Peripheral T-cell Lymphoma arising from Age-Related EBV-associated Lymphoproliferative Disorder (AR-EBVLPD)

Alaina Chodoff MSII, Guldeep Uppal MD, Jerald Gong MD
Department of Hematopathology, Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA

ABSTRACT
In the setting of underlying immune suppression, Epstein Barr Virus (EBV) is a well-recognized oncogenic agent that induces the malignant proliferation of B-cells. EBV-lymphoproliferative disorders (LPDs) have recently been linked to immunosenescence. We present a unique case of Age-Related EBV-Lymphoproliferative Disorder (AR-EBVLPD) in a 70 year old female that deviates from the characteristic progression of this disease. Over the course of 18 months, the patient’s clinical condition worsened without a definitive diagnosis to explain the severe, atypical widespread chronic inflammation spanning her gastrointestinal tract, from esophagus to small bowel. The diagnosis of AR-EBVLPD, polymorphic extranodal subtype, was delayed until the patient developed a synchronous peripheral T-cell lymphoma. At this time, the patient was very sick, with a jejunumostomy tube. To our knowledge, this is the first time that a T-cell lymphoma has arisen in the context of a diagnosis with AR-EBVLPD. This rare, EBV induced malignant transformation of T-cells may explain the patient’s rapid clinical deterioration.

CLINICAL HISTORY:
A 70 year old woman who presented in January, 2012 at an outside hospital with worsening nausea and vomiting following regular feeds and a 50 pound weight loss over the preceding 6 months. At this time, multiple endoscopies were taken with small bowel and gastric biopsies, revealing gastric outlet obstruction. Biopsy results were suggestive of severe gastritis. She was admitted to Jefferson in May, 2012 for workup of her gastric outlet obstruction. She was referred to the surgical service to undergo exploratory laparoscopy with perigastric lymph node biopsies and distal subtotal gastrectomy. Exsuditional biopsies revealed extensive chronic inflammation without evidence of lymphoma. The patient’s postoperative course was unremarkable. She initially did well, but her clinical condition continued to worsen with persistent nausea and vomiting, failure to thrive and generalized lymphadenopathy. Unable to eat, she began total parental nutrition (TPN) in July of 2013. In October, 2013, she was re-admitted and a jejunostomy tube was placed for her to receive enteral nutrition. Repeat GI biopsies and cervical lymph node exsuditional biopsies were performed, with the subsequent diagnosis of an EBV-associated LPD. At this time, the patient started treatment on Rituximab in an effort to decrease the B-cell population harboring the EBV virus. In December, 2013, her biopsy sections were sent to the National Institutes of Health (NIH), which confirmed the diagnosis of a new-onset peripheral T-cell lymphoma. The patient continued on Rituximab at home with no improvement and ultimately expired in February, 2014.

RESULTS:

BIOPSY RESULTS:
January 2012: Chronic active inflammation involving the esophagus, stomach and small bowel. Severe gastritis with underlying gastric outlet obstruction.
May 2012: Prominent lymphoplasmacytic inflammation in the stomach and small bowel with circumscribed ulceration. No evidence of lymphoma. In situ hybridization for EBV (EBER) is positive in scattered cells in the gastric and small bowel mucosas.
October 2013: Prominent widespread lymphoplasmacytic inflammation revealing ulceration throughout the esophagus, stomach and small bowel. EBER-positive cells are increased in the small bowel and cervical lymph node. CD3 immunohistochemical staining (IHC) involving the gastrointestinal tract and the lymph node showed increased T-cells with cytologic atypia consistent with a peripheral T cell lymphoma associated with an EBV driven B cell polyclonal proliferation.

ADDITIONAL RESULTS:

DISCUSSION: AR-EBVLPD
AR-EBVLPD is an aggressive subtype of EBV-driven LPDs that occurs in older patients >50 years of age with any known immunodeficiency. Etiology is attributed to immunosenescence. The diagnosis of AR-EBVLPD is associated with a wide clinicopathologic spectrum. Prognosis is dependent on variable factors. Our patient presented with a well-circumscribed EBV+ mucocutaneous ulcer with widespread involvement of the GI tract. AR-EBVLPDs in well-circumscribed extranodal sites are typically compatible with good prognosis, in contrast to the aggressive clinical course presented in this case.

CONCLUSION:
We presume that the patient’s progressive clinical deterioration over 1.5 years coincided with an increasing burden of EBV infected tumor cells, during which time she was being treated conservatively. The patient’s rapid decline coincided with an altered T-cell repertoire, and the development of a malignant T-cell population. We present a unique case of T-cell peripheral lymphoma arising in association with an EBV-driven B cell polyclonal proliferation. We are not yet certain of the mechanism underlying EBV infection of T-cells.

REFERENCES: