Post-chemotherapy Gastric Obstruction in Diffuse Large B-Cell Lymphoma: Endoscopic Dilation Can Fix It!

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Abstract
Treatment of diffuse large B-cell lymphoma (DLBCL) is based on immunochemotherapy with overall good outcomes. Complications related to the treatment or the disease itself can occur during follow-up. We herein report a case of a 37-year-old male who was diagnosed with stage IV gastric DLBCL. Subsequently, he underwent R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone) chemotherapy. After six cycles of treatment, complete remission has been achieved. But afterwards, the patient presented with a symptomatic gastric obstruction related to a tight stenosis in the antro-fundic junction. Endoscopic dilation was performed and multiple macrobiopsies within the stenosis were taken. Pathological examination concluded to the fibrous character of the stricture. In cases of post-chemotherapy obstruction in gastric DLBCL, endoscopic treatment should be attempted carefully in patients with no evidence of active lymphoma. Diagnosis of fibrosis can avoid surgery and its morbidity.
Introduction

Gastric diffuse large B-cell lymphoma (DLBCL) is the most frequent extranodal site of non-Hodgkin’s lymphoma [1]. Various modalities of treatment for this disease have been used [2]. R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone) is now the gold standard in the treatment of DLBCL [3]. Surgical complications like bleeding, obstruction, and perforation can occur in the course of treatment [4]. Their incidence is rare due to underreported complications in the literature [5]. Gastric stenosis management presents a controversy due to the lack of data. We report a case of post-R-CHOP fibrous gastric obstruction treated with endoscopic dilation.

