Case report

Spontaneous pathological splenic rupture as a first manifestation of mantle cell lymphoma – a case report and literature review

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Splenic rupture is a critical surgical condition that poses an immediate threat to the patient's life. In most cases, mechanical trauma to the organ results in the rupture of the capsule, leading to hemorrhage into the peritoneal cavity. Spontaneous (pathological) spleen rupture (SPSR) is considered when the etiology of the rupture is non-traumatic. Spontaneous (pathological) spleen rupture is most commonly associated with hematological malignancies, though it remains a rare condition. Only 8 cases described in the literature have been caused by mantle cell lymphoma (MCL). This review presents the case of a 59-year-old male patient who was treated with emergency splenectomy due to SPSR. Histopathological examination revealed MCL.

Key words: chemotherapy, MCL, splenectomy, spontaneous pathological splenic rupture.

Introduction

Splenic rupture is a life-threatening condition, typically resulting from mechanical trauma. Spontaneous (pathological) spleen rupture (SPSR) occurs when there is no traumatic background that could lead to this type of injury. Most often, SPSR is a complication of malignancy, such as acute or chronic leukemia, non-Hodgkin lymphoma (including mantle cell lymphoma – MCL), myeloproliferative diseases, myelodysplastic diseases, chronic lymphocytic leukemia or multiple myeloma. Spleen rupture can also be caused by infectious mononucleosis or malaria [1]. However, these causes are sporadic. To date, approximately 800 cases have been reported, with only eight attributed to MCL [2]. Patients diagnosed with SPSR most commonly complain of acute abdominal pain, pain in the left shoulder (Kehr's sign), and general malaise [3]. A highly valuable examination in the diagnostic process of SPSR is abdominal ultrasonography (USG). This inexpensive and non-invasive test provides a reliable evaluation of splenomegaly, numerous enlarged peritoneal lymph nodes, the presence of free fluid in the peritoneal cavity, as well as evidence of splenic trauma. If necessary, SPSR can be confirmed by contrast-enhanced computed tomography (CT) [3].

Case report

A 59-year-old patient was admitted to the emergency department (ED) due to abdominal pain that lasted for several days, with a rapid peak on the day of admission, and a 10% body weight loss over the last 6 months. The patient was in good general condition, with stable circulation and breathing (blood pressure 127/78 mm Hg, heart rate 63 beats per minute). He denied any trauma or other symptoms. The patient had undergone a right-sided nephrectomy in the past

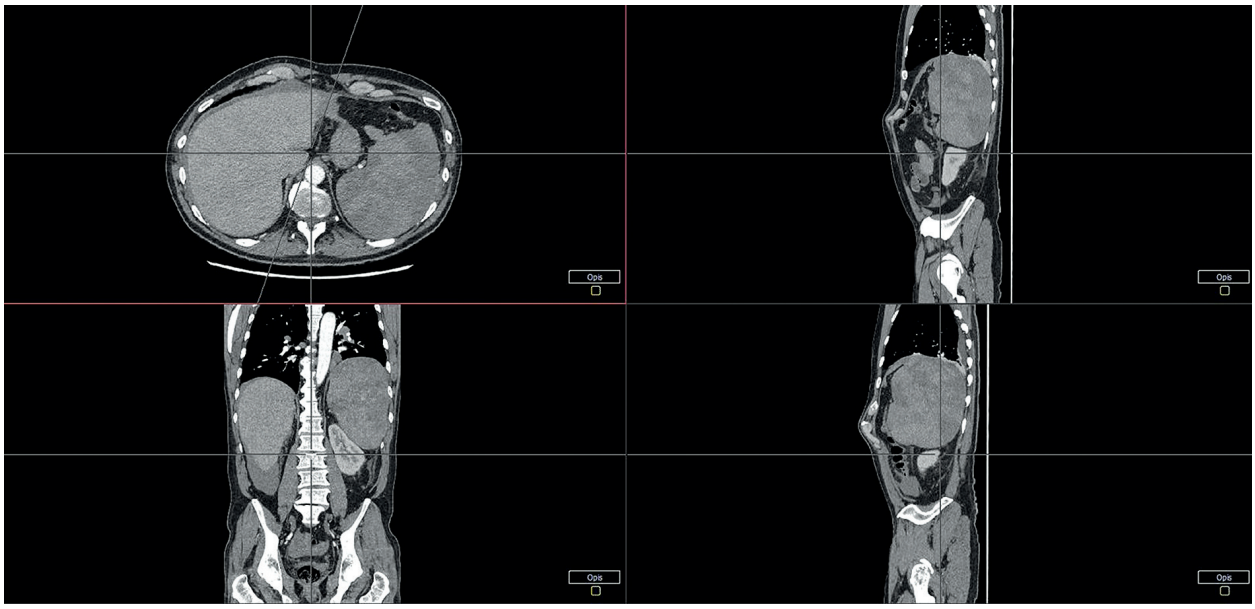

Figure 1. Computed tomography image, taken during emergency diagnostics in emergency room showing a significantly enlarged spleen suspected to be fractured and free fluid in the abdominal cavity with a density of blood

