*Case Report*

# Aggressive diffuse large B-cell lymphoma manifested by splenic rupture progressed 2 months after transverse myelitis: an autopsy case report

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*Background:* Splenic rupture by diffuse large B-cell lymphoma (DLBCL), which usually progresses insidiously, is extremely rare.

*Case Presentation:* A 60-year-old man presented with paralysis in his lower left extremity. A magnetic resonance imaging suggested transverse myelitis. No lymphadenopathy or organomegaly was noted. Two months after remission, he was referred to the emergency department complaining of presyncope. He was in preshock due to splenic rupture, and underwent laparotomy after attempts of transcatheter arterial embolization. Splenomegaly, hepatomegaly, and disseminated enlarged lymph nodes were observed. Histological examinations of the resected spleen showed DLBCL. He died of multiple organ failure associated with intractable bleeding. His autopsy revealed diffuse systemic invasions of lymphoma cells except for the brain and spinal cord. Microscopically, the spinal cord showed macular incomplete necrosis and histiocytic infiltration, suggestive of hemophagocytic syndrome.

*Conclusion:* The progression of DLBCL in our case is drastically rapid. Undiagnosed transverse myelitis preceded the onset.

**Key words:** Diffuse large B-cell lymphoma, hematologic malignancy, oncologic emergency, spontaneous splenic rupture, transverse myelitis

## INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is the most common form of non-Hodgkin lymphoma.[1] Despite 60%–70% of *de novo* cases being diagnosed as advanced stage, chemo-immunotherapies can still control up to 60% of the cases.[2] Thus, it is critical to make a diagnosis from biopsied lymph nodes. However, approximately 30% of cases show extranodal lesions and symptoms may not manifest until the stage advances. We herein report a case of splenic rupture due to DLBCL that was systemically disseminated in various organs within 2 months after undiagnosed transverse spinal cord myelitis.

## CASE REPORT

A 60-year-old man, whose medical history was significant for abdominal aortic dissection, hypertension, and dyslipidemia, was referred to the department of hematology in our hospital due to mild anemia with 13.3 g/dL of hemoglobin concentration (Hb) and thrombocytopenia with $14 \times 10^4$ cells/μL of platelets. After 6 months, he noticed numbness in his left trunk below the umbilical level and motor and sensory paralysis in his lower left extremity. A whole-body computed tomography (CT) did not show any abnormal findings except for stable aortic aneurysm. A magnetic resonance imaging (MRI) of the head and the spinal cord demonstrated high-intensity signals at T2-weighted sequences in the center of the spinal cord from the 2nd to the 12th thoracic level. Cerebrospinal fluid examination by lumber puncture showed no significant abnormalities. His soluble interleukin 2 receptor level was 397.2 U/mL, which was within the normal range. He underwent six plasma exchanges in addition to steroid pulse therapy for the suspected transverse myelitis followed by a course of its tapering, which ameliorated the condition. The high-intensity signals in the MRI at T2 weighted were attenuated 13 days after the first MRI. Two months after the manifestation of paralysis, he was brought by ambulance to the emergency department in our hospital due to a syncopal episode. On arrival, his Hb was 7.4 g/dL, platelets were $2.6 \times 10^4$/μL,

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prothrombin time was 16.6 s, D-dimer was 32.34 μg/dL, and serum lactate dehydrogenase was 666 U/L. A plain abdominal CT indicated a ruptured spleen with remarkable splenomegaly and intra-abdominal hemorrhage. Para-aortic lymphadenopathy was also noted. The volume of the spleen was shown to be more than two times compared with that observed in the CT performed 2 months before (Fig. 1). He underwent an emergent percutaneous transcatheter embolization, and extravasations in the spleen were detected and controlled by coil embolization. After his admission, his platelets continued to decrease despite repeated transfusions. On the 9th day, his spleen reruptured and his platelets showed $0.9 \times 10^4/\mu L$, and he subsequently underwent the second interventional radiology (IVR). For his refractory thrombocytopenia and uncontrollable splenic rupture, an emergency laparotomy was performed. His spleen was remarkably enlarged with a massive adhesion to the perisplenic tissues. Splenectomy with distal pancreatectomy was finally achieved by fractionating the spleen. After the splenectomy, his lactate dehydrogenase peaked at 1,560 U/L on the 13th day and then decreased to a normal range. The extracted spleen was enlarged with diameters of $15 \times 10 \times 8$ $cm^3$ (Fig. 2A). Histological examinations reported on the 24th admission day showed diffuse proliferation of atypical lymphocytes with large irregular nuclei, which was consistent with DLBCL (Fig. 2B). The immunohistochemical staining of the spleen was positive for CD20, CD10, CD79a, and Bcl-6; partially positive for Ki-67 (70%–80%); and negative for EBV-ISH, CD3, CD5, and Bcl-2 (Fig. 2C, D). Fluorescence *in situ* hybridization (FISH) demonstrated no translocation of c-Myc, BCL2, and BCL6. On the 24th day, he was found to have pancreatic fistula and CT-guided percutaneous drainage was performed, which was well-controlled thereafter. On the 50th day, he was revealed to have active bleeding from the stump of the pancreas, and surgical hemostat was performed. After this event, he underwent five laparotomies and two IVRs, during which he was also found to have gastric perforation. His soluble interleukin 2 receptor was 5,823.1 U/mL on the 25th day and 11,877.8 U/mL on the 67th day. His refractory thrombocytopenia persisted despite massive platelet transfusion, which reached 950 units in total. Despite these repeated procedures and treatments, he deceased of multiple organ failure on the 71st day.

