Unusual presentation of Gastric marginal-zone lymphoma in a young HIV positive patient-a case report with review of literature

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Abstract

Non-Hodgkin's lymphoma is the second most common malignancy in HIV-infected patients.[1] The proportion of extra nodal lymphoma is higher in these patients and gastrointestinal tract is the most common site. Gastrointestinal lymphoma in HIV-positive affects younger patients with male predilection, shows preferential involvement of distal gastrointestinal tract, and is more often high grade with Epstein Barr virus positivity. This report presents a rare presentation of Epstein - Barr virus negative Gastric marginal zone lymphoma presenting as an ulcero-proliferative growth in a HIV-positive female.

Key words: gastric, marginal zone lymphoma, Non-Hodgkin's

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Introduction

The gastrointestinal tract [GIT] is the most common primary site of extra nodal lymphomas accounting for 4-20% of all non-Hodgkin's lymphomas [NHL]. Stomach is the most commonly involved organ being most common site for marginal-zone B-cell lymphoma [MZL]. [1] People with AIDS are at increased risk for developing stomach carcinomas and NHLs. Although the incidence of NHL has decreased with improved treatments for HIV infection, HIV-infected individuals face continued risks of stomach malignancies including NHLs. [2]

We present a case report of a 38 year old HIV infected lady who had been suffering from refractory dyspepsia for few years. Her upper GI endoscopy revealed a gastric mass which turned out to be gastric MZL after HPE and ancillary tests. This case discussion emphasizes the need to consider a gastric malignancy including GI-lymphoma in HIV positive patients with dyspeptic symptoms.

Case report

A 38 year old lady presented with severe epigastric pain. In spite of medication [including anti- H.pylori treatment], her pain was not cured completely over few years and it started to become severe for last couple of months. As she was found to be at high-risk for HIV infection, she was referred to institute's Integrated Counseling and Testing Centre and she was found to be HIV positive. Her CD4 count was 69/mm^3. She was started on anti-retroviral therapy. Upper GI endoscopy showed an ulcero-proliferative growth in the body along the lesser curvature along with patchy areas of rugal thickening and redness. Biopsy was done and pathological examination revealed a poorly differentiated malignancy. Since the tumor cells were scant in this biopsy, immunohistochemistry [IHC] was not feasible. A partial gastrectomy was performed. Pathological examination of suspicious areas showed diffuse infiltrate of uniform small to medium-sized cells with irregular nuclei and distinct rim of clear cytoplasm. Tumor cells were predominantly seen in the mucosa [with expansion of lamina propria] and sub mucosa through multiple breakages of the muscularis mucosae. Careful search revealed that deepest invasion was till the muscularis propria without penetrating it [figure 1]. Multiple areas of mucosal ulceration, lymphoepithelial lesion and follicular colonization were also seen. IHC showed strong and diffuse positivity for LCA and CD20 [figure 2]; and negativity for CD10, CD5, bcl-6, cytokeratins and CD117. In situ hybridization for Epstein - Barr virus [EBV] was negative. Morphology and IHC was consistent with a diagnosis of gastric MZL. There was no regional lymph node involvement. Further work-up ruled out hepatosplenomegaly, bone marrow and lymph node involvement elsewhere. She continued anti-retroviral treatment and was referred to oncology department post-operatively for chemotherapy and is doing well on four months of follow-up.