Case Presentation

A 37-year-old male, with a family history of peptic ulcer disease and a personal history of hypertension, presented to our department with cramp-like paroxysmal epigastralgia and vomiting associated to night sweats and prolonged fever for more than 4 months. He had lost about 15 kg in 3 months. He was an active smoker. He was a consumer of neither alcohol nor drugs. He had no consumption of unpasteurized milk products and he had not traveled in the last 2 years. Physical examination was normal. Biology parameters showed an elevated white blood cell count at 14,000/mm³, microcytic hypochromic anemia at 7.9 g/dL. The ferritin level was in the normal range at 167. C-reactive protein was elevated at 294 mg/L. Lactic acid dehydrogenase was slightly high at 305. Laboratory tests of the liver and kidney were normal. Hypoalbuminemia was also noted at 27 g/L. The blood calcium level was normal. Tuberculin skin test, HIV screening, and viral hepatitis screening were negative. Esophagogastroduodenoscopy (EGD) was performed revealing a large circumferential ulcerative mass at the antro-fundic junction of the stomach, which easily bled with contact. The gastric lumen was reduced by the mass but, it remained crossable. Biopsy specimen and immunohistochemistry concluded to the presence of tumor cells positive for CD20 (CD; cluster of differentiation) and Mouse Monoclonal Antibody (MUM1). Consequently, diagnosis of gastric DLBCL was confirmed. A computed tomography (CT) of thorax, abdomen, and pelvis revealed a mass-like thickening of the stomach’s body with nodal involvement on both sides of the diaphragm. Intrapерitoneal effusion of moderate size, hepatomegaly, and enlarged spleen were noted. A CT exploring the cavum was normal. Bone marrow exam, immunoelectrophoresis-serum test and cerebrospinal fluid analysis were also normal. Thus, our patient was evaluated to have Ann Arbor stage IV gastric DLBCL and underwent six cycles of chemotherapy: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). Follow-up EGDs on third (after three courses of R-CHOP) and fifth month (after five courses) showed regression then complete disappearance of the ulcerative mass. However, a progressive shrinkage of the antro-fundic junction was noted at every endoscopic exam. Biopsy specimens confirmed absence of tumor cells at every time. Thoracic abdominal CT, at the sixth month, was performed to monitor treatment efficiency and concluded to complete response according to Cheson criteria. Then, our patient presented 1 month after six cycles of chemotherapy with repetitive vomiting with signs of dehydration. Laboratory findings showed functional acute kidney failure, hypokalemia, and hypochloremia. EGD revealed the presence of impassable stenosis at the antro-fundic junction. The patient was put on nasogastric tube drainage and total parenteral nutrition. Dilation with 16 and 18 balloons was performed without any incident. A second pneumatic dilation (with 25 mm) was pursued 1 month after (Fig. 1). Multiple macrobiopsies were taken in both endoscopies. Pathology analysis
showed no signs of active lymphoma but fibrosis and inflammatory cells (Fig. 2). The patient is now asymptomatic. He was referred to his hematologist and received two more courses of R-CHOP.
Gastric DLBCL is the most common gastrointestinal tract non-Hodgkin's lymphoma [1]. It mainly affects males after 60 years old with a mean age at presentation of 64 years [6]. The clinical presentation of the disease is varied. The occurrence of systemic “B” symptoms like night sweats, fever, and weight loss can reveal the disease in 30% of cases [7]. Similarly, in our case, the patient had these manifestations. That’s why we had to eliminate tuberculosis because of the epidemiological context of the country [8]. DLBCL is an aggressive tumor with high mortality without treatment [9]. A shift in the prognosis of the disease as well as the treatment modalities has been noted in the last 20 years. In fact, chemotherapy with immunotherapy regimens based on rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone (R-CHOP) replaced surgery and became the first-line treatment [10]. Promising results of R-CHOP were shared in literature with significant rates of complete remission (CR). For instance, Kadota et al. [5] reported an 86% rate of CR and a 3-year overall survival (OS) of 80% in their series. Previous studies also reported CR rates varying between 92.5% and 100% and 3-year OS rates ranging between 84.4% and 100% [11, 12]. On the other hand, CR was significantly correlated with the lymphoma stage and the International Prognostic Index [13]. It was lower in more advanced stages or higher risk groups according to the International Prognostic Index [5]. Our patient was identified in the high-intermediate risk category and was a candidate for an aggressive frontline chemotherapy treatment from the start. During the course of the disease, complications like bleeding, perforation, and obstruction can be related to both the lymphoma and the treatment. Incidence of these complications and mainly gastric obstruction is still underestimated due to the lack of reporting. This side effect has a remarkable impact on quality of life and can result in a lower OS because of treatment interruption [5]. As shown in Table 1, we tried to summarize the different cases of outlet gastric obstruction post R-CHOP chemotherapy and the treatment strategy opted at every time. We noted a clear male predominance with a mean age of 63.85 years. Most of cases presented with symptomatic stenosis after an average of four cycles of therapy. The disease was localized in 8 cases and advanced in 5. Only 5 of all patients had evidence of active lymphoma during the time of obstruction. Four of them died of active disease. Furthermore, signs of chronic inflammation and fibrosis were found in 83% of cases at biopsy and operative specimens of the stricture. Conversely, surgery was the most common treatment used for this complication’s management.

In our case, we opted for an interim evaluation by CT to evaluate the initial treatment response. CR in interim CT was demonstrated to be correlated to a higher survival rate [18]. For our patient, before performing the CT, a relapse or a progression of the disease in the form of gastric stenosis was first suspected. However, we had no evidence of an active lymphoma in the last monitoring morphological examinations. Thus, the stricture is most likely secondary to tumor necrosis, scarring, and fibrosis, which can be considered as a sign of healing. There is no clear consensus on the best way to manage this complication. We believe endoscopy could be, in specific cases, a better treatment method than surgical resection. In fact, the patient had no objective signs of active lymphoma. Opting for surgery would have put our patient at a higher risk of developing postoperative complications and, thus, a probability of interrupting chemotherapy especially that he needed additional R-CHOP courses. Further research is warranted to establish clear management algorithms.

