patient's condition was successfully treated by performing a timely splenectomy to reduce the tumor burden, followed by steroid pulse therapy and chemotherapy. Of note, surgery and subsequent chemotherapy may be life-saving in certain cases of LAHS, as this strategy may assist in avoiding chemotherapy-related fatal complications.

References

1. La Rosée P, Horne A, Hines M, von Bahr Greenwood T, Machowicz R, Berliner N, Birndt S, Gil-Herrera J, Girschikofsky M, Jordan MB, *et al*: Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. Blood 133: 2465-2477, 2019.
2. Henter JI, Horne A, Aricó M, Egeler RM, Filipovich AH, Imashuku S, Ladisch S, McClain K, Webb D, Winiarski J and Janka G: HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer 48: 124-131, 2007.
3. Lee JC and Logan AC: Diagnosis and management of adult malignancy-associated hemophagocytic lymphohistiocytosis. Cancers (Basel) 15: 1839, 2023.
4. Pasvolsky O, Zoref-Lorenz A, Abadi U, Geiger KR, Hayman L, Vaxman I, Raanani P and Leader A: Hemophagocytic lymphohistiocytosis as a harbinger of aggressive lymphoma: A case series. Int J Hematol 109: 553-562, 2019.
5. Li F, Li P, Zhang R, Yang G, Ji D, Huang X, Xu Q, Wei Y, Rao J, Huang R and Chen G: Identification of clinical features of lymphoma-associated hemophagocytic syndrome (LAHS): An analysis of 69 patients with hemophagocytic syndrome from a single-center in central region of China. Med Oncol 31: 902, 2014.

