

# Recurrent Gastrointestinal Near-Tetraploid Diffuse Large B-Cell Lymphoma Causing Intussusception and Ileal Ulceration

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## ABSTRACT

Polyploid karyotypes in diffuse large B-cell lymphoma (DLBCL) are rare and carry a poor prognosis. Extranodal polyploid lymphoma is uncommon. A 71-year-old man with back pain was found to have ileal intussusception. He underwent surgical resection and was diagnosed with DLBCL with a near-tetraploid karyotype. Despite rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone therapy, he developed recurrent disease for which he started a clinical trial. He then developed dark stools from an ileal ulcer due to progressive disease and died 2 weeks later. This is the first reported case of gastrointestinal DLBCL with polyploidy. These karyotypes require attention to extranodal disease and prompt initiation of therapy.

## INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin's lymphoma, accounting for nearly 40% of all lymphoma cases.<sup>1,2</sup> While gastrointestinal (GI) presentation of DLBCL is not uncommon, patients with polyploid karyotypes rarely present extranodally.<sup>3</sup> Polyploid karyotypes are associated with a poor prognosis, and to date, no primary GI cases of polyploid DLBCL have been reported.<sup>4,5</sup>

## CASE REPORT

A 71-year-old man with a medical history only notable for a right-sided inguinal hernia repair presented to the hospital with 2 weeks of back pain with periumbilical radiation, poor appetite with intermittent nausea, and nonbilious emesis. Over the preceding months, he reported 5 kg of weight loss, inability to tolerate food by mouth, and decreased stool caliber. His last colonoscopy over 10 years ago was normal.

Physical examination was unremarkable, and routine laboratory parameters were within normal limits. Computed tomography (CT) revealed a small bowel obstruction with transition point in the terminal ileum and 4 cm of intussusception at the site of a mass-like circumferential ileal wall thickening (Figure 1). He was taken for an emergent exploratory laparotomy and underwent a right hemicolectomy with side-to-side ileocolic anastomosis.

Pathology revealed a nongermlinal center DLBCL, specifically not otherwise specified activated B-cell type per WHO classification. Resection margins were negative. Cytogenetic analysis showed a near-tetraploid abnormal karyotype in 19 of 20 evaluated metaphase cells (Figure 2). Fluorescence in situ hybridization assays detected *BCL6* gene rearrangement and *BCL2* gene rearrangement with the lambda light chain immunoglobulin resulting in a t(18;22) translocation. *MYC*, *MYC-IGH*, and *IGH-BCL2* gene rearrangements were ruled out by the fluorescence in situ hybridization assays. A staging positron emission tomography-CT 1 week later

revealed only mild subcentimeter cervical and mesenteric lymph node avidity determined to be reactive without evidence of lymphomatous nodal involvement (Figure 3). He was started on chemotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. A mid-treatment CT revealed no evidence disease. After completing 6 cycles of