An autopsy revealed: (1) DLBCL of the spleen with invasion to multiple organs and systemic lymph nodes, including the cervical, pulmonary hilum, para-aortic, peripancreatic nodes, the bone marrow, liver, both lungs, heart, and bilateral adrenal glands; additionally, effusion into the body cavities were found. (2) All lymph nodes obtained from the neck, lung, para-abdominal aorta, and abdominal cavity showed invasions of large lymphoma cells that were identical with those found in the spleen. (3) The liver was significantly enlarged, weighing 2,750 g, with numerous white nodules of DLBCL in its parenchyma, invasive to the portal area, especially showing massive invasion to the portal vein (Fig. 3A, B). (4) Hemophagocytic syndrome in the bone marrow was remarkable. (5) Macular incomplete necrosis in and CD68-positive histiocytic infiltration to both white and gray matters of the spinal cord from cervical to sacral were seen (Fig. 3C, D). No infiltration of CD20-positive tumor cells was demonstrated. (6) No abnormal findings in the optic nerve, cerebrum, brain stem, and cerebellum were seen. Thus, the final diagnosis was DLBCL, not otherwise specified.

## DISCUSSION

DLBCL, THE MOST common type in non-Hodgkin lymphoma, is often aggressive, and its diagnosis-to-

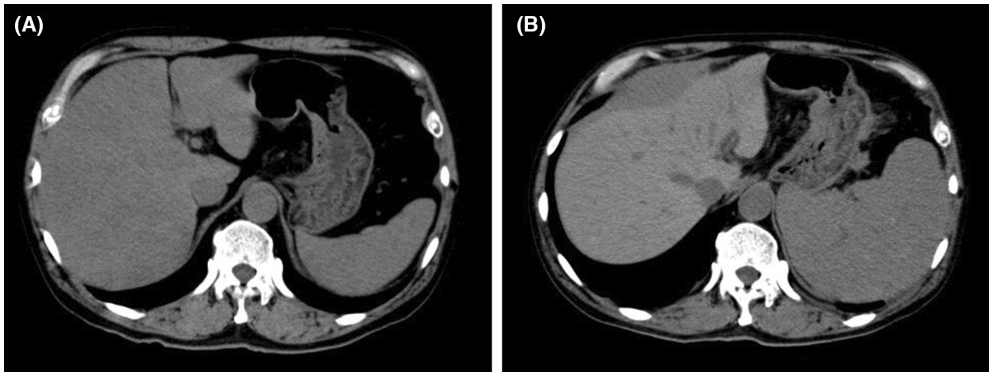


**Fig. 1.** Horizontal sections of computed tomography (CT) of the upper abdomen. (A) A horizontal section of the upper abdomen performed at the presentation of paralysis of the lower extremity. (B) A CT performed 2 months after the first CT presenting with a syncopal episode demonstrates a remarkably enlarged and ruptured spleen with intraperitoneal hemorrhage.

