Primary Follicular Lymphoma of the Duodenum Relapsing 11 Years after Resection

Masaya Iwamuro¹, Hiroyuki Okada², Katsuyoshi Takata³, Seiji Kawano², Yoshiro Kawahara², Junichiro Nasu¹, Katsuji Shinagawa⁴, Tadashi Yoshino³ and Kazuhide Yamamoto¹

Abstract

A 52-year-old Japanese woman was diagnosed with primary follicular lymphoma of the duodenum that was curatively resected by pancreatoduodenectomy. She remained in complete remission until 11 years after the surgery, when multiple enlarged intra-abdominal lymph nodes were demonstrated by computed tomography scans and positron emission tomography scans. Two years later, jejunal lesions were detected by endoscopy, and biopsy samples confirmed a recurrence of follicular lymphoma. This case indicates that primary gastrointestinal follicular lymphoma has a potential of relapse after an extended period of time, and thus patients must be followed up for over 10 years after complete remission.

Key words: follicular lymphoma, gastrointestinal endoscope, duodenal neoplasms, gastrointestinal lymphoma

(DOI: 10.2169/internalmedicine.51.7060)

Introduction

Primary gastrointestinal follicular lymphoma is a variant of systemic follicular lymphoma that was established within the last decade (1). Most cases of primary gastrointestinal follicular lymphoma arise in the small intestine, including the duodenum (2, 3). The representative endoscopic feature is small whitish polypoid nodules up to 2 mm in diameter (4, 5). Generally these lesions remain small, rarely forming bulky tumors, and therefore most of the cases are asymptomatic or have only symptoms not related to the lymphoma lesions, and the lesions are often diagnosed during routine esophagogastroduodenoscopy (5). Recently this disease entity gained recognition among endoscopists. Consequently, its occurrence has been increasingly reported, but the long-term prognosis of primary gastrointestinal follicular lymphoma has not yet been elucidated. Herein, we report a case of primary follicular lymphoma of the duodenum, which relapsed 11 years after curative resection.

Case Report

In 1996, a 52-year-old Japanese woman was diagnosed with primary follicular lymphoma of the duodenum by routine esophagogastroduodenoscopic examination. She had a previous history of gynecological surgeries due to an ovarian tumor and a uterine myoma, but she had no history of gastrointestinal disease. Physical examination revealed no abnormalities, and there was no evidence of hepatosplenomegaly or peripheral lymphadenopathy. Laboratory examinations revealed slight anemia (red blood cell count, 377×10⁴/mm³; hemoglobin, 11.9 mg/dL). Other laboratory findings, including the levels of lactate dehydrogenase (LDH), were within normal limits. The endoscopic examination showed a whitish elevated lesion with a hoof-like appearance around the ampulla of Vater in the duodenal second portion (Fig. 1A-C). Endoscopic ultrasonography for

¹Department of Gastroenterology and Hepatology, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Japan, ²Department of Endoscopy, Okayama University Hospital, Japan, ³Department of Pathology, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Japan and ⁴Department of Hematology and Oncology, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Japan

Received for publication December 6, 2011; Accepted for publication January 22, 2012
Correspondence to Dr. Masaya Iwamuro, iwamuromasaya@yahoo.co.jp
the lesion revealed a thickened mucosal layer and an intact submucosal layer (Fig. 1D). In the biopsy specimen from the duodenal lesion, small to medium-sized lymphoid cells had infiltrated the duodenal mucosa. The lymphoid cells were positive for CD79a, CD10, and BCL2, but negative for cyclin D1 (Fig. 2). Other examinations, including colonoscopy, small bowel follow-through, bone marrow aspiration and biopsy, abdominal ultrasound imaging, gallium scintigraphy, and computed tomography (CT) scans of the neck, chest, abdomen, and pelvis showed no abnormalities. Consequently, the patient was diagnosed with primary follicular lymphoma of the duodenum. The clinical stage was considered to be stage I, based on the Lugano staging system for the classification of gastrointestinal tract lymphoma (6, 7).

