CASE REPORT

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DIFFUSE LARGE B-CELL LYMPHOMA COMPLICATED BY BLEEDING FROM VARICOSE VEINS OF THE STOMACH AGAINST THE BACKGROUND OF SINISTRAL PORTAL HYPERTENSION. CASE STUDY AND LITERATURE REVIEW

Among 11,152 patients treated for complicated portal hypertension (PH) in the Kyiv Emergency Hospital in 2000—2023, 394 (3.5%) had sinistral portal hypertension (SPH), the etiological factor of which in one patient (0.25% of SPH cases, 0.009% of all PH cases) was diffuse large B-cell lymphoma (DLBCL). We provide an example of successful surgical treatment of a patient with DLBCL that was complicated by the development of SPH with bleeding from varicose veins of the stomach. A peculiarity and difference between SPH and other forms of PH is not only the preserved patency of the portal vein and the normal gradient of portal pressure but also the preserved liver function.

Keywords: diffuse large B-cell lymphoma, splenic vein thrombosis, sinistral portal hypertension, bleeding.

Sinistral, or left-sided, portal hypertension is a rare cause of upper gastrointestinal bleeding due to splenic vein obstruction and can occur secondary because of pancreatitis due to splenic vein thrombosis [1]. Based on a literature review using PubMed, CrossRef, and Google Scholar sources for the period from 1999 to 2024 on diffuse large B-cell lymphoma (DLBCL) and other types of non-Hodgkin's lymphomas, we did not find information on the development of sinistral portal hypertension (SPH) complicated by bleeding that required surgery, and the etiological factor of which was DLBCL. In this report, we present an example of successful surgical treatment of a patient with DLBCL complicated by the development of SPH with bleeding from varicose veins of the stomach.

A 49-year-old man was admitted to the intensive care unit of the Hospital of Emergency Medical Aid with acute upper gastrointestinal bleeding, manifested by vomiting of fresh blood and signs of hemorrhagic shock. During hospitalization, hemodynamic parameters were as follows: blood pressure

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80/40 mmHg, PR 110 bpm, and Hb 49 g/L. Bleeding from gastric varicose veins (IGV1 according to the Sarin classification) was detected during emergency esophagogastroduodenoscopy in the intensive care unit. From the anamnesis, it was known that over the past two years, the patient had been treated in the Department of Hematology for stage IV DLBCL, where he underwent several courses of chemotherapy. Also, the patient did not abuse alcohol and did not have chronic liver disease.

The data of the laboratory examination were as follows: Complete blood count: Hb 49 g/L; RBC 1.5 × × 10^{12}; WBC 2.0 × 10^9; PLT 42 × 10^9. Biochemical blood test: total protein 47 g/L; albumin 31 g/L; total bilirubin 10.7 μmol/L; direct bilirubin 4.2 μmol/L; ALT 0.4 mmol/h/L; AST 0.31 mmol/h/L; thymol test 4.3 units; urea 14.7 mmol/L; creatinine 80 μmol/L. Coagulogram: APTT 16 s; PTI 100%; total fibrinogen 3.1 g/L. Serological markers of viral hepatitis B and C were negative.

CT with contrast revealed a tumor spreading from the pancreas tail to the spleen and signs of PH with varicose veins of the stomach, which drain blood from the spleen, as shown in Figs. 1 and 2.

Based on the anamnesis and examination data, the diagnosis was established: diffuse large B-cell lymphoma stage IV with damage to the pancreatic lymph nodes, body and tail of the pancreas, and spleen. A sinistral form of portal hypertension. Varicose veins of the stomach of the III degree, complicated by bleeding. Hemorrhagic shock. Splenomegaly. Hypersplenism. Severe post-hemorrhagic anemia.

After stabilization of hemodynamic parameters, the patient underwent surgical treatment, which included splenectomy, ligation of v.gastricae sinister, and resection of the stomach fundus with varicose veins.

During the revision of the abdominal cavity organs, attention was drawn to the smooth liver surface, the biopsy of which did not reveal cirrhotic changes. A diffuse lesion of the liver and spleen, pancreatic lymph nodes, and the body and tail of the pancreas were diagnosed. Blood autoreinfusion was used, and a restrictive blood transfusion strategy was carried out to the target hemoglobin level of 70—80 g/L.

