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Case Report

# CLINICAL CASE OF A PATIENT WITH EXTRANODAL DIFFUSE LARGE B-CELL LYMPHOMA AND SURGICAL COMPLICATIONS

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## Summary

Diffuse large B-cell lymphoma (DLBCL) is one of the most common types of non-Hodgkin lymphoma in adults. In most of the cases a complete remission is possible to obtain by applying conventional immunochemotherapy (rituximab in combination with cyclophosphamide, doxorubicin, vincristine, methylprednisolone or R-CHOP). Its effect depends on some risk factors, cellular origin of the lymphoma and to some extend – the localization when extranodal involvement is confirmed.

We present the case of a patient with DLBCL of small intestine and non-specific clinical manifestation. Following treatment with standard therapy R-CHOP patient fail to achieve disease response and gastrointestinal track (GIT) complications were registered.

**Keywords:** intestinal lymphoma, surgical complications, therapy.

## Introduction

DLBCL is a heterogeneous group of aggressive non-Hodgkin lymphomas, morphologically characterized by the presence of large transformed B-cells and a diffuse growth pattern [1]. According to latest clinical data average age at the time of diagnosis is about 70 years and most of the patients present with advanced stage of the disease [2]. These specific features and the possibility for massive extranodal engagement may lead to therapy resistance. The disease may be “de novo” diagnosed or as a result of precedent indolent lymphoma transformation [1, 3].

DLBCL represents about 40% of all lymphomas worldwide [4, 5] with prevalence of 5-6 cases per 100 000 people and a marked increase to 15-25 per 100 000 in advanced age [6]. Diagnosis requires a comprehensive history with specific attention to B symptoms presence, objective status, hematological and chemistry panel, immunohistochemistry of tissue biopsy. In 40% of DLBCL cases an extranodular disease localization can be found

[7], involving one or more organs – GIT, soft tissues, muscles, bones, skin, endocrine glands. Mediastinal and abdominal disease engagement is often presented as a large tumor mass (so called Bulky disease), which is clinically associated with symptoms of underlying tissue and organ compression. DLBCL is diagnosed after excision biopsy of a lymph node, tissue or organ, following immunohistochemistry. Immunophenotyping allows the differentiation between germinal center (GC) or non-GC origin with a well-established panel: CD20, CD3, CD5, CD10, CD45, BCL2, BCL6, Ki-67, IRF4/MUM [2]. Helpful methods to differentiate between distinct subtypes of patients, their expected outcome and survival are cytogenetics and fluorescence in situ hybridization (FISH) for MYC, bcl2, bcl6 gene rearrangements. Imaging is recommended for DLBCL staging and can be performed with positron emission tomography (PET/CT) or computer tomography (CT) of neck, chest, abdomen and pelvis. Complex disease evaluation requires Ann Arbor staging (Lugano modification), International prognostic index (IPI) risk stratification and/or age-adapted IPI (aaIPI) [2].

## Clinical case

An average patient was admitted in Hematology Clinic in May, 2022 for diagnostics, staging and treatment. His main complaints started two months before - abdominal pain, periodically changing in intensity without association with food consumption. The abdominal CT confirmed a tumor mass, probably originating from small intestines, and mesenterial lymphadenomegaly. A midline laparotomy was made and the tumor mass with intestinal origin was confirmed, infiltrating omentum. Surgeons proceeded with intestinal resection, latero-lateral anastomoses and partial omentum resection. Immunohistochemistry of biopsied material confirmed high-grade B-cell lymphoma infiltration of DLBCL profile, non-GC type. High proliferative index was found - Ki-67 about 85-90%, positive staining for CD20, bcl2 and negative for bcl6, c-myc, CK AE1/AE3, S-100.

Next month a whole-body CT was performed, revealing a conglomerate of intestinal loops in the right abdominal cavity with adhesions and pathologically enlarged lymph nodes, reaching 134/70 mm in size. This tumor mass was close to the gall bladder, liver flexure and front abdominal wall on the right. Abnormal paracaval lymph nodes about 25mm in diameter were found, cecum and ascending colon dilated, reactive ascites was present. (Fig a,b )

Based on all these data and diagnostic procedures performed, the patient was staged as DLBCL of small intestines and mesentery IV E according to Ann Arbor, Lugano system and evaluated as a high risk patient (aaIPI).

According to current guidelines for the treatment of extranodal B-cell lymphomas R-CHOP regimen was initiated every 21 days.

