Complete Spontaneous Remission of Diffuse Large B-Cell Lymphoma of the Maxillary Sinus After Concurrent Infections

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Clinical Practice Points

- Diffuse large B-cell lymphoma (DLBCL) is an aggressive type of lymphoma that should be promptly treated with immunochemotherapy; rarely will patients experience spontaneous tumor regression before initiating treatment.
- We present a patient who experienced spontaneous regression of DLBCL of the maxillary sinus in the setting of concurrent pneumonia and *Clostridium difficile* colitis.
- A review, to our knowledge, of all previously reported cases of spontaneous DLBCL remission suggests that tumor location may be an important factor that affects tumor regression; almost all reported cases of spontaneous remission have occurred in patients with extranodal disease. In addition, several of the cases also occurred in the setting of concurrent infection.
- Although an antitumor immune response has been proposed as a likely cause of spontaneous remission, the specific mechanisms that underlie tumor regression in DLBCL are not known.
- Information gained through careful investigation of this phenomenon could potentially lead to a better understanding of DLBCL biology and more effective immune-mediated therapies.

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Case Description

A 67-year-old woman presented to her dentist for evaluation of painless, right-sided facial swelling that had been slowly increasing for approximately 4 weeks. The swelling did not improve after a course of oral antibiotics. One month after presentation, she was referred to an oral surgeon who extracted 2 teeth. During this procedure, a soft tissue mass that involved the right maxilla was noted, and biopsies of the mass were performed.

Histologic examination of the mass revealed sheets of monomorphic, large cells with vesicular chromatin and prominent nucleoli, with admixed scattered small lymphocytes (Figure 1). Immunohistochemistry stains showed positive CD 20, CD10, Bcl-2, Bcl-6, and MUM-1 with negative CD5, consistent with diffuse large B-cell lymphoma (DLBCL), activated B-cell-like subtype.[1] The Ki-67 proliferation index was 80% in the lymphoma cells, and Epstein-Barr virus (EBV) stains were negative. Kappa light-chain restriction on immunohistochemical stains confirmed clonality of the lymphoma cells. Karyotype of the paraffin-embedded tumor was normal (46,XX), and florescence in situ hybridization showed no evidence of Myc or Bcl-2 translocations.

Positron emission tomography with concurrently acquired computed tomography (PET-CT) showed a 5.1 × 4.2-cm soft-tissue mass in the right maxillary sinus, with erosion of the anterior and inferior portions or the sinus. The mass was intensely fluorine-18 fluorodeoxyglucose (FDG) avid and extended into the soft tissues of the cheek (Figure 2). No other FDG-avid masses or lymph nodes were identified in the head and neck area, but an 8-mm FDG-avid lymph node of unclear clinical significance was noted adjacent to the thoracic aorta. No abnormalities suggestive of lymphoma were seen in the abdomen or the pelvis. Bilateral bone marrow aspirates and biopsy specimens with flow cytometry and cerebrospinal fluid examination showed no evidence of lymphoma.

Based on the above information, the patient was diagnosed with stage IE DLBCL. Lactate dehydrogenase (LDH) was normal at the time of diagnosis, and Eastern Cooperative Oncology Group perfor-

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Figure 1 Tumor Pathologic Examination. Hematoxylin and Eosin Stain (A) Showing the Large Malignant Cells With Scattered Small Lymphocytes in the Background. Immunohistochemical Stains for CD10 (B), CD20 (C), Bcl-2 (D), Bcl-6 (E), and Mum-1 (F) Were Positive in the Malignant Cells, Consistent With Diffuse Large B-cell Lymphoma, Activated B-Cell–Like Subtype