without a history of malignancy and reported no other comorbidities. On physical examination, the patient's abdomen was soft, with tenderness in the left epigastric and umbilical regions. There were no signs of peritoneal irritation; peristalsis was normal. The spleen was not palpable through the abdominal wall. Physical examination revealed no lymphadenopathy or other abnormalities.

As part of emergency diagnostics in the ED, blood morphology was performed. The examination showed the following results: slightly decreased number of red blood counts (3.81 T/l), hemoglobin (11.7 g/dl) and hematocrit (35%). Conversely, C-reactive protein level was significantly increased (131.7 mg/l), despite a normal leukocyte count (9.4 G/l). The blood smear showed significantly increased quantity of lymphocytes (30%), monocytes (6%) and segmental granulocytes (62%). Moreover, the number of thrombocytes was slightly decreased to 127 G/l. Coagulation parameters and other marked values showed no deviations. The patient underwent an abdominal USG, which revealed a significantly enlarged spleen, retroperitoneal lymphadenopathy, and the presence of free fluid in the abdominal cavity. The diagnostic workup was extended with an intravenous contrast-enhanced CT scan of the abdominal cavity, which confirmed splenomegaly (160 × 90 mm) and advanced lymphadenopathy in the abdominal cavity (Figure 1). The density of the fluid in the abdominal cavity suggested blood origin. The patient was admitted to the General Surgery Department for further treatment.

During observation, the patient's condition progressively deteriorated despite conservative treatment. Due to hemodynamic instability despite intensive fluid resuscitation, the patient was qualified for urgent laparotomy. Massive internal bleeding into the abdominal cavity, from fractured, enlarged spleen was confirmed intraoperatively. Splenectomy was performed in a standard procedure, with-

