CASE REPORT

Rare Case of Primary Gastric Burkitt Lymphoma in a Child

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Primary gastric tumors are very rare in children. Burkitt lymphoma is a common type of non-Hodgkin’s lymphoma, and gastric Burkitt lymphoma usually occurs in the aged. When involving the gastrointestinal tract, primary gastric Burkitt lymphoma is very rare in younger childhood. Many gastric lymphomas including mucosa-associated lymphoid tissue lymphoma are associated with Helicobacter pylori infection or acute bleeding symptom. We report a seven-year-old boy who presented with only some vomiting and postprandial pain. His upper gastrointestinal endoscopy and biopsy revealed a large primary Burkitt lymphoma with no acute bleeding and no evidence of H. pylori infection. After chemotherapy, he remains in remission. (Korean J Gastroenterol 2016;68:87-92)

Key Words: Burkitt lymphoma; Gastric cancer; Non-Hodgkin lymphoma

INTRODUCTION

Primary gastric Burkitt lymphoma (BL) is extremely rare below age of ten. BL is a very aggressive non-Hodgkin lymphoma (NHL), and commonly presents in extranodal sites or as acute leukemia. The most common sites are lymph nodes of the head, the neck, and the abdomen. Rarely, it can involve the liver in adults. Primary gastrointestinal tract lymphomas among NHLs tend to occur in the stomach of adults as opposed to the cecum or the ileum in children. The global incidence of pediatric NHLs is reported diversely, and the incidence of childhood gastric BL is unknown, although likely very low compared to its adult counterpart. Kassira et al observed that the most common histologic type of primary gastrointestinal tract lymphoma was BL (52%), accounting for 140 patients among 265 pediatric patients below age of twenty. However, only four patients out of 116 children below the age of ten had gastric lymphomas (BL or others). NHLs commonly occur in the cecum or the ileum, but localized and primary gastric BL is very rare in children. Herein, we report a seven year old boy with primary gastric BL who was successfully treated with chemotherapy.

CASE REPORT

A previously healthy seven-year-old boy visited our pediatric department, presenting with nausea, vomiting, postprandial abdominal pain, and pale appearance that began...
one month prior. He had no specific history including drug or family history. He showed no systemic symptoms such as fever, weight loss or night sweating. His vital signs were stable and were within normal range (blood pressure, 100/55 mmHg; heart rate, 120 beats/minute; respiratory rate, 20 breaths/minute; body temperature, 36.8°C). On physical examination, a single, fixed, hard, 5×3-cm mass was palpated in the left upper quadrant of the abdomen. Abdominal examination revealed direct tenderness in the left upper quadrant. No lymphadenopathy of the neck or the inguinal area was identified.

Initial laboratory work-up showed normal white blood cell count, mildly decreased hemoglobin of 9.9 g/dL (normal range, 12-16 g/dL). Decreased mean corpuscular volume and mean corpuscular hemoglobin were consistent with iron deficiency anemia. His laboratory profiles showed normal liver and renal function. Serum lactate dehydrogenase (LDH) level was 1,604 IU/L (normal range, 218-472 IU/L) and erythrocyte sedimentation rate was 41 mm/hour (normal range, 0-20 mm/hour). Serum uric acid level was normal. Epstein-Barr virus (EBV) and cytomegalovirus polymerase chain reaction analyses were all negative. Furthermore, alpha-fetoprotein and carcinoembryonic antigens were undetected.