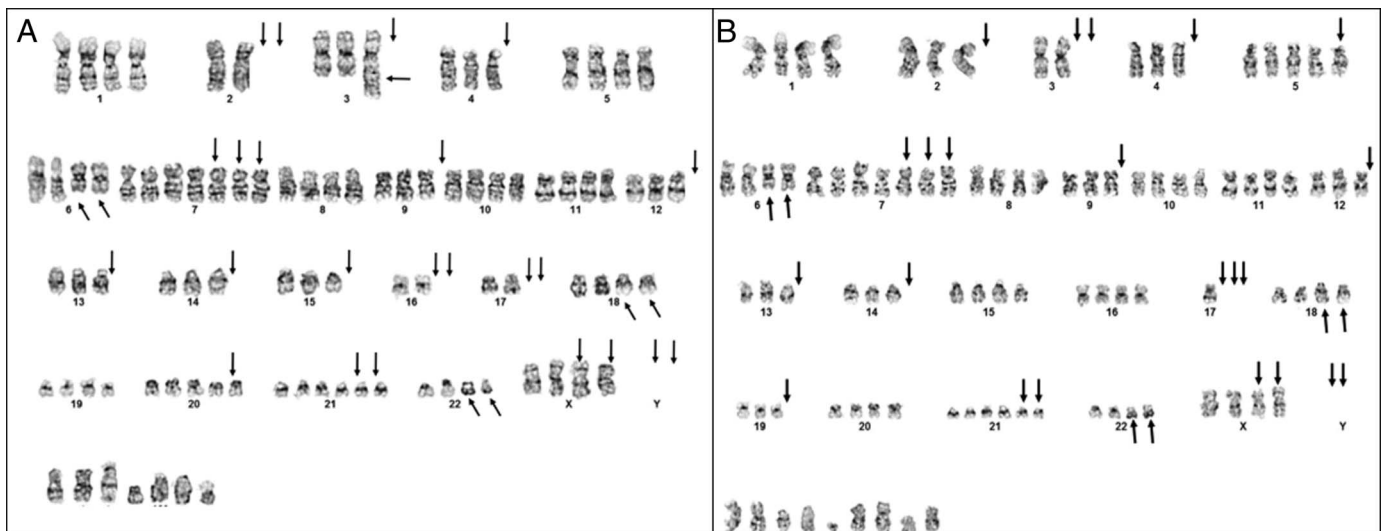
**Figure 1.** Computed tomography scan showing 4 cm of intussusception of the terminal ileum into the colon.

therapy, an end of treatment positron emission tomography-CT revealed newly avid peritoneal and mesenteric nodules compatible with recurrent disease (Figure 3). Given the radiographic recurrence and evidence of chemorefractoriness, he was started on a clinical trial with a combination of ibrutinib, lenalidomide, and rituximab.

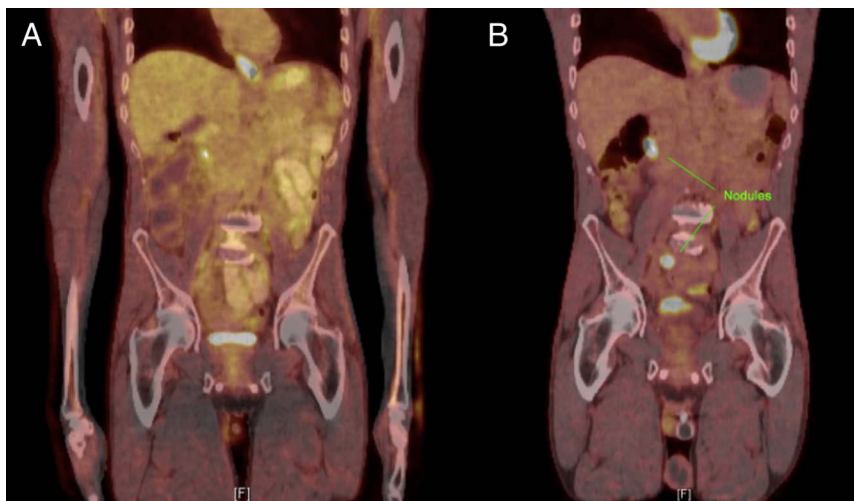
During the first cycle of treatment after 3 weeks of treatment, the patient again presented with anemia, dizziness, and dark stools. Given hemodynamic stability, luminal endoscopic evaluation was favored. Hemoglobin was found to be 8.8 g/dL, which dropped from 10.9 g/dL in 1 week. Although esophagogastroduodenoscopy was unremarkable, colonoscopy revealed a solitary, nonbleeding, 10-mm ulcerated polyp in the neoterminal ileum with surrounding healthy mucosa proximal to the site of the previous end-to-end ileocolic anastomosis (Figure 4). Pathology revealed recurrent DLBCL, and imaging confirmed progressive disease. Treatment with salvage chemotherapy was ineffective. He was transitioned to hospice and died 2 weeks later.