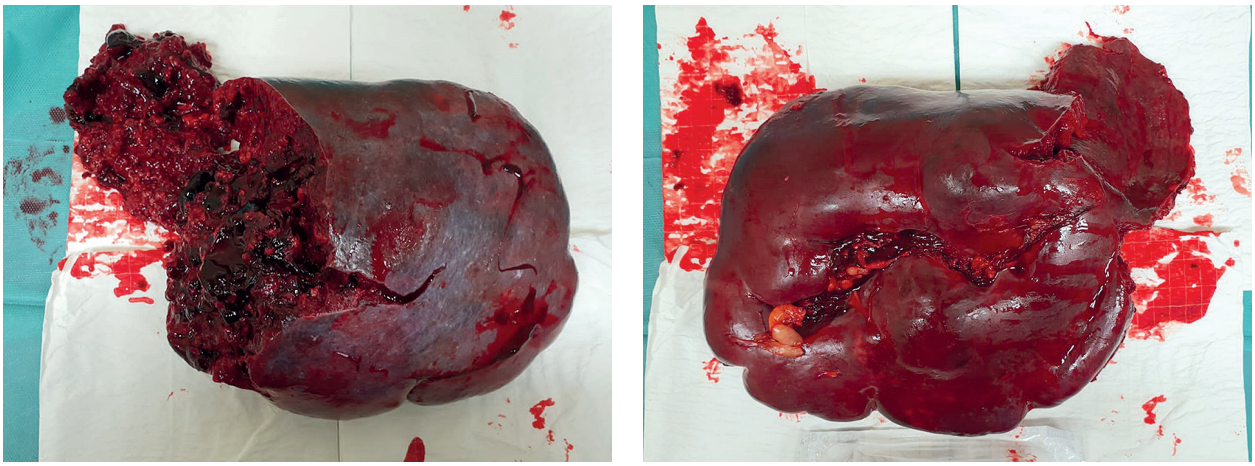

Figure 2. Intra-operative preparation – enlarged, fractured spleen

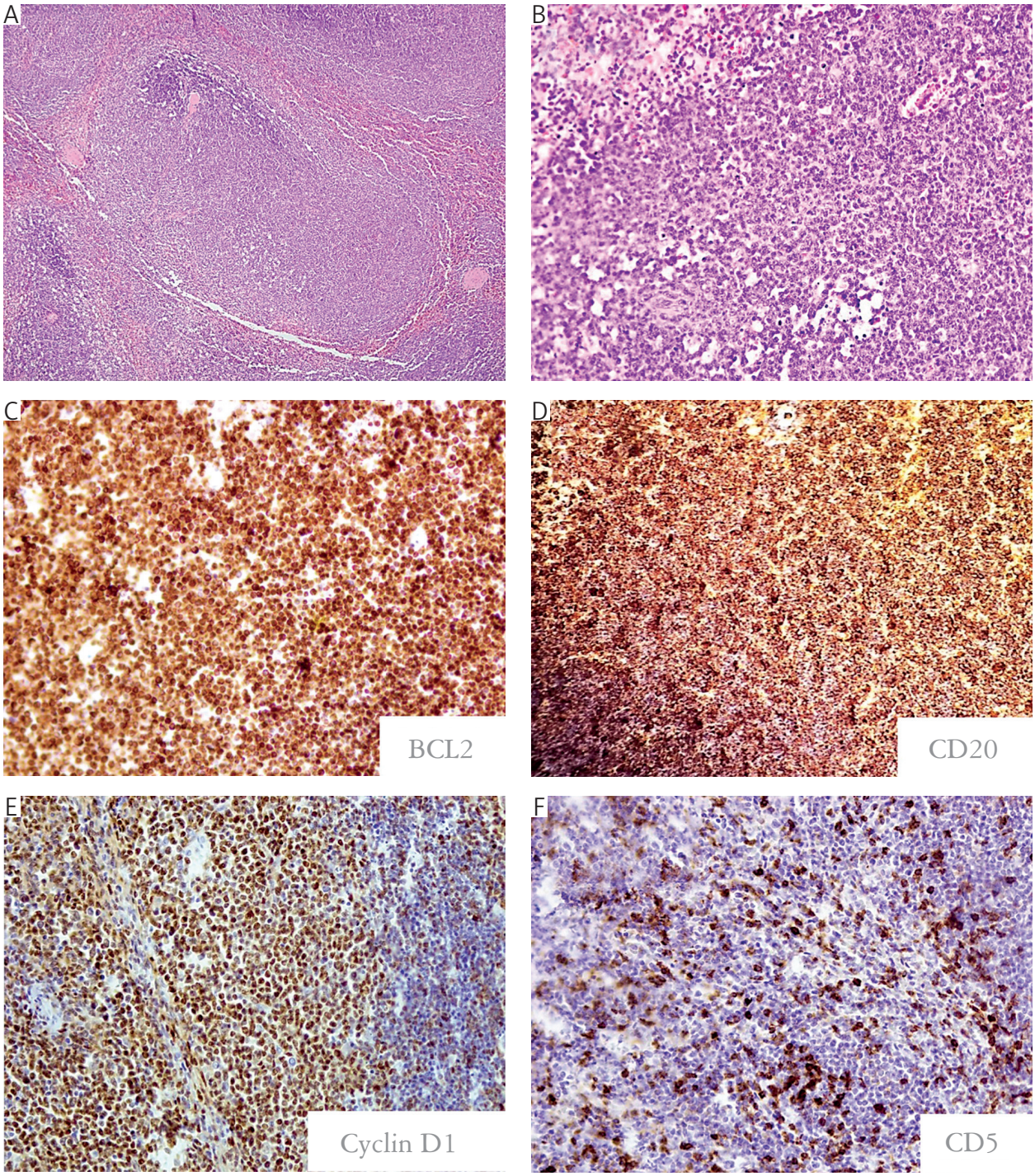

Figure 3. Histopathological image of the patient's spleen sections. A, B) Hematoxylin and eosin staining. Visible compound infiltration of monomorphic small cells. C) Immunohistochemical staining for CD20 expression (positive). D) Immunohistochemical staining for BCL2 expression (positive). E) Immunohistochemical staining for cyclin D1 expression (positive). F) Immunohistochemical staining for CD5 expression (positive reaction in a few tumor cells)

out intraoperative complications (Figure 2). During the perioperative period, 4 units of red blood cell concentrate, 4 units of fresh frozen plasma and 5 units of platelet concentrate were transfused to the patient. During the postoperative period, stabilization of the patient's condition and blood morphology parameters was observed, with no signs of active bleeding. Hospitalization was uncomplicated. The patient was discharged in good condition on postoperative day 6, with referral for vaccination against encapsulated bacteria.

