

PRIMARY MALIGNANT TUMORS OF THE SMALL INTESTINE: ANALYSIS OF 156 IRANIAN PATIENTS

H. SAADATNIA, M.D., S. SERESHKI, M.D., AND T. GHIASI
MOGHADAM, M.D.

*From the Departments of Medicine and Pathology, Ghaem Hospital, Mashhad University of Medical
Sciences, Mashhad, Islamic Republic of Iran.*

ABSTRACT

156 Iranian patients with primary malignant tumors of the small intestine were reviewed. Malignant lymphoma was the most common tumor type, comprising 128 patients (82%), followed by adenocarcinoma (22 patients, 14.1%), leiomyosarcoma (4 patients, 2.56%) and carcinoid tumor (2 patients, 1.28%).

Lymphomas and adenocarcinomas were primarily located in the duodenum or jejunum, whereas leiomyosarcomas were more common in the ileum. Abdominal pain (73%), weight loss (68%), diarrhea (41%), and nausea or vomiting (35%) were the most common symptoms with these tumors.

Among the lymphoma group 95 patients (74.2%) had non-IPSID (immunoproliferative small intestinal disease) lymphoma and 33 patients (25.8%) had IPSID related lymphoma.

In contrast to the western world and far east countries in which malignant small intestinal tumors are a disease of middle and old age groups and adenocarcinoma is the most common tumor type, in our area, similar to some other middle east and north African countries, lymphomas are much more frequent. Although Iran is endemic for IPSID related lymphoma, the majority of these tumors are non-IPSID lymphomas and appear in a very young age group (mean age 27 y).

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INTRODUCTION

Primary malignant tumors of the small intestine are rare and constitute approximately 0.5% of all malignancies in the body¹ or 1-3% of all gastrointestinal malignancies.^{1,2,17} The annual incidence has been reported to be 0.6-1.0 per 100,000 in epidemiological studies from the United States and Europe.^{3,5} Since the incidence in Asian people is also low, there are few reports from Asia which have evaluated the clinicopathological characteristics in a large number of

cases of small intestinal tumors.⁴ We reviewed 156 Iranian patients, and the characteristics of their small intestinal malignancies are discussed.

PATIENTS AND METHODS

We reviewed 156 Iranian patients who presented to Ghaem Hospital (a 1000 bed tertiary general hospital affiliated to Mashhad University of Medical Sciences at northeast of Iran) between 1972-1997 with primary malignant

Primary Malignant Small Intestinal Tumors

Table I. Anatomic and histological distribution of small bowel tumors in 156 Iranian patients.

	Duodenum	Jejunum	Ileum	Total
Lymphoma*	82	28	18	128
Adenocarcinoma	15	5	2	22
Leiomyosarcoma	1	0	3	4
Carcinoid	0	2	0	2
Total				156

* Patients with IPSID-related lymphoma had diffuse involvement of the duodenum and jejunum.

small intestinal tumors (PMSIT). All cases of PMSIT indexed in the files of the Department of Pathology were reviewed and re-examined by one of us (T.G. Moghadam) and classified. Of 188 cases reviewed 32 were excluded because pathologic material was considered inadequate or the small intestine was not the initial site of involvement by tumor. PMSIT was defined as a tumor initially presenting as small intestinal disease with pain, obstruction, perforation, hemorrhage, malabsorption, or other related symptoms. Patients who had palpable peripheral lymphadenopathy, mediastinal lymphadenopathy upon radiographic evaluation, abnormal peripheral blood smear or bone marrow examination, evidence of hepatic or splenic tumoral involvement except via direct extension from primary bowel tumor were not considered as PMSIT (Modified Dowson's criteria).¹⁸ Tumors invading the ampulla of Vater of the duodenum were not included to prevent confusion with periampullary and pancreatic tumors, and lesions of the

ileocecal valve were also excluded. All tumors were resected surgically (58%) or sampled endoscopically (42%) and were confirmed histopathologically to be malignant tumors of small intestine. Although precise diagnosis and classification of PMSIT may need a variety of ultrastructural and histochemical techniques, classifications based on site of tumor, cell type, radiological appearance, geographic distribution, presence or absence of underlying mucosal disease and alpha heavy chain in serum is reasonable for epidemiological studies and we used this approach for classification. Lymphomas were further divided to non-IPSID lymphomas (including Western lymphoma (WL), enteropathy associated T-cell lymphoma (EATCL), Burkitt's and Burkitt's-like lymphoma (BL), multiple lymphomatous polyposis (MLP), and IPSID lymphomas (Mediterranean lymphoma and alpha-heavy chain disease were included in the IPSID group).

RESULTS

In our series malignant lymphoma was the most common tumor type, comprising 128 cases (82%). Twenty-two patients had adenocarcinoma (14.1%), 4 had leiomyosarcoma (2.56%) and only two patients had carcinoid tumor (1.28%). In total there were 87 males and 69 females (male:female ratio= 1.26:1). Malignant lymphoma was 1.32 times more common in males (73 cases) than females (55 cases). On the other hand an equal number of males and females had adenocarcinoma (11 cases each), leiomyosarcoma (2 cases each) and carcinoid tumor (1 case each). The age of the patients ranged from 11 to 65 years but the majority presented in their third decade. The average age was 27 years for patients with lymphoma, 49 for those with adenocarcinoma, 40 for those with leiomyosarcoma and 54

Table II. Symptoms associated

Symptoms	Tumor location			Total (%)
	Duodenum	Jejunum	Ileum	
Pain	21	48	45	114(73)
Weight loss	24	50	22	106(68)
Diarrhea	11	30	23	64(41)
Nausea, Vomiting	4	32	19	54(35)
Bleeding	6	12	5	23(15)
Anorexia	3	8	3	14(9)
Constipation	2	4	5	11(7)
None	1	1	3	5(3.2)

in patients with carcinoid tumor.