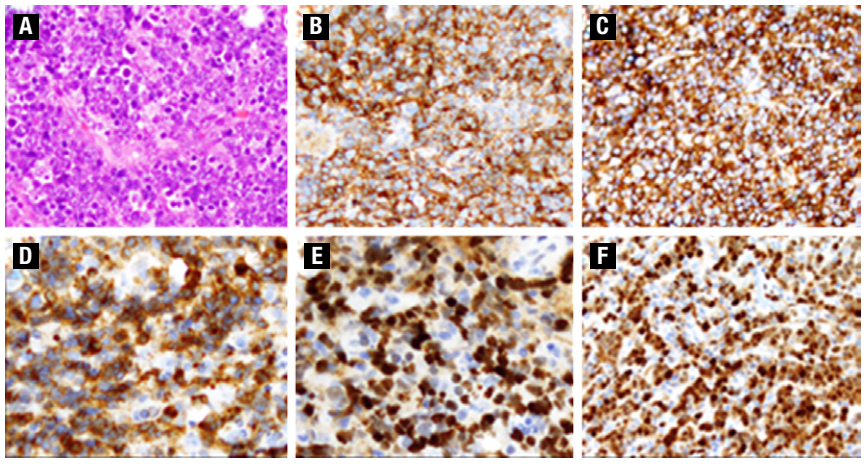
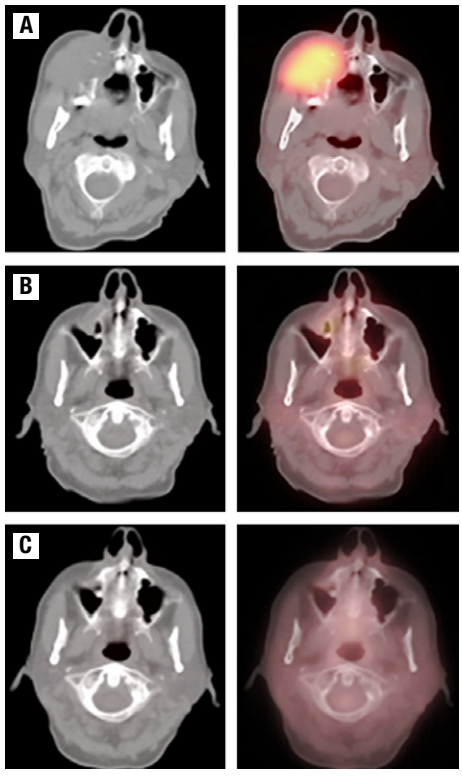


Figure 2 Tumor Imaging. Computed Tomography and Positron Emission Tomography Images (left and right images, respectively) at (A) Diagnosis, (B) 2 Months Later, and (C) 7 Months Later



mance status was 1. The international prognostic index score for the patient was calculated to be 1 (age > 60 years). She was scheduled to start chemotherapy shortly after the staging evaluation was completed.

Two days before the planned initiation of chemotherapy, the patient presented to the emergency department with fever that had started earlier that day. She started to have nausea, vomiting, and diarrhea 4 days before presentation, followed 2 days later by the onset of cough. Her stool was positive for *Clostridium difficile* toxin, and a chest radiograph revealed a left lower lobe opacity. She was treated with metronidazole for colitis, as well as with levofloxacin and clindamycin for empiric treatment of possible bacterial pneumonia. Notably, the swelling on the right side of her face had begun to decrease in size about the same time or just after the onset of these symptoms. CT with intravenous contrast of the maxillofacial area showed that the right facial mass had decreased in size to 3.8 × 3 cm; no drainable fluid collection was seen. Chemotherapy was not given as planned due to the presence of the infections.

The patient's facial swelling resolved during the hospitalization. A repeated PET-CT 1 month later showed that the mass had further decreased in size (to 2 × 1 cm) and was only mildly FDG avid; the lymph node adjacent to the thoracic aorta was not visualized. A second follow-up PET-CT 7 months after the patient's initial presentation showed that the facial mass was no longer present (Figure 2). The patient never received chemotherapy and currently remains well, with no evidence of disease more than 1 year after initial presentation.

Discussion

DLBCL is the most common non-Hodgkin lymphoma, which accounts for approximately 30% of all non-Hodgkin lymphoma cases.[2] Spontaneous remission of DLBCL is exceedingly rare, with only a handful of case reports that describe the phenomenon present