Histopathological examination of splenic sections showed a malignant neoplasm composed of a monomorphic population of cells destroying the splenic parenchyma (Figure 3A, B) derived from B lymphocytes (showing expression of CD20 protein) (Figure 3C). The tumor cells had a centrocyte-like morphology with diffuse chromatin with an invisible nucleus

or blastoid or pleomorphic morphology. On immunohistochemical examination, the cells showed the phenotype: CD20+, CD23–, CD123–, CD3–, CD5+/– (expression in few cells), Cyclin D1+, bcl 2+, bcl 6–, CD10–, CD138–, SOX-11+ (weakly), CD30–, CD11c–, CD25–, CD38–, CD23+, Annexin 1-, $\kappa > \lambda$, Ki-67 index: approximately 20–25% (expression of cyclin D1, BCL2 and CD5) (Figure 3D, F). The immunophenotype was consistent with cells derived from the mantle zone. Despite the positive expression of CD5 in a few tumor cells, the overall morphology, immunophenotype and clinical picture allowed to establish the diagnosis of mantle zone lymphoma in the classic variant (Figure 3).

After an extended investigation, the patient was diagnosed with Ann Arbor IV MCL with intermediate risk (MIPI 6.3, Ki-67 25%). As part of his qualification for hematological treatment, a positron emission tomography and computed tomography (PET-CT) was carried out. It showed metabolically active lymph nodes in the neck, chest (mediastinum, axillary, and hilar lymph nodes of the lung), abdomen and pelvis.

Hematological treatment was started about two months after the splenectomy, using cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate and prednisone (CHOP) without rituximab due to ongoing vaccination. The treatment was well tolerated by the patient. In the next cycle, chemotherapy containing rituximab, dexamethasone, cytarabine, and cisplatin (R-DHAP) was administered, resulting in transient acute kidney injury, which resolved after conservative treatment. A bone marrow examination showed lymphoma infiltration (12%).

Subsequently, immunochemotherapy was implemented according to the R-CHOP (rituximab + CHOP) regimen, which proceeded without complications. At a later stage, the patient received cycles of rituximab and high-dose cytarabine (R-HD-Ara-C) chemotherapy, including stem cell mobilization. The treatment was complicated by gastritis. A follow-up PET-CT showed a metabolically active left external iliac lymph node – an unsuccessful attempt at a nodular surgical biopsy was made (the lesion was not visualized intraoperatively). Mobilization of hematopoietic cells was completed successfully with cytapheresis, resulting in an adequate CD34+ count.

The patient was qualified for autologous stem cell transplantation (aSCT) after conditioning treatment according to the carmustine, etoposide, cytarabine and melphalan (BeEAM) regimen. The transplant was performed without complications, while the period of drug aplasia was complicated by bacterial and fungal infections as well as pneumonia. After intensive antibiotic and supportive therapy, improvement was achieved. The patient was discharged in good general condition with a regenerating hematopoietic system.

A follow-up PET scan performed three months after aSCT showed no metabolically active lymphoid lesions, except in the area of the gastric cardia which required further diagnosis. Since then, the patient has remained in remission and under the ongoing care of a hematology outpatient clinic. Recent hospitalizations for pneumonia and gastroscopy have shown no signs of relapse, and the patient remains in good health.

Discussion

This case illustrates the clinical picture of MCL with a pathological rupture of the spleen. Mantle cell lymphoma is a subtype of non-Hodgkin's lymphoma (NHL), accounting for approximately 6% of NHL cases and is characterized by a chromosomal translocation t(11; 14) (q13; q32) leading to overexpression of cyclin D1 [3–5]. Overproduced cyclin D1 actively formulates retinoblastoma 1 proteins causing the overactivation of the transcription factor E2F and resulting in cellular pathway dysregulation and cell entry into the S phase of the cell cycle [6]. This alteration also impacts signaling pathways involving the TP53 and mammalian target of rapamycin proteins [6, 7]. This mutation is found in about 8% of all B-cells; such cells can remain in a long latency period of around 12 years. Thus, not every cell with the aberration will be a precursor to cancer [6, 7]. There are four types of MCL: classic, small cell, pleomorphic, blastoid, and 3 histological patterns: mantle zone, follicular, diffuse [5]. Mantle cell lymphoma is more common in men (M : F 3 : 1), with a median age of diagnosis of 60–70 years [3, 5, 8]. The incidence of MCL varies by race. Statistical analysis based on SEER data from 1992–2004, shows a predominance of Caucasians (0.61/100,000) compared to African Americans (0.32/100,000) or other communities/groups (0.27/100,000) [9]. Another analysis, conducted in 2012, confirmed a higher incidence among Caucasians compared to other groups. The incidence was 0.9/100,000 among Caucasians, followed by 0.6/100,000 among Hispanics, 0.36/100,000 among Black individuals, and 0.3/100,000 among Asians [8]. Mantle cell lymphoma is most commonly diagnosed at stage III or IV (Ann Arbor) in 74.6% of cases [9]. The 5-year related survival rate in 2014–2020 was 74.3%, although the leukemic phase present in 30% of cases worsened the prognosis [10–17]. Splenomegaly has also been associated with an exacerbated prognosis [17]. Typical presentations in MCL morphology are cells with irregular or cleaved nuclei, in some cases resembling small lymphocytes. Mantle zone extension may also be present [18].