The laboratory parameters in the postoperative period were the following: Complete blood count: Hb 82 g/L; RBC 2.3 × 10^{12}; WBC 20 × 10^9; PLT 391 × 10^9;

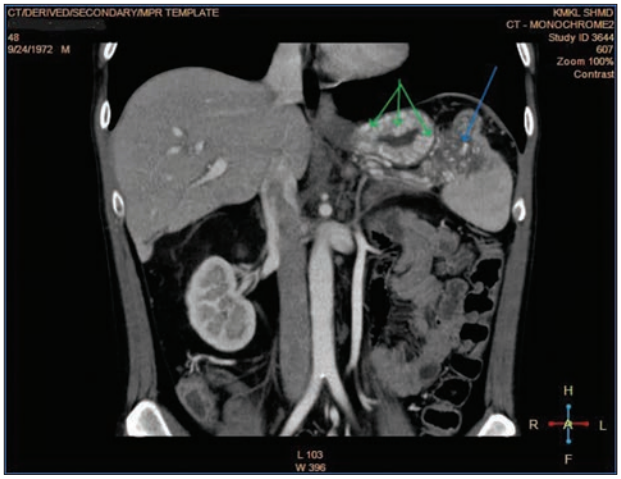

Fig. 1. Computed tomography with contrast in the portal vein phase demonstrates the presence of varicose veins of the stomach, which are visualized as multiple sinuous tubular structures with an uneven outline (green arrows), and a large heterogeneous mass of B-cell lymphoma spreading from the pancreas tail to the spleen (blue arrow)

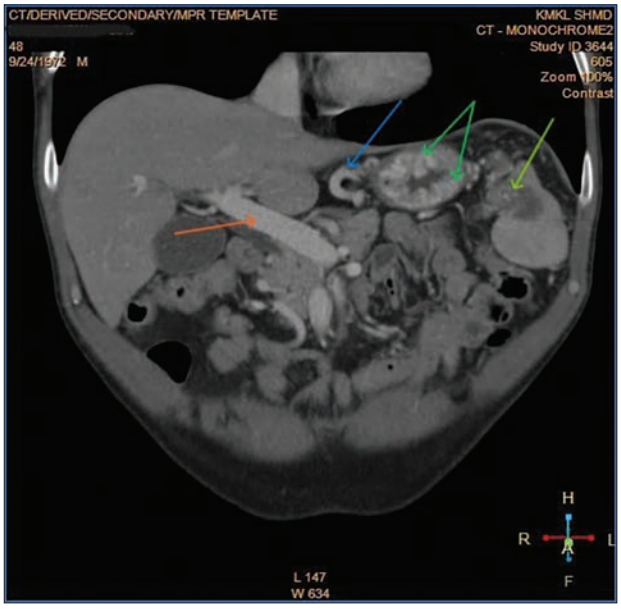

Fig. 2. Computed tomography with contrast enhancement in the portal vein phase shows: dilated portal vein (orange arrow), dilated v.gastrica sinister (blue arrow), the presence of B-cell lymphoma spreading to the spleen (yellow arrow), and multiple varicose veins (green arrows)

total protein 49 g/L; albumin 34 g/L; total bilirubin 13.7 μmol/L; direct bilirubin 2.9 μmol/L; ALT 0.2 mmol/h/L; AST 0.19 mmol/h/L; thymol test 4.3 units; urea 5.8 mmol/L; creatinine 80 μmol/L; prothrombin time 17 s; prothrombin index 94%; and total fibrinogen 3.1 g/L. In the postoperative period, the patient received antibacterial third-generation cephalosporins, anticoagulant therapy, which in-

cluded the introduction of low molecular weight heparin from the 2nd day of the postoperative period, and early enteral nutrition with protein mixtures. The postoperative period proceeded without complications. The patient was discharged from the hospital in satisfactory condition on the 8th day of the postoperative period. No recurrence of bleeding was observed during the follow-up.

