

Burkitt's Lymphoma of the Abdomen: The Northern California Kaiser Permanente Experience

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Citation

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Abstract

We retrospectively reviewed the experience of the Kaiser Permanente Northern California Region (KPNCR) with Burkitt's lymphoma and studied patients with abdominal Burkitt's lymphoma. During a 16-year period from 1987-2002, 7868 patients with lymphoma were entered into the California Cancer Registry (CCR) of KPNCR. Of these patients, 121 patients (1.5%) were found to be Burkitt's type of lymphoma. Of the 121 patients, 36 were associated with HIV infection and an additional 35 patients had Burkitt's lymphoma presenting at a site outside of the abdomen. The charts and computerized medical records of 50 cases of abdominal Burkitt's lymphoma form the basis of this study. Of these 50 patients with intra-abdominal Burkitt's lymphoma, involvement of mesenteric, retroperitoneal or pelvic structures was so extensive that the diagnosis was made by fine-needle aspiration, core biopsy or biopsy of a regional lymph node in 24 patients. Investigation of vague upper gastrointestinal symptoms led to CT scan and endoscopic stomach biopsy which demonstrated involvement with Burkitt's lymphoma in three patients. Seven additional patients had open biopsies of large intraabdominal masses showing Burkitt's lymphoma. The primary treatment of these patients was chemotherapy. Sixteen patients from the CCR had surgical exploration and resection of their tumor. One patient had disease of the jejunum. Two patients had isolated disease of ileum. Seven had disease of the ileum and cecum and six were felt to have disease primarily of cecum. When possible, abdominal Burkitt's lymphoma was resected. All patients were also treated with chemotherapy.

INTRODUCTION

Burkitt's lymphoma is a rare neoplasm that can occur in virtually any location in the body. When it occurs in the abdomen, it can present as a large mesenteric, retroperitoneal or pelvic mass. In other cases, however, it can be isolated to the gastrointestinal tract leading to a mass, intussusception, obstruction or bleeding. In this study, we review the Kaiser Permanente Northern California Region experience.

RESULTS/METHODS

The charts of patients with intra-abdominal Burkitt's lymphoma were reviewed for this study. Two patients were identified from our own personal experience. Fourteen additional patients were identified from the California Cancer Registry (CCR) of Kaiser Permanente Northern California Region. Kaiser Permanente is a large integrated health care system which includes Kaiser Health Plan, Kaiser Foundation Hospitals and The Permanente Medical Group and currently provides comprehensive medical care to 3 million members in the northern half of California. As such, this series reports on the experience of over 1% of Americans. During the period from 1987 to 2002 (sixteen

years), 121 patients with Burkitt's lymphoma were entered into the Cancer Registry. During the same time span, our membership has averaged just over 2.5 million members. This leads to an incidence of approximately 3.0 cases per million per year. The 121 patients are divided into three groups: 36 patients had HIV-associated Burkitt's lymphoma, 35 patients presented with extra-abdominal Burkitt's lymphoma and 50 patients presented with Burkitt's lymphoma arising in the abdomen. This final group of 50 patients is subdivided into 34 patients with extensive, unresectable disease and 16 patients where primary disease involved the gastrointestinal tract and could be resected. Of the 34 patients with unresectable disease, diagnosis was established with endoscopic stomach biopsy in three patients, open biopsy in seven patients and FNA or core biopsy of mass or peripheral node in 24 patients.

The treatment of the sixteen patients with resectable gastrointestinal Burkitt's lymphoma of the gastrointestinal tract will be discussed in depth. Seven of the patients were children ranging in age from three to thirteen years. Nine of the patients were adults from 19 to 84 years. Twelve patients

were male and four were female. All patients had abdominal pain when seen by a surgeon. Vomiting was present in 4/9 patients (44%) when mentioned. Rectal bleeding was present in 3/9 patients (22%); in two the bleeding was present for only two days. One patient reported bleeding for about two months. Duration of symptoms ranged from two weeks to more than a year. Seven patients had symptoms of from one day to a month. The other patients' symptoms were reported from one to 12 months duration. None of the patients was found to have fever. An abdominal mass was palpable in half of the patients. Varying degrees of abdominal tenderness were found on the right side of the abdomen in all patients. Hematocrit values ranged from 25-48%. The hematocrit was <30% in 4/13 patients.