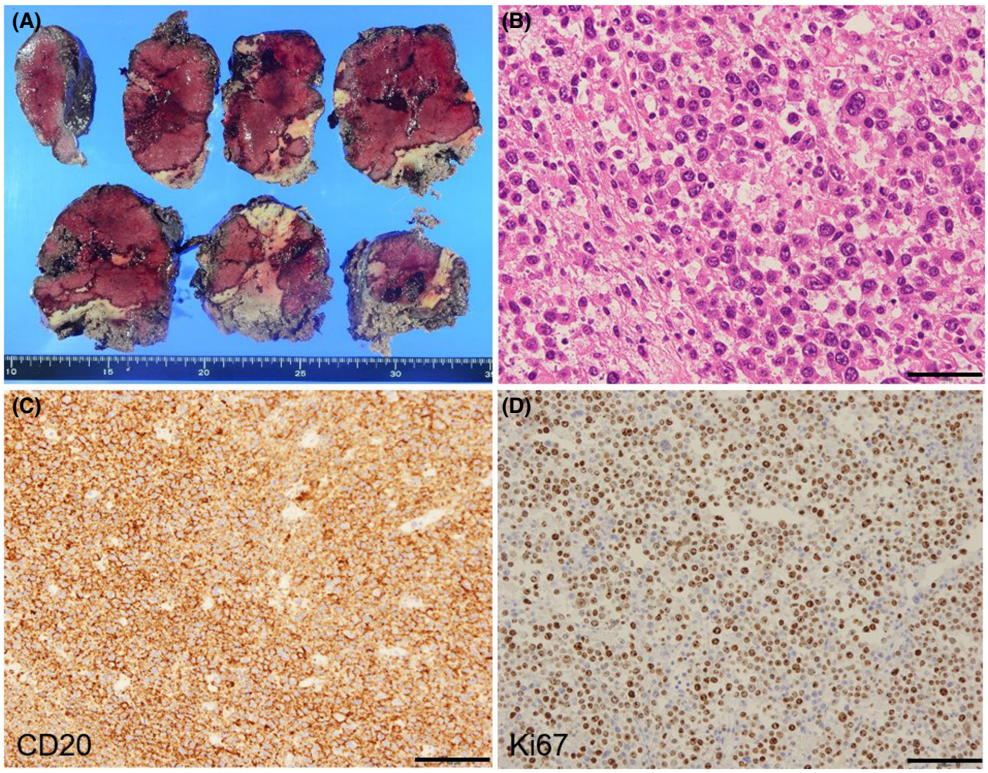


**Fig. 2.** The pathological examinations of the extracted spleen. (A) Gross anatomical examinations show infarcted areas (white) and multiple nodules. The size of the spleen was 15 × 10 × 8 $cm^3$ in diameter. (B) Histological examinations with hematoxylin and eosin staining show diffuse invasion of large lymphoma cells with large and irregular-shaped nuclei. (C), (D) Staining of CD20 and Ki67, respectively. Scale bars depict 100 μm.

treatment intervals are critical because a 2-year delay in diagnosis causes poor outcome.[1,3] Our patient's clinical course was drastic and unique. Initially, the patient showed asymptomatic mild anemia and thrombocytopenia, and he did not have any symptoms including lymph adenopathy. Two months before his rupture of splenomegaly, he had transverse myelitis. As of this moment, his abdominal organs, including the spleen, were normal with no lymphadenopathy. His myelitis was cured by steroid and plasma exchanges. The autopsy showed systemic invasions of lymphoma cells except in the brain and spinal cord, and microscopic examinations showed diffuse proliferation of atypical large lymphoma cells. Although intravascular large B-cell lymphoma (IVLBCL) can be accompanied with encephalitis and myelitis,[4,5] IVLBCL is unlikely in our case due to diffuse systemic disseminations of lymphomas.[6] The histological examination of the spinal cord did not show invasions of lymphoma cells but it did show demyelination with histiocyte invasion. Possible speculative interpretations for the spinal cord lesions are[1] simple observation of healed myelitis of unknown cause[2]; healed lesions of malignant lymphoma after steroid therapy[3]; and inflammatory lesion as paraneoplastic effects by latent lymphomas. As it was impossible to obtain histological specimens during myelitis, and the latter two scenarios were never reported, the myelitis might have been a separate event from lymphoma. Transverse myelitis could be a manifestation of human T-lymphotropic virus type 1 (HTLV-1)–associated myelopathy; however, the patient was not from the Kyushu District, nor the pathology did reveal any evidence of HTLV-1 infection. Hemophagocytic lymphohistiocytosis is a rare clinical manifestation of DLBCL.[7]

Our patient developed systemic invasions of lymphoma cells in only 2 months, which is similar to the clinical course of high-grade B-cell lymphoma. However, the FISH test did not show rearrangements of c-Myc, BCL2, and BCL6, which is inconsistent with high-grade B-cell lymphoma.[8] We do not know potential unknown genetic causes because we have not performed whole-genome sequences for germline and somatic genetic variants, which is beyond the scope of this case report.[9]