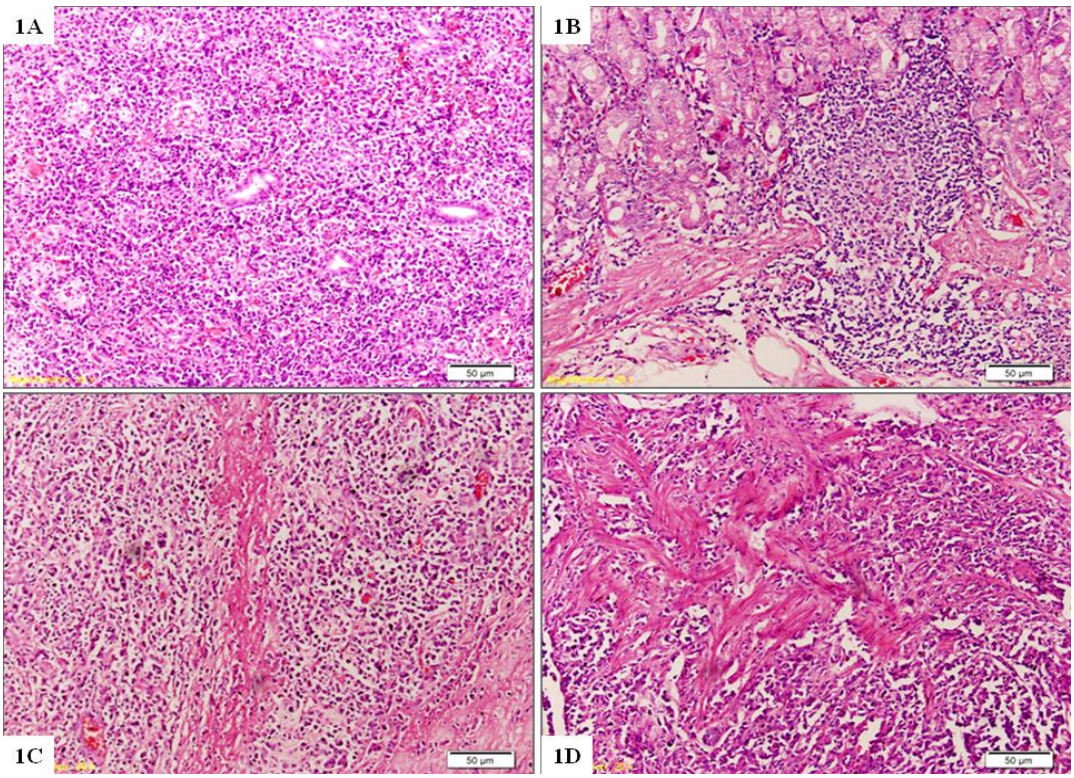

Fig. 1(A): tumor cells sparing the glands (H & E, 4X)
Fig. 1(B): areas showing colonized follicles (H & E, 10X)
Fig. 1(C): tumor cells penetrating through the muscularis mucosae (H & E, 10X)
Fig. 1(D): deepest extent of the tumor invading up to the muscularis propria (H & E, 40X)