Chest and abdomen radiograph showed elevated left phrenic shadow and mass-like lesion in the epigastric and the left infra-phrenic region (Fig. 1). Abdominal ultrasound revealed diffuse thickening of the stomach wall. CT of the abdomen showed homogeneous diffuse gastric wall thickening (6 cm in the maximal thickness) with necrotic cyst-like portion. There were 1 to 2 cm lymph node enlargements around the stomach (Fig. 2). The gastroscopy revealed a huge well-demarcated ulcerative lesion with neighboring mucosal elevation and irregular margin, but no acute bleeding in the cardia (Fig. 3). We performed multiple gastric biopsies during endoscopy. Histologic examination of biopsy samples revealed gastritis, and no evidence of Helicobacter pylori, but lymphocyte proliferation was suggestive of lymphoma (Fig. 4A).
Negative \textit{H. pylori} infection was confirmed through the \textit{Campylobacter}-like organism test. Serum IgG-anti \textit{H. pylori} was negative. In immunohistochemistry, the tumor cells stained with CD20 (Fig. 4B), CD10 (Fig. 4C), and Bcl-6 (Fig. 4D), but not with CD3, CD5, Bcl-2, CD56, Tdt, Mum-1, and CyclinD1 antibodies. \textit{In situ} hybridization using EBV-encoded small RNA probes was performed, and EBV transcripts were not detected in tumor cells. All of the neoplastic cells were positive for Ki-67 (Fig. 4E). These findings pointed toward a diagnosis of BL. Spinal tap and bone marrow aspiration reported no involvement of the central nervous system and the bone marrow. No anomalous heart function or structure was seen in echocardiogram.

Fludeoxyglucose (FDG) scan revealed FDG-avid lymphoma involving gastric mucosa and lymph nodes (left internal mammary, left paravertebral, and anterior diaphragmatic lymph nodes). Multifocal peritoneal lymphomatosis was seen on the dependent portion of the pelvis and the peritoneum (Fig. 5). The boy was diagnosed with stage II (St. Jude/Murphy staging system) BL. He was started on a chemotherapy protocol consisting of intravenous adriamycin, cyclophosphamide, vincristine, and oral prednisone. After six cycles of chemotherapy, no evidence of disease recurrence was found in recent gastroscopy (Fig. 6).

**DISCUSSION**

Worldwide, pediatric gastrointestinal tumors tract account for only 5% of all malignancies. Gastric tumor is the fifth most common malignancy after the lung, breast, pros-
tate, and colorectum in adults. In children, however, gastric tumors are very rare, so there is little research regarding optimal management and outcome. Curtis et al. reported incidence of primary gastric tumors in children at Children’s Hospital Los Angeles over a 55-year period. The tumors were identified as follows: six stromal tumors, four teratomas, four lymphomas, two adenocarcinomas, two myofibroblastic tumors, two hamartomas, and one rhabdomyosarcoma. In Korea, ten children among 1,284 children who underwent upper gastrointestinal endoscopy were reported with gastric tumors in a 10-year period at a single center. Six children with ectopic pancreas, two children with rhabdomyosarcoma, one child with gastrointestinal stromal tumor (GIST), and one with hamartoma due to Peutz-Jegher syndrome were diagnosed by gastroscopy. There was no gastric lymphoma. As for GIST, only two children (aged nine and 17 years) were recently reported with gastric masses in Korea. Two children with signet ring cell carcinoma and one child with adenocarcinoma were reported as having gastric malignancy in Asia. Gastric malignancy in children is very rare. In Korea, despite increased pediatric gastroscopy, reports of gastric tumors in children are rare, compared to adult.

BL has a short doubling time of roughly 24 hours, and thus grows rapidly. It spreads diffusely and quickly becomes a large mass. FDG PET/CT is a very sensitive study for initial diagnosis and later evaluations, because BL has a high glycolytic rate. The mesenteric or intraperitoneal lymph nodes are commonly involved. The involved large mass in the lymph node, liver, kidney, or the spleen is easily detected by CT or ultrasonography. Generally, ultrasound is initially used in the children with abdominal or pelvic mass, while CT scan is performed for tumor staging. Due to radiation hazard, repeated CT examination has been recently replaced with magnetic resonance imaging. If bone involvement is suspected, radionuclide bone scans are recommended. A distal ileal mass causes constriction of the gastrointestinal tract and associated obstruction symptoms. These aggressive lesions lead to malignant ascites, intraperitoneal seeding, intussusception, or perforation. Gastric or colonic BL may be asymptomatic by the diffuse thickening of submucosal infiltration until it becomes bulky. However, the main symptom of advancing gastric tumors is bleeding. In the literature, most pediatric gastric BL cases display bleeding symptoms. Nonspecific symptoms like abdominal pain and vomiting may occur, as in this case. Pediatric upper gastrointestinal endoscopy is a useful tool for evaluation of gastric tumors in children as this case.