The anatomic and histological distribution of the lesions are shown in Table I. 95 patients (74.2%) with a mean age of 27.6 years had WL, located in the duodenum or jejunum in the majority of patients (86%). Diffuse mixed, diffuse large cell and small lymphocytic lymphomas were the most frequent types.

33 patients (25.8%) had IPSID-related lymphoma. Mean age was 26 years. Tumors always involved the duodenum and jejunum diffusely. 36% of those tested had abnormal alpha-heavy chain in their serum. EATCL and MLP were not seen. 9 patients with BL (mean age 12.6 years) were also seen during this period but were not included in the present study because the ileocecal region was always involved, with evidence of ascites and extensive lymph node spread in the majority of them. Hodgkin's lymphoma was not seen in our patients.

Adenocarcinomas tended to be located in the duodenum (69%) and jejunum (25%) and they showed a decreasing frequency as one progressed distally. In three out of four patients (75%) with leiomyosarcoma, the tumor was in the ileum, and the average age was 40 years. Two patients had carcinoid tumors located in the mid-jejunum.

The predominant symptoms were abdominal pain (73%), weight loss (68%), diarrhea (41%), nausea and/or vomiting (35%) and bleeding (15%). Pain was more frequent in jejunal and ileal tumors; otherwise, there was no correlation between the location of tumors and their symptoms as shown in Table II.

DISCUSSION

Although the small intestine is the site for almost 90% of the alimentary tract's mucosal surface area, it is the site of only a small percentage of intestinal neoplasms, and only rarely is a malignancy found there.¹⁷ Adenocarcinomas or carcinoid tumors have been reported to be the most or second most common type of small intestinal tumors in the western world. Reviewing reports from the United States and Europe, the incidence of adenocarcinoma and carcinoid tumor ranged from 20% to 40%, and from 21% to 45%, respectively, of all malignant tumors in the small intestine.^{3,5,7} However, the incidence of various small bowel tumors differs among the races. For instance, blacks have a higher incidence of adenocarcinomas and carcinoids than whites, but lower rates of lymphomas and leiomyosarcomas.^{3,8} In Jews, lymphomas are the most common intestinal tumor while adenocarcinomas or carcinoid tumors are rare.^{9,14} In contrast to western and far east countries we found that lymphomas are the most common intestinal tumors in Iranian patients, adenocarcinomas are second in frequency and only two patients had carcinoid tumors.

The sex ratios of non-IPSID lymphoma (1.32:1), IPSID-related lymphoma (1.3:1) and adenocarcinoma (1:1) is in

agreement with other reports. The average age of Iranian patients was markedly lower than western patients (27.5 years. 26 years and 49 years for non-IPSID lymphoma, IPSID related lymphoma and adenocarcinoma, respectively). The average age of our patients with leiomyosarcoma (40 years) and carcinoid tumor (54 years) was also slightly lower than western patients.

Although Iran is endemic for IPSID-related lymphoma¹⁴⁻¹⁶ most of our patients had non-IPSID lymphoma. Lymphomas have been reported to develop less frequently in the duodenum (0-11%) than in the jejunum (28-42%) or the ileum (55-70%).^{2,6,8,11} In our study, most non-IPSID lymphomas were located in the duodenum (64%), and the jejunum and ileum were involved less frequently (22% and 14%, respectively). Patients with IPSID-related lymphomas had diffuse involvement of the duodenum and jejunum and occasional involvement of the ileum. IPSID related lymphomas appeared mostly in the second and third decade of life and males were slightly more affected. 36% of those tested had alpha-heavy chain in their serum. None of our lymphoma patients had predisposing factors for the development of lymphoma (i.e., non-tropical sprue, AIDS, cyclosporine therapy, etc). Primary Hodgkin's lymphoma of the intestine is extremely uncommon and was not seen in our series.

Adenocarcinoma of the small intestine tended to develop in the proximal rather than in the distal portion of the small intestine in our series (69%, 24%, and 6% in the duodenum, jejunum and ileum, respectively). This proximal localization is more prominent in our patients than patients from western reports.^{5,6,8,11,13} In two of four patients with leiomyosarcoma, the tumor was located in the jejunum; previous reports from Europe and the United States found rates of 0-22% in the duodenum, 22-58% in the jejunum and 25-56% in the ileum.^{2,8,11,12}

It has been reported that more than 66% of carcinoid tumors are located in the ileum.^{2,3,6,8,11,12} Our only two patients with carcinoid tumor had the jejunum involved.

Because the majority of non-IPSID lymphomas, all IPSID-related lymphomas and a large number of adenocarcinomas in our area have duodenal involvement when suspected, upper gastrointestinal endoscopy and biopsy is an extremely important diagnostic technique.

Pain was the most notable symptom of small bowel tumors in our series (73% of cases) and others (65-86%).^{6,7,9} In our series pain tended to be more frequent in jejunal and ileal tumors. The incidence of nausea and vomiting (35%) and that of bleeding (15%) in our series was comparable to previous reports.^{6,7,9} Diarrhea (41%) occurred more frequently in our series than in others, because patients with IPSID-related lymphoma usually have diarrhea and a significant number of our patients had this tumor.

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