Discussion

Among a significant number of non-Hodgkin lymphomas, DLBCL is the most common. It affects various organs and tissues including not only the abdominal cavity. The most common primary extranodal localizations of DCL are the gastrointestinal tract, head-and-neck, and skin/soft tissues [2]. DLBCL is the most common type of lymphoma, accounting for about a third of all cases worldwide. According to the 5th edition of the World Health Organization Classification of Haematolymphoid Tumours, DLBCL, not otherwise specified (NOS), is the most common entity of the family of large B-cell lymphomas comprising 17 specific entities other than DLBCL, NOS [3]. DLBCL mainly occurs in the oropharynx, especially in the tonsil on one side, and if endoscopy reveals yellow-white pseudomembranous adhesion on the tonsil surface, and ultrasound examination reveals multiple enlarged lymph nodes in the neck, DLBCL should be excluded [4].

Primary gastric lymphoma is a high-grade malignancy gastric lymphoma, more common than lymphoma of the mucosal layer associated with lymphoid tissue (MALT), characterized by a poorly differentiated lesion and is usually secondary to *H. pylori* infection [5].

Gastric DLBCL accounts for nearly 59% of all gastric lymphomas, and there are no definitive prognostic markers for this disease, but many studies suggest that bulk formations, advanced stage, aggressive histology, B-symptoms, high serum β2-microglobulin levels, and LDH may have prognostic value [6]. In addition, gastric DLCBCL is one of the most common extranodal lymphomas with a limited number of published series with nonspecific clinical signs of the disease, which may contribute to diagnostic delay and progression of the disease stage when detected [7].

Primary pancreatic lymphoma and DLBCL are rare diseases, accounting for 0.1% of all malignant lymphomas, for which there are no well-defined diagnostic and therapeutic protocols [8].

DLBCL mimics antinuclear autoimmune hepatitis, which occurs with liver damage and can be confirmed by biopsy [9].

DLBCL which appears in the spleen, also known as primary DLBCL splenic lymphoma, is a rare form of malignant lymphoma and is defined as lymphoma that is limited to the spleen or also involves splenic lymph nodes located in the spleen gate [10]. Also, DLBCL is one of the most common non-Hodgkin's lymphomas, which does not have typical or specific clinical signs and can manifest itself as a spleen abscess [11]. Therefore, primary splenic lymphoma is a rare lymphoproliferative disease that affects the spleen, has a variety of clinical manifestations, and does not have a clear consensus on treatment strategies [12].

Identification of DLBCL of the duodenum is difficult due to the presence of nonspecific symptoms such as hematemesis, melena, and obstructive jaundice [13]. Male sex, advanced stage of tumors, and certain histological variants, including T-cell lymphoma, B-cell lymphoma, and DLBCL, are associated with poor prognosis [14].

Obstructive jaundice caused by papillary duodenal lymphoma is extremely rare. For diagnosis and treatment, it is necessary to conduct histological, immunohistochemical, and molecular studies [15].

Though the risk of death from esophageal-gastric varicose bleeding caused by portal hypertension is the highest in patients with gastrointestinal bleeding, diagnosis and treatment require further improvement [16]. Left-sided portal hypertension is a rare form of extrahepatic portal hypertension, which is also known as a localized, regional, or sinusoidal portal hypertension, and is characterized by increased pressure on the left half of the portal system, secondary to compression or obstruction of the splenic vein with normal liver function and portal vein patency [17]. Various diseases of the pancreas, including malignant ones, cause LPH and need to be corrected [18, 19].

LPH, or segmental portal hypertension, has also been described in diseases of the abdominal organs (retroperitoneal fibrosis or abscess) or after pancreatic surgery (caudal pancreatectomy with ligation of splenic vessels but preservation of the spleen or pancreatoduodenectomy with ligation of the splenic vein) or the liver transplantation, as well as

a complication of certain endovascular procedures [20]. The isolated gastric varicose veins are a typical manifestation of LPH, resulting in severe or persistent gastrointestinal bleeding [21, 22].

