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Primary appendiceal lymphoma: clinical characteristics and outcomes of 116 patients

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ABSTRACT

Background: Primary appendiceal lymphoma (PAL) is extremely rare with limited data available in literature. In this study, we sought to describe clinical features and identify factors affecting survival in patients with PAL using a large population cohort.

Methods: Surveillance, Epidemiology, and End Results database was queried for patients with PAL between 1973 and 2012. Patient demographics, tumor characteristics, and outcomes were assessed.

Results: One hundred sixteen patients with PAL were included. The mean age (standard deviation) at diagnosis was 48 y (±22). PAL primarily afflicted males and white race. Diffuse large B-cell lymphoma was the most common histologic subtype (34.5%). Patients with Burkitt lymphoma presented at an earlier age compared with follicular lymphoma and diffuse large B-cell lymphoma (33 *versus* 59 and 53 y, respectively, [$P < 0.001$]). Mean overall survival (OS) for the whole cohort was 185 mo with a 5-y survival rate of 67%. No statistically significant survival difference was observed between gender, race and histologic subtypes. Right hemicolectomy conferred no survival benefit over appendectomy and/or partial colectomy ($P = 0.501$). In multivariate analysis, increasing age at diagnosis ($P < 0.001$) was associated with increased hazards of death while gender, race, tumor histology, disease stage, and nature of resection were not significantly associated with OS.

Conclusions: This is the largest series of PALs. Our results demonstrate that age at diagnosis is an independent predictor of poor survival. Gender, race, histologic subtypes have no effect on OS, and hemicolectomy provides no survival benefit over appendectomy and/or partial colectomy. Additional prospective, multicenter studies including details about chemotherapy and immunotherapy are needed to guide management.

Introduction

While gastrointestinal (GI) involvement by malignant lymphoma is not uncommon, primary lymphomas are rare in the alimentary tract, representing approximately 1%-4% of all GI tumors.[1] Primary GI lymphoma was first defined by Dawson as "predominantly GI tract lesion, with or without spread to regional nodes, no involvement of the peripheral or mediastinal nodes, no involvement of the liver or spleen, and a normal white cell count and differential."[2] Primary appendiceal lymphomas (PALs) are exceedingly rare, constituting around 0.015% of all GI lymphoma cases.[3] Similar to primary GI lymphomas, PALs primarily constitutes lymphomas limited to the appendix. Our current knowledge about PALs is based on

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anecdotal reports and one small retrospective series with a total of around 60 cases reported to date.[4-6] Most of these cases are non-Hodgkin's lymphomas (NHL) with only four cases of Hodgkin's disease reported previously. In most cases, a multimodality approach including chemotherapy, surgical resection, radiotherapy, and immunotherapy is considered to be the optimal management. However, there are insufficient data to determine the correct management of these tumors.

In this study, we sought to evaluate the clinical characteristics, treatment, and survival outcomes of patients with PALs using a population-based database. In addition, we aimed to review previously reported cases in the literature and summarize the current knowledge about PALs.

Materials and methods

Study population

National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database was used for data mining. SEER database is a set of 18 cancer registries that covers approximately 28% of the US population. We queried SEER 18 Registries Research Data, November 2014 Sub (accessed April 2016)[11] and first identified 8526 cases with histologically confirmed primary appendiceal cancer between 1973 and 2012, using the primary site code for appendix (C18.1). Next, all patients with appendiceal lymphomas ($n = 136$) were extracted using the World Health Organization (WHO) 2008 lymphoma classification.[12]

Patients with tumor histology of mucosa-associated lymphoid tissue ($n = 6$), Hodgkin's lymphoma ($n = 2$), and plasmacytomas ($n = 2$) were excluded because of the unique management of these patients (i.e., proton pump inhibitors in combination with antibiotic therapy can lead to complete remission in patients with mucosa-associated lymphoid tissue[13]). A small number of patients who did not undergo surgical resection ($n = 6$) and those who received radiotherapy after surgical resection ($n = 4$) were excluded to ensure robustness while analyzing the data.

Covariate selection

We retrieved data on patient demographics (age at diagnosis, gender, and race), tumor characteristics (stage and histology), treatment (extent of resection), and overall survival (OS). Race was recoded into white and others (including Blacks, American Indian, Asian, and Pacific Islander). Tumor histology was consolidated into four groups using International Classification of Diseases (ICD) oncology codes and based on similar histopathologic and clinical features. The groups consisted of diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, Burkitt lymphoma, and "others". Due to a small number of cases with mantle cell lymphoma, small lymphocytic lymphoma, peripheral T-cell lymphoma, and "NHL not otherwise specified" (NOS), these tumors were included in "others" category.

Tumors were staged according to the Ann Arbor classification for lymphomas.[14] Briefly, stage I disease corresponds to localized involvement of a single extralymphatic site; stage 2 disease constitutes localized involvement of single extralymphatic site and its regional lymph nodes (with or without other lymph nodes regions on the same side of the diaphragm); involvement of lymph nodes on both sides or diaphragm or involvement of the spleen or both designates stage 3; stage 4 disease corresponds to multifocal involvement of one or more extralymphatic organs or isolated extralymphatic organ involvement with distal nodal involvement.

Table 1 – Clinical characteristics of patients with primary appendiceal lymphoma ($n = 116$).

Variable	*n* (%)
Age, y	
<50	60 (51.7)
≥50	56 (48.3)
Gender	
Male	95 (81.9)
Female	21 (18.1)
Race	
White	94 (81)
Others	22 (19)
Tumor histology	
DLBCL	40 (34.5)
Burkitt lymphoma	30 (25.9)
Follicular lymphoma	17 (14.7)
Others	29 (25.0)
Disease stage	
Stage I	59 (50.4)
Stage II	27 (23.1)
Stage III	2 (1.7)
Stage IV	22 (18.8)
Unknown	7 (6.0)
Nature of resection	
Local excision/destruction, NOS	30 (25.9)
Appendectomy/partial colectomy	69 (59.5)
Right hemicolectomy or greater	17 (14.7)

DLBCL = diffuse large B-cell lymphoma; NOS = not otherwise specified.
"Others" race = Blacks/American Indian/Asian/Pacific Islander; "others" histology = mantle cell lymphoma, small lymphocytic lymphoma, peripheral T-cell lymphoma, and "NHL (NOS)".

For extent of surgical resection, procedure codes used for data mining include "site-specific surgery" codes (10 and 20 = local tumor destruction/excision, 30 = appendectomy [including partial colectomy], 40 = hemicolectomy or greater, and 90 = surgery NOS) from 1983 to 1997 and "surgery primary site" codes (20-27 = local tumor destruction/excision, 30-32 = appendectomy [including partial colectomy], 40-41 = hemicolectomy or greater, and 90 = surgery NOS) from 1998 onwards. OS was defined as time interval from the time of initial diagnosis to the date of last contact (or the date of death, if the patient was deceased).

Statistical analysis

The difference between mean age at diagnosis among histologic subtypes was calculated using analysis of variance test.