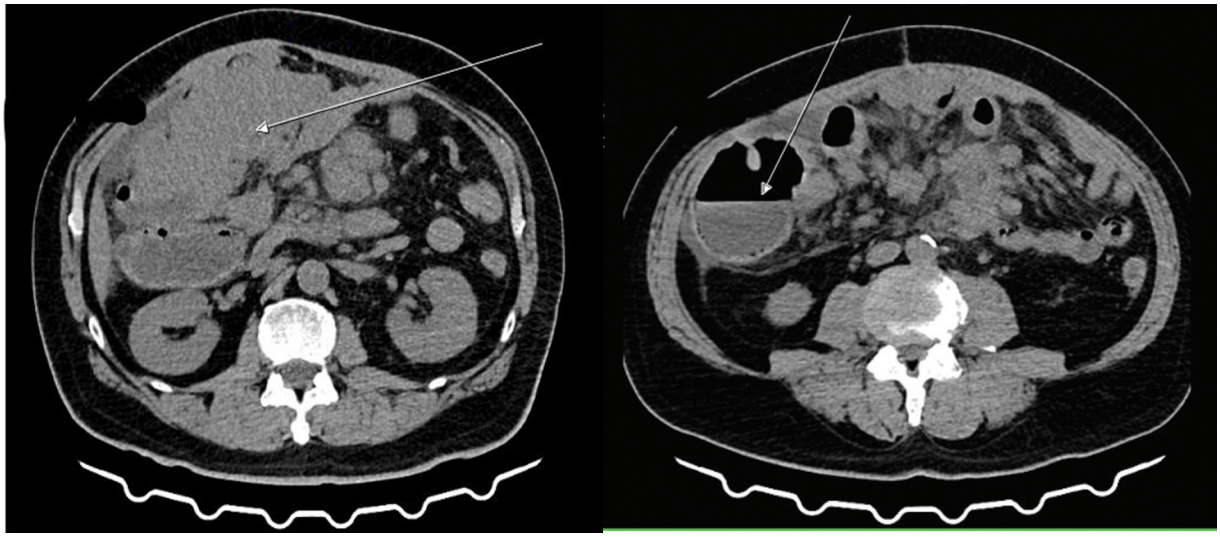

**Figure 1.** Abdominal CT coronal view. **a*\ a conglomerate of intestinal loops with adhesions and pathologically enlarged lymph nodes (arrow) **b*\ dilated colon (arrow).

However, 5 days after cycle 3 finished patient was urgently hospitalized in surgery clinic because of intensive abdominal pain and a suspicion for acute surgical abdomen. Latter was denied and a conservative treatment was done. After cycle 4 patient experienced negative change in his physical condition, without any tumor mass reduction and significant abdominal pain, rigid abdominal wall, hematemesis and melaena, registered later on. Given the clinical course and lack of improvement, after patient was stabilized and bleeding was resolved first cycle of hyper-CVAD (cyclophosphamide, vincristine sulfate, doxorubicin and dexamethasone) regimen was initiated

## Discussion

Lymphomas, originating from extranodular organs, represent about one third of all non-Hodgkin lymphoma cases. Most common localizations are GIT, Waldeyer ring, skin and bones [8]. GIT lymphomas are hard to diagnose because of their asymptomatic course. Usually stomach is involved, followed by small intestines around the area of ileum [9]. Intestinal lymphomas affect patients, aging from 13 to 65 years, with a male prevalence. Signs and symptoms are unspecific – abdominal pain, ileus, diarrhea, weight loss, GIT bleeding, anemia, palpable tumor mass [10,11]. Diagnosis relies on a precise excision biopsy of the affected organ [12]. Common complications before diagnosis and in the postoperative period are melena and adhesive ileus – prevalence of the latter reaches 93% when operation was performed and a mortality rate, ranging from 3% in obturation ileus to 30% in strangulation ileus [13]. At present, therapy for extranodal B-cell lymphomas (DLBCL inclusive) is standard immunochemotherapy – R-CHOP. Patients with GIT lymphomas always have a risk for bleeding or perforation in the course of treatment – factors, that may influence their survival negatively. On the other hand, DLBCL patients may be resistant to the gold standard in their treatment – R-CHOP. Integrating targeted therapy to R-CHOP remains challenging [14] results from recent clinical trials (GOYA, ROBUST, REMODL-B, PHOENIX, MAIN), comparing different regimens, do not show any improved efficacy over conventional R-CHOP.

## Conclusions

Lack of specific symptoms in primary DLBCL of GIT origin, risk of surgical and non-surgical complications in the course of treatment, absence of established therapy guidelines for this patient population and their potential resistance to conventional regimens lead to the conclusion that more clinical data are needed on patients with this specific subtype of DLBCL and localization to optimize their management and outcome.

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