Gastrointestinal involved lymphomas classified as T-cell lineage and B-cell lineage origin. B-cell type of lymphoma can be subdivided to extranodal marginal zone B-cell lymphoma, diffuse large B-cell lymphoma, mantle cell lymphoma, follicular lymphoma, Burkitt lymphoma, and Hodgkin lymphoma. Cytologic features of the BL include uniform medium-sized rounded cells with multinucleoli, scattered chromatin, numerous mitotic figures, and basophilic cytoplasm.
The nucleus has 3 to 5 nucleoli, and is slightly indented. Macrophages laden with apoptotic cellular debris exhibit the “starry sky” appearance on basophilic background. As a rapidly growing tumor, it shows a high proliferation proliferation. Immunohistologic findings can be helpful to differentiate BL from others, such as negativity of TdT, Mum-1, cyclin D1, CD5, CD23, CD34, CD44, Bcl-2, but positivity for CD10, 19, 20, 22, 24, 37, 38, Bcl-6, Tcl-1, and a very high (above 95%) Ki-67 proliferation. The cells of African BL are CD21-positive, but those of American cases are negative.

In this case, CD20, CD10, Bcl-6, and Ki-67 were positive results. At the molecular level, translocation between C-myc gene and IgH gene t(8;14)(q24.1;q32.3) is the major chromosomal abnormality in BL. Other translocations between C-myc proto-oncogene and kappa t(2;8) or lambda t(8;22) light chain are also present in BL.

H. pylori infection, inflammatory bowel disease, celiac disease, underlying immunosuppression, and malaria or EBV infection may be risk factors for BL. In adults, gastric lymphoma, underlying immunosuppression, and malaria or EBV lymphoma. Hence, eradication of H. pylori suggested that H. pylori may be a cofactor in the development of BL and eradication should be performed concurrently with chemotherapy regimens in H. pylori-positive lymphoma. In this case, although the patient showed negative result of H. pylori infection in mucosal biopsy, the possibility of false negativity remains, due to patch distribution. However, BL is a high-grade B-cell lymphoma and does not show T cell proliferation, unlike MALT lymphoma. There are a few cases supporting the causal link between gastric BL and H. pylori. Moreover, the prevalence rate of H. pylori infection is very high in children. To verify this relationship, further experimental data is necessary.

Aggressive chemotherapy is the first-line therapy for induction of remission in BL. Surgical resection is no longer favored due to the benefits of chemotherapy such as high chemosensitivity, dramatic response, and quick recovery. Combination chemotherapy including cyclophosphamide achieves a high cure rate and excellent survival rate in children. However, tumor lysis syndrome or chemotherapy-associated toxicities are life-threatening complications. Rapid breakdown of malignant cells results in tumor lysis syndrome. In event of tumor lysis, hyperkalemia, hyperphosphatemia, and hyperuricemia are observed in lab test results. Prophylactic measures with bicarbonate hydration, allopurinol, and rasburicase are required. Hemorrhagic cystitis, neuropathy, vomiting, mucositis, gastrointestinal bleeding, bowel obstruction, and bone marrow suppression are severe toxic complications. Patients with low stage (stage I or II) disease have good prognosis with disease-free survival of over 95% after chemotherapy.

In NHL, bone marrow and central nervous system involvements are the main prognostic factors regardless of location of the tumor. LDH levels, performance status, Ann Arbor staging, and the presence of extranodal disease are other prognostic factors. After treatment, early relapse (below three months) or late relapse (over three months) may occur. In the early stages, the tumor usually grows at the original site. The new tumor arises at an uninvolved site in late relapse. In this case, our patient has not relapsed during the three years since diagnosis. We report a seven-year-old boy with primary BL in stomach who complained of nonspecific gastrointestinal symptoms including abdominal pain and vomiting. He achieved successful remission with chemotherapy and no relapse.

REFERENCES