6. Wang H, Xiong L, Tang W, Zhou Y and Li F: A systematic review of malignancy-associated hemophagocytic lymphohistiocytosis that needs more attentions. Oncotarget 8: 59977-59985, 2017.
7. Fischer AH, Jacobson KA, Rose J and Zeller R: Hematoxylin and eosin staining of tissue and cell sections. CSH Protoc 2008: pdb.prot4986, 2008.
8. Moreau EJ, Langerak AW, van Gastel-Mol EJ, Wolvers-Tettero IL, Zhan M, Zhou Q, Koop BF and van Dongen JJ: Easy detection of all T cell receptor gamma (TCRG) gene rearrangements by Southern blot analysis: Recommendations for optimal results. Leukemia 13: 1620-1626, 1999.
9. van Dongen JJ and Wolvers-Tettero IL: Analysis of immunoglobulin and T cell receptor genes. Part I: Basic and technical aspects. Clin Chim Acta 198: 1-91, 1991.
10. Southern E: Southern blotting. Nat Protoc 1: 518-525, 2006.
11. Kim B, Lee ST, Kim HJ and Kim SH: Bone marrow flow cytometry in staging of patients with B-cell non-Hodgkin lymphoma. Ann Lab Med 35: 187-193, 2015.
12. Carbone PP, Kaplan HS, Musshoff K, Smithers DW and Tubiana M: Report of the committee on Hodgkin's disease staging classification. Cancer Res 31: 1860-1861, 1971.
13. Schwartz J, Padmanabhan A, Aqui N, Balogun RA, Connelly-Smith L, Delaney M, Dunbar NM, Witt V, Wu Y and Shaz BH: Guidelines on the use of therapeutic apheresis in clinical practice-evidence-based approach from the writing committee of the American society for apheresis: The seventh special issue. J Clin Apher 31: 149-162, 2016.
14. Li B, Guo J, Li T, Gu J, Zeng C, Xiao M, Zhang W, Li Q, Zhou J and Zhou X: Clinical characteristics of hemophagocytic lymphohistiocytosis associated with non-hodgkin B-Cell lymphoma: A multicenter retrospective study. Clin Lymphoma Myeloma Leuk 21: e198-e205, 2021.
15. Yao S, Jin Z, He L, Zhang R, Liu M, Hua Z, Wang Z and Wang Y: Clinical features and prognostic risk prediction of non-hodgkin lymphoma-associated hemophagocytic syndrome. Front Oncol 11: 788056, 2021.
16. Che Y, Xu L, Zhang X, Qiu X, Song J, Ding X and Sun X: Secondary hemophagocytic lymphohistiocytosis triggered by peripheral T-cell lymphoma: An unusual case report. Clin Case Rep 10: e6528, 2022.
17. Paluszkiewicz P, Martuszewski A, Majcherek M, Kucharska M, Bogucka-Fedorczuk A, Wróbel T and Czyż A: Hemophagocytic lymphohistiocytosis secondary to peripheral T cell lymphoma with rapid onset and fatal progression in a young patient: A case report and review of the literature. Am J Case Rep 22: e932765, 2021.
18. Iizuka H, Mori Y, Iwao N, Koike M and Noguchi M: Hemophagocytic lymphohistiocytosis associated with Epstein-Barr virus-positive diffuse large B-cell lymphoma, NOS of bone marrow-liver-spleen type: An autopsy case report. J Clin Exp Hematop 61: 102-108, 2021.
19. Tang S, Zhao C and Chen W: Aggressive diffuse large B-cell lymphoma with hemophagocytic lymphohistiocytosis: report of one case. Int J Clin Exp Pathol 13: 2392-2396, 2020.
20. Patel R, Patel H, Mulvoy W and Kapoor S: Diffuse large B-cell lymphoma with secondary hemophagocytic lymphohistiocytosis presenting as acute liver failure. ACG Case Rep J 4: e68, 2017.
21. Hu Y, Zhou W, Sun S, Guan Y, Ma J and Xie Y: 18F-fluorodeoxyglucose positron emission tomography-based prediction for splenectomy in patients with suspected splenic lymphoma. Ann Transl Med 9: 1009, 2021.
22. Pata G, Bartoli M, Damiani E, Solari S, Anastasia A, Pagani C and Tucci A: Still a role for surgery as first-line therapy of splenic marginal zone lymphoma? Results of a prospective observational study. Int J Surg 41: 143-149, 2017.
23. Kennedy ND, Lê GN, Kelly ME, Harding T, Fadalla K and Winter DC: Surgical management of splenic marginal zone lymphoma. Ir J Med Sci 187: 343-347, 2018.
24. Archibald WJ, Baran AM, Williams AM, Salloum RM, Richard Burack W, Evans AG, Syposs CR and Zent CS: The role of splenectomy in management of splenic B-cell lymphomas. Leuk Res 128: 107053, 2023.
25. Ma J, Jiang Z, Ding T, Xu H, Song J, Zhang J, Xie Y and Wang W: Splenectomy as a diagnostic method in lymphoma-associated hemophagocytic lymphohistiocytosis of unknown origin. Blood Cancer J 7: e534, 2017.
26. Jing-Shi W, Yi-Ni W, Lin W and Zhao W: Splenectomy as a treatment for adults with relapsed hemophagocytic lymphohistiocytosis of unknown cause. Ann Hematol 94: 753-760, 2015.
27. Fouquet G, Larroche C, Carpentier B, Terriou L, Urbanski G, Lacout C, Lazaro E, Salmon Gandonnière C, Perlat A, Lifermann F, et al: Splenectomy for haemophagocytic lymphohistiocytosis of unknown origin: risks and benefits in 21 patients. Br J Haematol 194: 638-642, 2021.
28. Howard SC, Jones DP and Pui CH: The tumor lysis syndrome. N Engl J Med 364: 1844-1854, 2011.
29. Han SM, Teng CL, Hwang GY, Chou G and Tsai CA: Primary splenic lymphoma associated with hemophagocytic lymphohistiocytosis complicated with splenic rupture. J Chin Med Assoc 71: 210-213, 2008.
30. Griffin G, Shenoi S and Hughes GC: Hemophagocytic lymphohistiocytosis: An update on pathogenesis, diagnosis, and therapy. Best Pract Res Clin Rheumatol 34: 101515, 2020.
31. Hunt DJ, Royer AM and Maxwell RA: Post splenectomy tumor lysis syndrome. Am Surg 78: E299-E300, 2012.
32. Daver N, McClain K, Allen CE, Parikh SA, Otrock Z, Rojas-Hernandez C, Blechacz B, Wang S, Minkov M, Jordan MB, et al: A consensus review on malignancy-associated hemophagocytic lymphohistiocytosis in adults. Cancer 123: 3229-3240, 2017.
33. Song Y, Wang J, Wang Y, Wu L and Wang Z: Requirement for containing etoposide in the initial treatment of lymphoma associated hemophagocytic lymphohistiocytosis. Cancer Biol Ther 22: 598-606, 2021.