Colorectal lymphoma in Mexico: clinico-pathological and survival analysis

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Contributions: (I) Conception and design: All authors; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: None; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval: All authors.

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Background: Primary colorectal lymphomas (PCLs) are very rare. We analyze a series of PCL to establish an approximate frequency of the disease and their clinico-pathological characteristics.

Methods: A retrospective cross-sectional study in a third-level hospital from 2006–2016. Clinico-pathologic features of 18 cases are presented.

Results: PCL corresponded to 1.5% of malignant colorectal neoplasms. Ten cases presented in men, the median age was 57 years, diffuse large B-cell lymphoma (DLBCL) was the most common subtype (55.6%), 55.6% presented in cecum, 83.4% as unique polypoid tumor and the median size was 52.5 mm. The most prevalent presentation symptom was abdominal pain (61.1%). Six cases (33%) received initial surgery followed by chemotherapy, 7 cases (39%) received only chemotherapy, 2 cases received only surgery and 3 cases no-treatment. The 2-year disease specific survival was 62.7%. The only factors associated with improved survival in univariate analysis were use of surgery followed by chemotherapy (P=0.043) and HIV (P=0.043). On multivariate analysis none factor was an independent risk factor for decreased survival.

Conclusions: The improved overall survival rates in our series emphasize the importance of surgery followed systemic therapy in the treatment of this disease.

Keywords: Colorectal lymphoma; survival; neoplasms

doi: 10.21037/jgo.2017.10.08

View this article at: http://dx.doi.org/10.21037/jgo.2017.10.08

Introduction

Lymphomas are the most frequent malignant tumors in the lymph nodes, although a substantial number occur at extranodal sites. (1) Extranodal lymphomas are more frequently located in the gastrointestinal tract, lungs, axial skeleton and skin (2). Gastrointestinal lymphomas are rare and they represent between 1–4% of all malignant gastrointestinal neoplasms (3), and less than 1% of colorectal malignances (4). In the gastrointestinal tract, 10–20% are present in the colorectum (5). The age of presentation has a bimodal distribution, with a peak of frequency before 15 years of age, and another between the fifth and sixth decade of life (6).

In view of the recent outcomes when treating this disease utilizing combined therapeutic modalities (7), it has become necessary to promptly identify the symptoms patients present with this type of neoplasm in order to facilitate an early diagnosis and to define the best treatment.

The median survival of the reported cases ranges from 24 to 36 months (4), but some authors have reported an improvement of up to 36 to 53 months with the use of adjuvant chemotherapy (8).

In Mexico and Latin America, there are few data...
regarding the frequency of this condition, so we consider it necessary to establish an approximate frequency of
the disease, and to identify the clinico-pathological characteristics of these patients in order to increase their
detection and improve their prognoses.

Methods
A retrospective cross-sectional study was carried out on patients from a third-level hospital (Instituto Nacional de
Cancerología de México). From the pathology files, all consecutive cases of colorectal tumors from January 01,
2006 to December 31, 2016 were reviewed. A primary colorectal lymphoma (PCL) was defined following
Dowson et al.’s (9) criteria as a case of a histopathologically confirmed lymphoma that presented in the colon or rectum
without any evidence of synchronous affection at the extra-colorectal sites and without a history of lymphoma in
another localization, and normal blood cell counts, and, finally, we accepted cases that showed lymph node
involvement at the drainage site of the colorectal lesion.

The clinical pathological variables recorded from the clinical and pathological records were age, sex, a personal
history of systemic arterial hypertension, diabetes, obesity, constipation, digestive bleeding, diarrhea, body mass index,
abdominal distension, date of diagnosis, date of last follow-up, treatment, B symptoms, tumor location, tumor size,
number of lesions, depth of invasion and outcome of the patient. For the outcome, the patients’ condition at the time
of their last visit is considered, thus placing them in one of the following categories: free of disease, died from the
disease, alive with the disease and died from another cause.

To analyze the data, we performed descriptive statistics with frequencies expressed as numbers, medians with
interquartile range and inferential statistics, contrasting between groups using a Chi square or Fisher’s exact test for
the categorical variables, and a Mann-Whitney U test for the numerical variables, with a level of significance P<0.05.
A survival analysis was performed using the Kaplan-Meier method. A multivariate analysis was performed using the
Cox proportional hazards model with a stepwise forward selection. All the P values were two-sided, with the hazard
ratios at 95% confidence intervals.

Results
We retrieved 1,229 cases of colorectal neoplasms; of these, 1,083 (88.1%) were carcinomas, 56 (4.5%) were
neuroendocrine neoplasms, 40 (3.3%), were gastrointestinal stromal tumors (GISTs), 6 (0.49%) were sarcomas and
44 (3.6%) were lymphomas, but only 18 (1.5% of the total) were considered to be PCL.