Various radiographic imaging modalities were used in these sixteen patients. In six out of ten patients where abdominal x-rays were done, bowel gas pattern was consistent with small bowel obstruction. Barium enema was performed in seven patients and was abnormal in each. In five patients the barium enema correctly demonstrated an intussusception. In one patient, the films showed a "string sign" in the terminal ileum consistent with inflammatory bowel disease or tumor. In the seventh patient, a right lower quadrant mass was seen. Abdominal CT scan was performed in five patients. In three, a complex mass was seen in the right lower quadrant; in two, intussusception was suspected. Abdominal ultrasound was abnormal in three patients where used, showing a mass in the right lower quadrant in two and suspected intussusception in one. A single patient had colonoscopy which demonstrated intussusception and biopsy showed an atypical lymphoid infiltrate. In a second patient with a small bowel tumor, colonoscopy was normal.

Operative findings were described in 15/16 patients. In eight patients, intussusception was found; one jejunal, one ileal and six ileocolic. In six patients, a resectable mass was found in the right lower quadrant without intussusception. Similarly, one patient was found with bulky but resectable disease of small bowel. Six of ten patients had involvement of lymph nodes found.

Fourteen of sixteen patients survived longer than one month after operation. One patient was recovering from operation but died of septic complications after a first round of chemotherapy. The second patient who died of septic complications was a heart transplant recipient one year previously. All 14 patients who survived more than one month after operation were treated with chemotherapy. Two of these patients died of septic complications during their

chemotherapy treatment. A third patient developed tumor recurrence after a full course of chemotherapy and died of disease. Ten patients, who received their initial operation and chemotherapy from two to more than fifteen years ago, are alive without evidence of disease.

Most patients in this series received surgical care by a general surgeon.

DISCUSSION

The general surgeon is frequently asked to evaluate patients with abdominal pain and tenderness, mass, bowel obstruction or intussusception. In many practice settings, general surgeons care for both adults and children. Yet the rarity of abdominal Burkitt's lymphoma means that most general surgeons will never care for one of these patients.

The incidence of Burkitt's lymphoma in general and abdominal Burkitt's lymphoma is not known. Levine estimated the incidence to range from one case per million for children less than ten years old, 0.7 per million from 10 to 20 and 0.6 per million from 20 to 30 [1]. He indicated that Burkitt's lymphoma was rare in patients older than 30. In this review of the Kaiser Permanente Northern California Region experience, we have attempted to estimate the incidence of Burkitt's lymphoma in a defined population group. When patients with known HIV infection are excluded (36 patients), 85 patients have been diagnosed and treated for Burkitt's lymphoma. This incidence is approximately 2.1 cases per million members per year. Of these 85 patients, 50 presented with primarily intra-abdominal disease, 16 of whom could be resected with curative intent.

All studies show that Burkitt's lymphoma is more common in males than females. Stein found 64% of patients were male [2]. All of Kaufman's patients were male [3]. In our own study, 71% of patients were male. The pattern of presentation was the same for adults and children with involvement of the ileocecal region as the primary site noted. Six of seven children survived their disease versus five of nine adults. The small sample size does not allow statistical comparison. It is important to note, however, that Burkitt's lymphoma is considered among the most responsive to chemotherapy.

Most large reviews of Burkitt's lymphoma describe the disease in children or have appeared in the pediatric surgery literature [2,3,4,5,6,7,8]. All of the patients in these reviews are younger than 21 years old. Magrath's review of 68 patients

included 66 patients younger than 15, one aged 25 and one aged 60 [9]. In Kemeny's review of the NIH experience, about one third of the patients were older than 20 [10]. This is the first review in the past 20 years that includes significant numbers of adult patients with abdominal Burkitt's lymphoma. Our patients ranged in age from 3 to 84. Of our patients with abdominal Burkitt's lymphoma, slightly more than half were older than 20.

