Chemotherapy-Related Chronic Myelogenous Leukemia: A Case Series of Patients With Germ Cell Tumor

Germ cell tumors (GCTs) are the most common cancer in young men ages 15 to 35 years and are uniquely responsive to chemotherapy, with cure rates approaching 80%. Late adverse effects of treatment can manifest throughout the lifetime of a cured patient who will be at increased risk of solid and hematologic malignant neoplasms. 1, 2 Etoposide has become one of the cornerstones of platinum-containing regimens for GCT. Treatment with etoposide entails a known risk of secondary leukemia that typically exhibits a short latency period, a chromosomal translocation (11q23 and 21q22), and rearrangement of the mixed-lineage leukemia gene.

Methods | We observed 3 patients with Philadelphia chromosome-positive chronic myelogenous leukemia (CML) following therapy for GCT.

Results | Case 1. In 1999, a man in his mid-30s with nonseminomatous GCT (NSGCT) was treated with orchectomy followed by 4 courses of bleomycin, etoposide, and cisplatin. In September 2011, he was noted to have a white blood cell count (WBC) of 111,700/μL (111.7 × 10⁹/L). Bone marrow examination showed morphologic findings of chronic-phase CML, and a t(9;22)(q34;q11) was identified. The patient started treatment with imatinib and achieved a complete molecular remission. Unfortunately, in 2014, he developed malignant transformation of teratoma to an undifferentiated neuroendocrine carcinoma with unresectable hepatic metastases and died of his disease.

Case 2. In 2006, a man in his early 30s had orchectomy for clinical stage I NSGCT and elected to receive a single cycle of BEP. In November 2006, the disease relapsed, and he was treated with 3 cycles of etoposide, ifosfamide, and cisplatin (VIP). In 2007, the patient experienced a second relapse and was treated with 2 cycles of high-dose carboplatin and etoposide followed by peripheral blood stem cell rescue. In 2011, he was found to have leukocytosis (WBC, 91,700/μL [91.7 × 10⁹/L]). Bone marrow examination confirmed chronic-phase CML with t(9;22)(q34;q11). The patient was treated with dasatinib and achieved a molecular remission. To date, he continues to be in remission for his CML and recurrent GCT.
Case 3. In 2012, a young adult man with history of Klinefelter syndrome presented with intermittent chest pain and was found to have a 15-cm primary mediastinal NSGCT. He was treated with 4 cycles of VIP followed by resection of residual mediastinal mass, which revealed teratoma. In 2014, he was found to have leukocytosis (WBC, 44,000/μL [4.4 × 10⁹/L]). Bone marrow examination confirmed chronic-phase CML by morphologic characteristics, and a t(9;22)(q34;q11) was identified by chromosome analysis. The patient started treatment with dasatinib and achieved a hematologic response. To date, his BCR/ABL transcript declined appropriately from 55% to 9%. He continues to be in remission for his GCT.

Discussion | There have been reports of chemotherapy-related Philadelphia-chromosome leukemias in patients with antecedent malignant neoplasms. Past treatments for GCT with cisplatin-etoposide–containing regimens or HDCT with carboplatin-etoposide have been linked to an increased risk of secondary acute leukemia and solid tumors. A review of the literature reveals 7 cases of GCT with subsequent development of CML. In this series, we present 3 cases of patients with GCT who achieved remission with chemotherapy and later developed BCR/ABL-positive CML. These findings raise the question of a causal relationship between etoposide and/or platinum-containing chemotherapy and the development of CML with t(9;22)(q34;q11).

Etoposide-based chemotherapy in patients with GCT is leukemogenic. It is not clear whether combination chemotherapy with cisplatin and bleomycin contribute to this result. While its association with AML is well established, questions regarding the connection of etoposide and cisplatin-containing combination chemotherapy and secondary CML are posed herein. The relatively low risk of secondary leukemia in patients treated with potentially curative combination chemotherapy for GCT continues to be reassuring. However, physicians should be aware of possible late toxic effects of these treatment regimens and the need for diligent follow-up in these patients.

Nabil Adra, MD
Hamid Sayar, MD
Lawrence H. Einhorn, MD

Author Affiliations: Indiana University, Indianapolis, Melvin & Bren Simon Cancer Center, Division of Hematology/Oncology, Indiana University School of Medicine, Indianapolis.

Corresponding Author: Nabil Adra, MD, Indiana University, 535 Barnhill Dr, RT 400, Indianapolis, IN 46202 (nadra@iu.edu).


Author Contributions: Dr Adra had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: All authors.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Adra, Einhorn.

Critical revision of the manuscript for important intellectual content: All authors.

Administrative, technical, or material support: Adra.

Study supervision: Sayar.

Conflict of Interest Disclosures: None reported.

Funding/Support: Dr Einhorn supported in part by the National Cancer Institute (NCI) (I R01 CA157823-1A1).

Role of the Funder/Sponsor: The NCI had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: We thank the patients for granting permission to publish this information.


Disease-Specific Hashtags for Online Communication About Cancer Care

Increasingly, patients, caregivers, and health care professionals (HCPs) go online to learn about and discuss cancer care. However, finding other people or organizations with similar interests can be difficult without some structure.

Hashtags are user-generated tags that can organize and aggregate content on social networks. In July 2011, 2 patient advocates started a breast cancer chat on Twitter using the tag #bcsms (breast cancer social media); one of us (D.J.A.) joined as a comoderator. This same model but with hashtag #btmsm was used to discuss brain tumors in January 2012. Both tags are now regularly used on Twitter by patients, caregivers, and HCPs.

Dedicated hashtags may make it easier to engage in relevant conversations online for other types of cancer. In this study, we describe a way to use disease-specific hashtags similar to #bcsms and #btmsm to organize and increase online discussion of cancer care.

Methods | Based on the models using the #bcsms and #btmsm hashtags, 2 of us (M.S.K. and P.F.A.) developed a set of 23 new cancer-specific tags that met the following criteria: disease specific, short, unique or minimally used on Twitter, and ending in “sm” for “social media” (as a prompt that online use is public). We selected this design to balance practical use with the ability to organize content. Initially proposed in July 2013, this cancer tag ontology (CTO) was posted on Symplur in November 2013 after public commentary and engagement (Table).

We analyzed the number of tweets and users of the tags quarterly from April 2011 through June 2015 using Symplur...