The data of the 18 cases of PCL are summarized in Tables 1 and 2. Ten cases (55.6%) presented in men, with a
median age of 57 years (interquartile range, 43.5–66.25 years). As shown in Table 1, diffuse large B-cell lymphoma
(DLBCL) was the most common subtype with 55.6% of cases, followed by mantle cell lymphoma (16.7%),
plasmablastic and Burkitt lymphomas (11.1% for each), and follicular lymphoma (5.6%).

The most common location was the cecum, with 10 cases (55.6%), followed by the rectum with 3 (16.7%), the
ascending and transverse colon with 2 cases each (11.1%), and 1 case in the anus. Most of the tumors (83.4%)
presented as unique polyloid tumors. The median size was 52.5 mm (interquartile range, 38.75–122.5 mm), with 50%
of tumors invading the entire wall depth until the subserous adipose tissue, whereas 27.8% presented in the submucosa,
but 22.2% extended to the serosa and contiguous tissues.

The most prevalent symptom was abdominal pain (61.1%), followed by weight loss (50%), constipation (44.4%),
gastrointestinal bleeding (44.4% corresponding to 8 patients, of which 7 presented as rectorragia or melena,
and only 1 case presented with fecal occult blood), “B” symptoms (33.3%), abdominal distension (27.8%), diarrhea
(22.2%) and hyporexia (11.1%).

The patients’ personal backgrounds showed that 27.8% were diabetic, 5 (27.8%) had a background of cancer
(familial), 4 (22.2%) had an HIV infection, 2 (11.1%) had systemic arterial hypertension and two were obese. The
median body mass index was 23.67 (interquartile range, 21.15–27.37).

With regard to the outcome, the patients were followed up at a median of 371.5 days (interquartile range,
72–755.5 days), 6 cases (33%) received initial surgery followed by chemotherapy, 7 cases (39%) received only
chemotherapy, two cases received only surgery and three cases did not receive treatment. At the final visit, 3 patients
(16.7%) had died of disease and 9 patients (50%) were alive with the disease, while only 4 (22.2%) were alive and free of
the disease. Two cases had been lost at the follow-up. The 2-year disease-specific survival rate in our series was 62.7%
(Figure 1), with a mean survival rate of 79.7 months.

The only factors associated with improved overall survival in the univariate analysis were the use of surgery
followed by chemotherapy (P=0.043, Figure 2) and an
HIV-negative status (P=0.043). Age, sex, surgery, subtype, symptoms, weight loss, BMI, obesity and tumor size were not significantly associated with survival.

In the multivariate analysis none of the factors was an independent risk factor for decreased survival.

**Discussion**

PCL is a very rare disease; in our series it corresponded to 1.46% of the primary colorectal neoplasms. From 18 cases, 55.6% presented in men, the median age was 57 years, all the cases were B-cell lymphoma, eight cases received surgery, seven cases received chemotherapy and three cases did not receive treatment. The factors associated with poor prognosis in the univariant analysis were an HIV-positive status and non-surgical treatment.

PCL represents from 0.1% to 0.6% of colorectal malignances (10-13), but in our institution we found a higher frequency (1.4%), perhaps due to the fact that our institution is a national cancer center, with a concentration of rare or difficult cases. The median age in our series was in agreement with the published literature in Caucasian populations (6-10), but higher than in Asian populations, where the median age ranges from 34.1 to 51 years (13,14). According to published studies, our cases were more prevalent in men and, interestingly, four patients had an HIV infection. This finding was only found in one case out of the 43 patients reported by Drolet et al. (10). In addition,

Table 1  Clinicopathologic data of 18 cases of primary colorectal lymphomas in Mexico, 2006–2016