Most studies agree that patients present with abdominal pain, tenderness, intestinal obstruction, a mass or intussusception. Fever is unusual. Rectal bleeding occurred in several of our patients with intussusception.

Workup often includes abdominal CT scan, upper or lower endoscopy, ultrasound or barium enema. Laboratory values often show anemia. While radiology studies often show a mass, intussusception or intestinal obstruction, Burkitt's lymphoma is rarely considered in the differential diagnosis.

The role of surgery in treating patients with Burkitt's lymphoma has been examined by many authors. When preoperative examination or radiographic studies suggest unresectability, fine-needle aspirate cytology or core biopsy usually provides an accurate diagnosis. Many patients with abdominal Burkitt's lymphoma, however, are treated for acute abdominal symptoms for which they are explored. When the general surgeon operates for a mass, bowel obstruction or intussusception, operative decisions often must be made without knowing the true pathologic diagnosis. Patients with larger, fixed tumor are beyond the scope of resection but incisional biopsy should provide adequate tissue to establish diagnosis. Faced with a potentially resectable mass and an uncertain diagnosis, most surgeons favor resecting the tumor with the involved intestine.

Pre-operative examination and radiographic studies often reveal extent of disease and suggest unresectability. In the NIH experience, all patients with abdominal Burkitt's lymphoma had a laparotomy prior to referral to NIH [10]; 41 of their 69 patients had either incomplete resection (5 patients) or biopsy only (36 patients) to establish diagnosis. In the current series, 34 patients had unresected abdominal disease. The diagnosis was confirmed with percutaneous FNA and core biopsy in 24 patients, by endoscopic gastric biopsy in 3 and by open incisional or core biopsy in seven.

Burkitt's lymphoma is characterized by rapid growth and is composed of small, non-cleaved lymphocytes. The diagnosis

is established by a combination of cytogenetic, histopathologic and immunohistochemistry techniques.

Most authors have found that the surgically resected patients have a slightly higher survival rate [56710]. A contrasting view is presented by Miron from France. Survival in their patients who were treated by chemotherapy alone was slightly better than in the resected group and they felt that resection unnecessarily delayed chemotherapy [8].

Figure 1
Table 1: Survival in Resected and Unresected Abdominal Burkitt's Lymphoma

#patients	Patient Survival	
	Resected Patients	Unresected Patients
Gahukamble (7)	31	83% 21%
Shamberger (6)	38	83% 45%
Stovroff (5)	28	83% 53%
Kemeny (10)	69	61% 36%
Current series	50	63% 41%
Miron (8)	35	71% 93%

The primary treatment of Burkitt's lymphoma is with chemotherapy. All patients in the current series, including those in whom all gross tumor was resected, were treated with chemotherapy. It is not the purpose of this article to discuss the medical treatment of Burkitt's lymphoma. We should emphasize, however, that some of the patients who died in our series experienced neutropenia and sepsis during chemotherapy. Another risk of the chemotherapeutic treatment of abdominal Burkitt's lymphoma is related to tumor lysis. It is logical to assume that this risk is greater in patients who have had only a biopsy in whom the tumor burden is so great. Despite the risks inherent in chemotherapy, significant numbers of patients with unresectable abdominal Burkitt's lymphoma are cured of disease with chemotherapy. In our patients with abdominal disease which was not resected, 14/34 patients are disease free. In our series, 10/16 patients are free of disease after combined resection and chemotherapy.

In conclusion, we attempt to estimate a population-based incidence of Burkitt's lymphoma in the Kaiser Permanente Northern California Region. We excluded patients known to have HIV infection. Of the remaining patients, 41% presented with disease outside the abdomen and 59% presented with primarily intra-abdominal disease. Of the patients with abdominal disease, 32% were amenable to surgical resection. Long-term survival was better in patients where gross disease was removed. All patients were also

treated with chemotherapy. The general surgeon should be aware that abdominal Burkitt's lymphoma often causes symptoms that lead to surgical consultation and treatment. Surgical management should include complete resection where possible and sufficient biopsy material to establish a diagnosis when resection is not feasible. All patients with Burkitt's lymphoma should be referred for chemotherapy.

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