Therapeutic strategies for the treatment of bleeding of gastric varices (GV) include endoscopic intervention, partial splenic embolization, and splenectomy, which are widely used for gastroesophageal varicose veins in patients with cirrhosis of the liver but have a high failure rate in the treatment of gastrointestinal bleeding caused by LPH [23].

Some authors demonstrate the efficacy and safety of the embolization and injection of cyanoacrylate into gastric varices under the control of endoscopic ultrasound equipment [24, 25]. A single-center retrospective study to compare the safety and clinical outcomes of combined transjugular intrahepatic portosystemic bypass grafting (TIPS) in combination with varicose obliteration using TIPS alone for the treatment of gastric varices (GVs) showed that the incidence of GV eradication is significantly higher after combination therapy, with no associated increase in the complications of portal hypertension [26].

The authors evaluated short-term and long-term mortality and rebleeding with endoscopic cyanoacrylate compared to retrograde transvenous balloon obliteration (BRTO) in ARV bleeding and concluded that BRTO is associated with a lower incidence of rebleeding but does not change mortality [27].

The efficacy and safety of embolization under the control of endoscopic ultrasound navigation with cyanoacrylate injection have achieved excellent clinical success, with a lower incidence of rebleeding and repeated interventions than with coil-alone treatment [28—30].

Endoscopic cyanoacrylate glue injection is the standard therapy for acute hemostasis; however, it can be associated with serious complications, and at the same time, endoscopic thrombin injection is similar to glue injection in achieving successful hemostasis in gastric varicose veins [31, 32].

DLBCL, affecting various structures and organs of the abdominal cavity, causes hemodynamic disorders in the basin of the portal system due to the compression of the splenic vein, which leads to the development of SPH complicated by profuse bleeding from the varicose veins of the stomach.

To identify the cause and form of portal hypertension, it is necessary to perform computed tomography with contrast enhancement.

This clinical case highlights a successful surgical treatment of SPH-associated gastric varicose vein bleeding in the context of DLBCL. The authors aim to draw attention to the hematological disease that causes the obstruction of the splenic vein and the development of a regional form of portal hypertension, to propose a variant of treatment tactic for controlling bleeding from gastric phlebectasia.

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Conflict of interest: none.

Compliance with ethical requirements

Ethical approval of the Commission on Bioethics of O.O. Bogomolets NMU was obtained. The written consent was obtained for using patient's data in a case report publication. The study was completed in accordance with the recommendations of the committees on the ethics of biomedical research, the legislation of Ukraine on health care, the Declaration of Helsinki of 2000, and the European Community Council Directive 86/609 on human participation in biomedical research.

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ДИФУЗНА ВЕЛИКОКЛІТИННА В-КЛІТИННА ЛІМФОМА, УСКЛАДНЕНА КРОВОТЕЧЕЮ З ВАРИКОЗНО РОЗШИРЕНИХ ВЕН ШЛУНКА НА ТЛІ СИНІСТРАЛЬНОЇ ПОРТАЛЬНОЇ ГІПЕРТЕНЗІЇ. ВИПАДОК З ПРАКТИКИ ТА ОГЛЯД ЛІТЕРАТУРИ

Серед 11152 пацієнтів, які перебували на лікуванні з приводу ускладненої портальної гіпертензії (ПГ) в лікарні швидкої медичної допомоги м. Києва протягом 2000—2023 рр., 394 (3,5%) мали синістральну портальну гіпертензію (СПГ), етіологічним фактором якої в одного (0,25%) пацієнта була дифузна великоклітинна В-клітинна лімфома (ДВКЛ), яка становила щодо всіх пацієнтів з ПГ 0,009%. У статті наведено приклад успішного хірургічного лікування хворого з ДВКЛ, ускладненою розвитком СПГ з кровотечею з варикозних вен шлунка. Поєднання цих патологічних станів визначає особливості клінічного перебігу та процесу лікування. Особливістю і відмінністю СПГ від інших форм ПГ є не тільки збережена прохідність ворітної вени, нормальний градієнт портального тиску, але й збережена функція печінки.

Ключові слова: дифузна великоклітинна В-клітинна лімфома, тромбоз селезінкової вени, синістральна портальна гіпертензія, кровотеча.