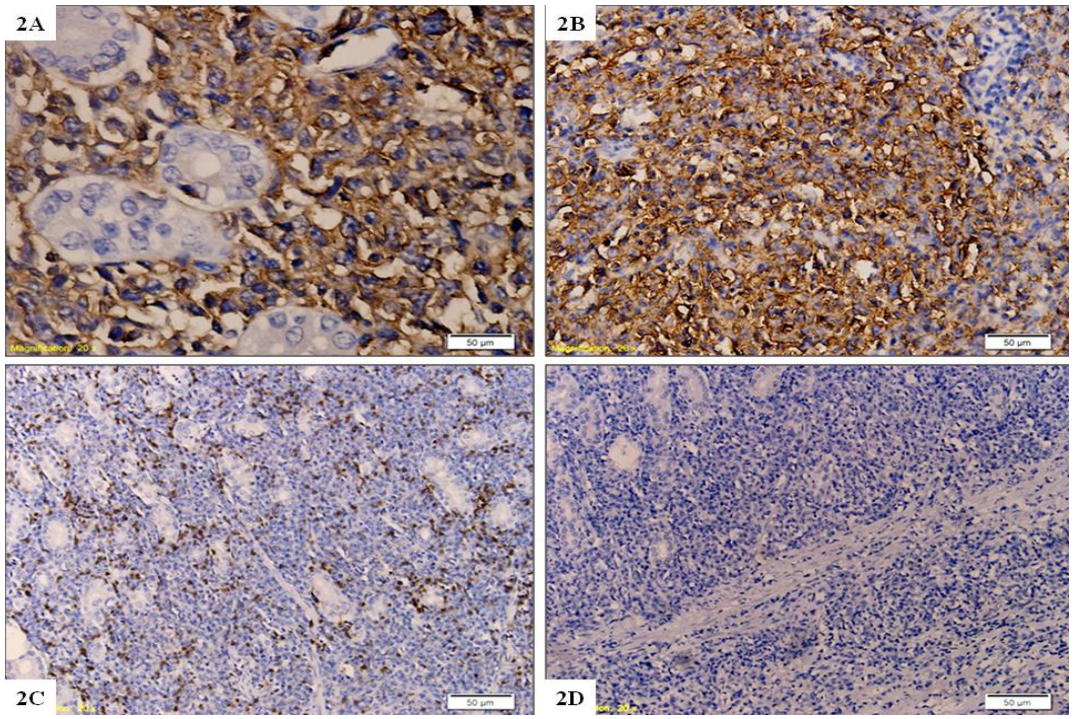

Fig. 2(A): LCA positive tumor cells (IHC, 40X)
Fig. 2(B): CD 20 positive tumor cells (IHC, 20X)
Fig. 2(C): CD 3 negative tumor cells with scattered CD 3 positive T-cells (IHC, 10X)
Fig. 2(D): CK negative tumor cells (IHC, 10X)

Discussion

HIV patients harbor a greater risk of malignancy including lymphomas, which are usually extra nodal, involve GIT most often and occur in younger patients, commonly homosexual men and mostly B-cell lymphomas. [1]

In the first decade of AIDS epidemic, it was seen that 32% of GI neoplasia in AIDS were mainly Kaposi Sarcoma and symptomatic NHL.[3] In spite of improved treatment for HIV, these patients are at increased risk for developing carcinoma and NHL at various sites including the stomach. Though, most of the AIDS related stomachs NHL are diffuse large B-cell lymphoma [DLBCL], there is also an increased risk of MALT lymphoma.[2]

The GI tract [main site for extra nodal AIDS-related NHL followed by CNS involvement [4,5]] can be involved primarily or secondarily. A diagnosis of primary GI lymphoma can be established by Dawson's criteria. [6] Accordingly, our patient was primary GI lymphoma which is rare and account for 1-4% of the tumors of small intestine, stomach and colon.[5] The incidence is 0.8-1.2 cases per 100,000 persons per year.[7,8]

On endoscopy or gross examination, gastric lymphomas show erosions, shallow ulcers, mucosal granularity or thickened mucosal folds and less commonly, a polypoidal or exophytic growth, mimicking carcinoma. [1] Our patient's endoscopic finding was more in favor of carcinoma due to the presence of ulceroproliferative growth apart from changes suggesting associated gastritis. Lymph node involvement is more expected when there is invasion into muscularis propria.[1] However, our patient did not have lymph node involvement in spite of involvement of muscularis propria. Usually, lymphomas involve only one portion of stomach; wide spread and multifocal tumors are well known. [1] But, our patient had single grossly visible tumor along with multiple microscopically visualized foci of tumor with free resected margins, which is not a common occurence. Once the diagnosis of GI lymphoma is established, staging becomes mandatory for planning the treatment. Using Lugano Staging System[9] our patient presented in stage I.

DLBCL being frequent, constituted one of the important differential diagnoses. It is characterized by large B-cells with prominent nucleoli, basophilic cytoplasm and diffuse growth pattern which was not seen in this case. Morphology and IHC did not support the diagnosis of DLBCL and other less common low grade lymphomas [follicular lymphoma and mantle cell lymphoma].

The pathogenesis of HIV related lymphoma is multifocal including- chronic immunosuppression, chronic antigenic stimulation, cytokine deregulation and association with EBV and HHV8.[10-13] Although association of EBV is seen in HIV related lymphomas[1], our patient was found to be negative. Gastric MZL arise from a background of gastritis with a component of acquired H. pylori-induced MALT. However, only a small proportion of them develop MZL. It implies that apart from H. pylori, host factors and environmental factors play a role in its pathogenesis. Cases where there is no evidence of H. pylori infection, it is not clear whether infection was present previously and resolved at a stage after the lymphoma attained autonomous growth, or whether there are other unknown etiological factors.[1] Though our patient was H. pylori negative; it remained unclear whether she was infected earlier as she received treatment before presenting to the authors and harbored frank malignancy at presentation.

Thus, we conclude that EBV negative MZL presenting as ulceroproliferative growth is rare and lymphomas should be considered in differential diagnosis of dyspepsia in HIV patients in spite of unusual endoscopic finding.

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