Physical examination for lymphadenopathy, together with histopathological evaluation, provides the greatest diagnostic yield in MCL, with 63% of patients presenting with this feature [19]. The di-

agnosis is confirmed by immunohistochemical examination, which confirms the presence of CD5, CD10, CD20 and, most crucially, cyclin D1 overexpression [20]. The most essential factor in preventing splenic rupture in patients with MCL is USG, which is an easily accessible test that allows to confirm possible splenomegaly and the presence of fluids in body cavities. Additional methods that can confirm splenomegaly include other imaging studies, e.g. CT, PET, and X-ray [21]. Laboratory tests include CBC, liver, and kidney function tests.

The treatment of MCL consists of combination chemotherapy (R-CHOP, R-DHAP), radiotherapy, immunotherapy, and targeted therapy using monoclonal antibodies, proteasome inhibitors or kinase inhibitors [22, 23]. The choice of therapy depends on the patient's age, general health and tumor stage. Although MCL remains mostly an incurable disease and treatment regimens are still not unified, many publication authors agree that R-CHOP/R-DHAP therapy (6 cycles of chemotherapy administered every 21 days) lasting several months with subsequent aSCT is the most favorable therapy for young/healthy patients [24–27]. In addition, studies have shown that administration of rituximab after aSCT improves progression-free survival (83% vs. 64% at 4 years) and overall survival (89% vs. 80% at 4 years) after 3 years of rituximab compared to observation without the drug [28, 29].

Older patients with MCL often have limited ability to tolerate intensive chemotherapy regimens. In their case, treatment is based on immunochemotherapy. There are two main approaches: either treatment with CHOP combination therapy or bendamustine-based regimens [30]. Immunotherapy uses immunomodulatory drugs such as lenalidomide. Currently, there are also ongoing studies on the use of chimeric antigen receptor T-cell therapy for relapsed or refractory lymphoma, with axicabtagene coalesced or tisagenlecleucel [23]. Despite intensive therapy, most patients experience relapses [31].

Nowadays, the method of treatment for SPSR is splenectomy; non-operative treatment (e.g., by vascular embolization) has been abandoned due to the high mortality rate [21]. The splenectomy procedure can be executed by three methods: laparotomy, laparoscopy, and the method using robotic systems, which has been rapidly developing over the past decades. Of the methods mentioned above, laparoscopy and the robotic method are the most preferred due to their advantages and lower complication rates [32]. The first method is associated with an incision of the abdominal cavity layers, either in the midline of the body, up from the umbilicus, or obliquely on the left side, a few centimeters below the left rib arch [3], closing the arterial and venous vessels of the spleen, and then dissecting the organ. In laparoscopic surgery, small incisions are made through which a camera and other instruments are inserted to allow for precise dissection of the spleen. Due to the precision guaranteed by the use of a robot during operation, the robot-assisted method is becoming more widely used [3]. Removal of the spleen can lead to the appearance of abscesses or cysts in its place of adhesions to neighboring organs. Adjacent intestinal segments can also move into the free space. All of these consequences may manifest as nonspecific pain symptoms, which in each case require medical consultation. The patient after splenectomy is at increased risk of infections, particularly those caused by enveloped bacteria. Therefore, prophylactic vaccinations against pneumococcus, meningococcus, Haemophilus influenzae type b, and seasonal flu are recommended after the procedure. Preventive antibiotic therapy is also often suggested [32].

Conclusions

Spleen rupture is a sudden, life-threatening condition with a high mortality rate. Because SPSR may be associated with malignant disease, patients should receive appropriate oncological follow-up after the procedure. Although treatment regimens for MCL have not yet been standardized, current therapeutic trends offer hope for gradual improvement in patient outcomes.

Disclosures

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4. Conflicts of interest: None.

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