## DISCUSSION

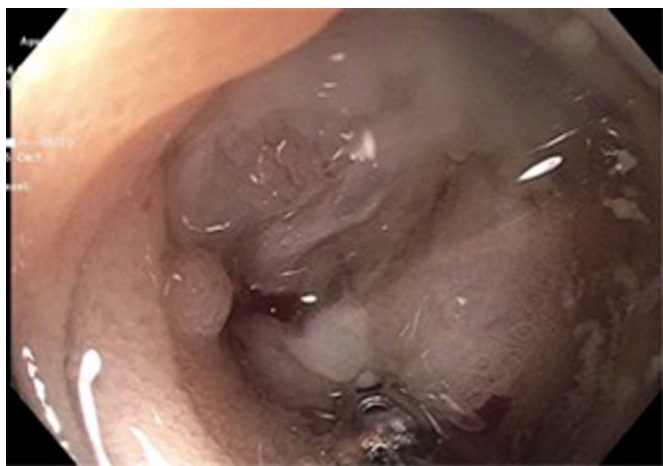
Extranodal presentation occurs in up to 40% of patients with DLBCL and is most commonly found in the GI tract, primarily the stomach.<sup>1,2</sup> The marked heterogeneity in clinical presentation and treatment response in DLBCL is thought to be due to unique molecular subtypes, genetic mutations, immune phenotypes, and cell morphology that compromise individual disease makeup.<sup>6</sup> These features are being used increasingly to tailor diagnostic evaluation and enhance targeted therapy. Polyploidy is one such feature that refers to more than 2 sets of homologous chromosomes—a result of abnormal cell division and replication of DNA. These karyotypes are uncommon,



**Figure 2.** Two karyotypes depicting components that made up the composite karyotype obtained from 19 metaphase cells are as follows: 86~97<4n>,XX,+X,+X,-Y,-Y,-2,-2,-3,add(3)(q27),4,+5,(6)(p10) × 2,+7,+7,+7,+8,-9,-12,-13,-14,-15,-16,-17,-17,t(18;22)(q21.3;q11.2) × 2,-19,+21,+21,-22,+4~9mar[cp19]/46,XY.<sup>1</sup>



**Figure 3.** (A) Postresection positron emission tomography-computed tomography (PET-CT) showing no evidence of active diffuse large B-cell lymphoma (DLBCL). (B) PET-CT after 6 cycles of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone therapy showing abdominal and retroperitoneal nodules consistent with recurrent DLBCL.



**Figure 4.** Colonoscopic view of the solitary ulcerated ileal polyp confirmed to be recurrent diffuse large B-cell lymphoma.

accounting for only 3% of DLBCL cases, and portend a poor prognosis with reduced overall survival.<sup>3</sup> Pathologic findings of polyploid DLBCL include higher proportions of huge and multinucleated cells.<sup>3</sup> Additionally, mutations in *p53* have been linked to genesis of polyploid chromosomal abnormalities.<sup>4,6,7</sup> One study found that patients with polyploid DLBCL only had significantly worse survival in patients who received rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone regimens, which may explain the poor survival seen in this case.<sup>4</sup> Previous studies have posited that this finding may be due to drug resistance as a result of a link between chromosomal instability and intratumor genetic heterogeneity.<sup>8,9</sup>

Extranodal infiltration of polyploid DLBCL is rare, with no reported cases of primary GI disease.<sup>4</sup> This patient's

presentation with intussusception and ileal recurrence may point toward the aggressive nature of DLBCL with polyploidy, particularly in the GI tract. To date, we believe this is the first reported case of GI DLBCL with polyploidy. Understanding clinical presentation with molecular and genetic features may have significant implications on the prognosis and management. Early identification and attention to extranodal disease and enrollment on clinical trials are preferred which may optimize potential treatment outcomes in these patients.

## DISCLOSURES

Author contributions: SN Mathews wrote the article and is the article guarantor. S. Mathew oversaw cytogenetic and karyotype analysis. R. Niec, JN Allan, and CV Crawford treated the patient and approved the article.

Financial disclosures: None to report.

Previous presentation: This case was presented at the American College of Gastroenterology Annual Scientific Meeting, October 5–10, 2018, Philadelphia, Pennsylvania.

Informed consent could not be obtained from the family of the deceased. All identifying information has been removed from this case report to protect patient privacy.

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