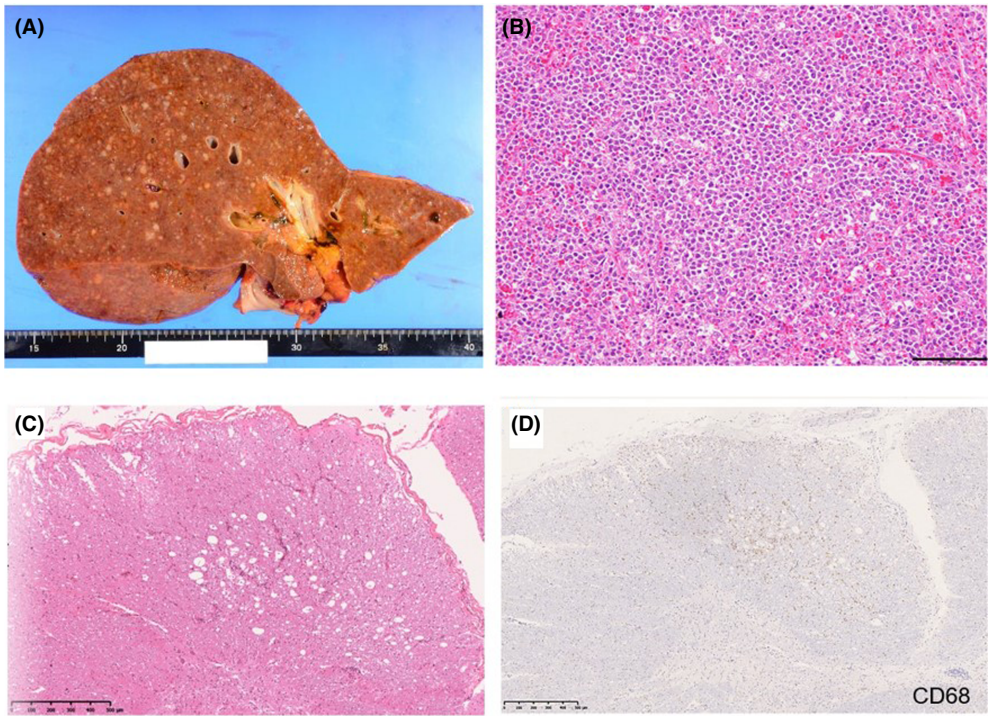


**Fig. 3.** Autopsy results of the liver and the spinal cord. (A) The cross section of the liver shows multiple white nodules indicating invasions of lymphoma cells in parenchyma and portal veins. (B) A histological examination revealed diffuse invasions of lymphoma cells as seen in the spleen. Scale bars depict 100 μm. (C) A transverse section with hematoxylin and eosin staining. Note that the vacuoles and demyelization occurred but no apparent invasion of lymphoma cells is seen. (D) CD68 staining. Diffuse invasion of histiocytes can be seen.

The reason the patient required multiple operations and IVRs should be discussed. First, he was given multiple plasma exchanges and a steroid pulse therapy for suspected transverse myelitis 2 months before the splenic rupture. Second, he was already shown to have advanced DLBCL and refractory thrombocytopenia at the first operation. These complications may have compromised his coagulability and caused tissue fragility. Every operation was mostly due to intractable bleeding and disruption of the tissues.

It can be controversial that chemotherapy could have been started after the splenectomy even when the patient's condition was critical. In this case, the pathological diagnosis was reported on the same day as the pancreatic fistula became obvious. Therefore, chemotherapy could not be started before the diagnosis of DLBCL as well as after the manifestation of pancreatic fistula.

The patient manifested a drastic course with rapidly progressed systemic DLBCL and multiple organ failure. The autopsy showed systemic invasions of lymphoma cells to multiple organs with hemophagocytic syndrome which was not observed at least 2 months before the splenic rupture, suggesting that his DLBCL was a fulminant type, although the result of FISH was inconsistent with high-grade B-cell lymphoma. In addition, intractable thrombocytopenia and tissue fragility which required multiple operations and transfusions could have largely affected his systemic condition causing multiple organ failure.

Although hematologic malignancy with acute onset necessitating emergency surgery is very rare, not only the proper surgical procedure but also deliberate postoperative management is crucial. Emergency physicians should well be prepared and communicate with specialists in oncology and hematology regarding decisions made on the treatment.

## CONCLUSION

WE EXPERIENCED a case of spontaneous ruptured splenomegaly due to DLBCL, not otherwise specified. This is a unique case because of the following reasons: first, splenic lymphoma involving multiple abdominal organs is extremely rare; second, hemophagocytic lymphohistiocytosis is a rare clinical manifestation of DLBCL; and third, splenic rupture and systemic metastases developed only in 2 months without the rearrangement of c-Myc, BCL2, and BCL6.

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## DISCLOSURE

APPROVAL OF THE Research Protocol: Not applicable.

Informed Consent: Informed consent for publication was obtained from the patient.

Registry and Registration No. of the Study/Trial: Not applicable.

Animal Studies: Not applicable.

Conflict of Interest: None declared.

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