Therefore, we chose to dilate gradually to prevent the known risk of perforation [5]. The thickness of the gastric wall can remarkably reduce this risk.

In addition to that, it is worth noting that low serum albumin can be a predictive factor of this complication in gastric DLBCL, like in our case, which was demonstrated before to be
| Author          | Age   | Gender | Stage | Cycles received, n | Status of the disease at the time of obstruction | Histology of stenosis | Location of the stenosis | Treatment                        |
|-----------------|-------|--------|-------|-------------------|------------------------------------------------|-----------------------|---------------------------|----------------------------------|
| Sepetre et al.  | 70 (died) | F | IV    | 6                | Active disease                                        | DLBCL                 | Cardia, lesser curvature | Irradiation and salvage chemotherapy |
|                 | 80 (died) | F | IV    | 4                | Active disease                                        | DLBCL                 | Cardia, body            | No treatment                  |
|                 | 44     | F | II    | 4                | CR                                                   | Fibrosis              | Antrum                   | Gastrectomy                   |
|                 | 79     | M | I     | 6                | N/A                                                 | N/A                   | Antrum, body            | Gastroenterostomy            |
|                 | 42     | M | I     | 4                | CR                                                   | Normal gastric mucosa | Antrum, body            | Conservative treatment        |
|                 | 48     | M | I     | 2                | CR                                                   | Fibrosis              | Antrum                   | Gastrectomy                   |
|                 | 77     | M | II    | 3                | Active lymphoma                                       | Chronic active gastritis Helicobacter pylori | Antrum                   | Conservative treatment        |
|                 | 68     | F | II    | 8                | CR                                                   | Mild chronic gastritis | Cardia, body and antrum | Conservative treatment        |
| Muto et al.     | 67     | M | N/A   | 3                | CR                                                   | Fibrosis              | Antrum                   | Total gastrectomy             |
| Tamai et al.    | 59     | M | III   | 2                | N/A                                                 | Fibrosis              | Antrum                   | Gastrojejunal bypass          |
| Benatta et al.  | 45     | M | II    | 3                | CR                                                   | Fibrosis              | GEJ                      | N/A                             |
| Kadota et al.   | 67     | M | IV    | 4                | CR                                                   | Fibrosis              | Antrum                   | Gastrojejunalostomy           |
|                 | 76 (died) | M | IV    | 3                | Residual disease                                     | N/A                   | Antrum                   | Endoscopic balloon dilation    |
|                 | 72 (died) | F | I     | 2                | Residual disease                                     | N/A                   | Antrum                   | No treatment                  |
| Genser et al.   | N/A   | N/A  | N/A   | 6                | CR                                                   | Fibrosis              | Antrum                   | Total gastrectomy             |

GEJ, gastroesophageal junction.
a surrogate marker of the severity of the disease [19]. Hence, our patient was referred to hematologists for additional chemotherapy cycles.

To sum up, our case is of clinical significance because it puts the light on an underestimated complication of R-CHOP therapy. Our approach combining conservative endoscopic treatment and aggressive chemotherapy could help reduce both morbidity and mortality.

**Statement of Ethics**

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

**Conflict of Interest Statement**

No competing interests were disclosed.

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**Author Contributions**

As per the guidelines of the International Committee of Medical Journal Editors (ICMJE), Khalaf Ben Abdallah contributed in writing and case conceptualization; Asma Ben Mohamed contributed to discussion, case conceptualization, and reviewing the manuscript; Manel Yacoubi contributed to writing and reviewing the manuscript; Amal Khsiba contributed to case conceptualization and discussion; Amel Dougaz contributed to case conceptualization and pathology examination; Emna Chelbi contributed to discussion and validation; Lamine Hamzaoui contributed to the performance of endoscopic procedure, reviewing the manuscript, and validation.

**Data Availability Statement**

All data underlying the results are available as part of the article and no additional source data are required. Further inquiries can be directed to the corresponding author.

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