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex, age</th>
<th>Diagnosis</th>
<th>Follow-up (days)</th>
<th>Tumor site</th>
<th>Size (mm)</th>
<th>No. of lesions</th>
<th>Depth of invasion</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
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<td>1</td>
<td>F, 59</td>
<td>Follicular lymphoma</td>
<td>49</td>
<td>Cecum</td>
<td>120</td>
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<td>Serosa</td>
<td>Surgery</td>
<td>LF</td>
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<td>2</td>
<td>M, 56</td>
<td>LBDL</td>
<td>66</td>
<td>Cecum</td>
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<td>1</td>
<td>Contiguous tissues</td>
<td>Surgery and CT</td>
<td>AWD</td>
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<td>Cecum</td>
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<td>Transverse colon</td>
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<td>Contiguous tissues</td>
<td>CT</td>
<td>AWD</td>
</tr>
<tr>
<td>6</td>
<td>M, 28</td>
<td>Plasmablastic lymphoma</td>
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<td>Anus</td>
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<td>Submucosa</td>
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<td>M, 44</td>
<td>Burkitt lymphoma</td>
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<td>Rectum</td>
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<td>Cecum</td>
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<td>Subserosa</td>
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<td>LF</td>
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<td>M, 34</td>
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<td>311</td>
<td>Ascending colon</td>
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<td>Surgery and CT</td>
<td>AWD</td>
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<td>LBDL</td>
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<td>Subserosa</td>
<td>CT</td>
<td>DWD</td>
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<tr>
<td>12</td>
<td>F, 60</td>
<td>Burkitt lymphoma</td>
<td>1,330</td>
<td>Transverse colon</td>
<td>150</td>
<td>1</td>
<td>Subserosa</td>
<td>Surgery and CT</td>
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<td>13</td>
<td>M, 58</td>
<td>Mantle cell lymphoma</td>
<td>1,369</td>
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<td>Submucosa</td>
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<td>Mantle cell lymphoma</td>
<td>365</td>
<td>Cecum</td>
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<td>Surgery and CT</td>
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<td>M, 51</td>
<td>Plasmablastic lymphoma</td>
<td>147</td>
<td>Cecum</td>
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<td>AWD</td>
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<td>16</td>
<td>M, 44</td>
<td>Mantle cell lymphoma</td>
<td>363</td>
<td>Cecum and descending colon</td>
<td>43</td>
<td>Several</td>
<td>Submucosa</td>
<td>CT</td>
<td>AWOD</td>
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<td>F, 76</td>
<td>LBDL</td>
<td>427</td>
<td>Rectum</td>
<td>4</td>
<td>Several</td>
<td>Submucosa</td>
<td>CT and RT</td>
<td>AWD</td>
</tr>
<tr>
<td>18</td>
<td>M, 73</td>
<td>LBDL</td>
<td>21</td>
<td>Cecum</td>
<td>50</td>
<td>1</td>
<td>Subserosa</td>
<td>No treatment</td>
<td>AWD</td>
</tr>
</tbody>
</table>

LBDL, large B-cell diffuse lymphoma; LF, lost in follow-up; AWD, alive with disease; AWOD, alive without disease; DWD, dead with disease; CT, chemotherapy; RT, radiotherapy.
Tevlin et al. (6) in their series of 11 patients, two presented immunosuppression secondary to transplantation.

Regarding the lymphoma subtypes, most of the reported PCLs were of B-cell lineage, ranging from 82% to 100%, where only the Asian series had an occurrence of T cell lymphomas (13,14). In a SEER-based analysis performed by Cai et al. (12) in the U.S., they found a similar proportion of B-cell vs. T-cell lymphomas (53% and 47%, respectively), although they studied cases in adults and children; other series including children also demonstrated the occurrence of T cell lymphomas (13), a fact that appears to be rare in adults. Between the cell subtypes, the most frequent is DLBCL, ranging from 45% to 74% (10-13), and our data are according to this subtype. The second most prevalent subtypes are variegated between the series. The most common location of PCL is the cecum, followed by the rectum (around 60% and 20%, respectively), and the most prevalent symptom is abdominal pain (6,10-14). Our results agree with these findings.

Almost all patients with PCL reported in the literature underwent a surgical resection (3,4,8-14), and the median survival in these series was generally low, ranging from 24 to 36 months. In most series, the majority of patients received adjuvant systemic chemotherapy, whose use has been associated with improved outcomes reaching a 2-year survival rate of around 60% (10,14) and a 5-year survival rate of 53–57% (12-14). However, in one of the largest series, and precisely in Mexican patients, Avilés et al. described an overall survival rate of 83% at 10 years (15). Our findings agree with most series with a 2-year disease specific survival rate of 62.7% with a mean survival rate of 79.7 months. These results suggest that an aggressively treated colorectal lymphoma could improve the prognosis.

### Table 2 Clinical features and presenting symptoms of 18 cases of primary colorectal lymphomas in Mexico, 2006–2016

<table>
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<tr>
<th>Patient No.</th>
<th>DM</th>
<th>SAH</th>
<th>Obesity</th>
<th>HIV</th>
<th>Constipation</th>
<th>Diarrhea</th>
<th>Bloating</th>
<th>GIB</th>
<th>WL</th>
<th>&quot;B&quot; symptoms</th>
<th>Hyporexia</th>
<th>Pain</th>
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SAH, systemic arterial hypertension; HIV, human immunodeficiency virus; GIB, gastrointestinal bleeding; BMI, body mass index; WL, weight loss.
Conclusions

In conclusion, most patients present with nonspecific symptoms, which often lead to delays in diagnosis and an advanced stage at presentation. The majority of patients have DLBCL. We found cases associated with immunosuppression (HIV infection). The treatment of colorectal lymphoma generally consists of surgery followed by systemic chemotherapy, and this treatment is the best approach.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by the Instituto Nacional de Cancerología (NO. 17/139) and written informed consent was not necessary because the retrospective/observational nature of the study and data does not contain identifying information of the patients.

References


Figure 1 Kaplan-Meier curves of survival of 18 cases with primary colorectal lymphomas. The estimated 2-year overall survival was 62.7%.

Figure 2 Kaplan-Meier curves of survival of 18 cases with primary colorectal lymphomas stratified according treatment.