Pancreatoduodenectomy with lymph node dissection was performed as a curative treatment. In the resected specimen, the lymphoma cells were localized in the mucosal layer of the duodenum, although partial infiltration to the inferior pancreatic head lymph node was suspected (Fig. 3). The neoplastic follicles were composed of uniform small-cleaved cells (2). The postoperative diagnosis was primary follicular lymphoma of the duodenum, Grade 1, pathological stage II-1. After the surgical resection, physical examination, complete blood count, and routine biochemical profile tests were performed every 3 months until 2004, and every 6 months from 2005 to 2008. Annual follow-up by esophagogastro-duodenoscopy was carried out until 2008. Abdominal CT scanning was performed yearly until 2004, but was not done from 2005 to 2008.

In 2008 (137 months after the resection), multiple enlarged lymph nodes were demonstrated in abdominal CT scans. Those lymph nodes were positive on positron emission tomography (PET) scans (Fig. 4), and therefore intraperitoneal recurrence of the follicular lymphoma was highly suspected. Esophagogastro-duodenoscopic examination, peroral double-balloon enteroscopy, and colonoscopy were also performed; however, gastrointestinal recurrence was not detected. Laboratory findings including the levels of LDH and soluble interleukin-2 receptor (sIL-2R), bone marrow aspiration and biopsy, and gallium scintigraphy showed no abnormalities at that time. Treatment for the relapsed follicular lymphoma was not initiated and “watch and wait” strategy was conducted, because the patient had no systemic symptoms related to the lymphoma. Subsequently, blood tests, CT scanning, and esophagogastro-duodenoscopy were performed every 3 months, 6 months, and 12 months, respectively. In 2010, esophagogastro-duodenoscopic examination and peroral double-balloon enteroscopy revealed multiple
Discussion

Only a few relapsed cases with primary gastrointestinal follicular lymphoma have been reported. Yamamoto et al. summarized 249 patients with gastrointestinal follicular lymphoma that had been reported in the literatures (5). They noted that 106 of the 249 cases achieved complete remission and only 16 cases had recurrences. The time to recurrence in 16 cases ranged from 1 to 98 months. Recently, case series of gastrointestinal follicular lymphomas have been reported by several institutions (8-10) as well as our latest report (3). Among these articles, relapses occurred reportedly up to 72 months after complete remissions (8). Consequently, the 11 years (137 months) described in the present case report is the longest recorded period until a relapse.

The majority of the patients with follicular lymphomas of nodal origin are in advanced stage III or IV. For these patients, no curative therapy has been established (11). Although only one-third of patients with nodal follicular lymphomas are in stage I or II at the time of the diagnosis (2), those patients have superior prognosis compared to patients with widespread disease. Campbell et al. evaluated the long-term outcomes of their 237 patients with limited-stage nodal
follicular lymphoma who received radiotherapy alone (12). They found only two patients who developed recurrent disease beyond 10 years, and they concluded that disease recurrence after 10 years is uncommon in patients who had limited-stage follicular lymphomas. In contrast to the nodal-origin follicular lymphomas, almost all patients with primary gastrointestinal follicular lymphoma are at limited stages by definition. Patients with widespread disease involving gastrointestinal lesions are likely to have been diagnosed with systemic follicular lymphoma, and thus they are excluded from the category of ‘primary’ gastrointestinal follicular lymphoma. We assume that the primary gastrointestinal follicular lymphomas have similar prognosis to limited-stage nodal follicular lymphomas, or have even better prognosis, especially in cases with duodenal involvement (3, 13). Therefore, recurrence beyond 10 years can probably be considered rare, but this frequency needs to be investigated hereafter. At present, it is important to collect data in terms of long-term (over 10 years) outcomes of this disease entity.

There is still no consensus regarding the choice of treatment modality for primary gastrointestinal follicular lymphoma. The initial treatment may be radiotherapy, surgical resection, systemic chemotherapy, monoclonal antibody monotherapy, a combination of these therapies, or a “watch and wait” policy (3, 5, 10). Several authors stated that the watch and wait strategy can be an acceptable initial approach for primary gastrointestinal follicular lymphomas, because aggressive therapies did not have a significantly different outcome from that of the watch and wait strategy, based on their results from case series (8-10, 14). Consequently, though there are not enough objective data to make treatment decisions yet, the watch and wait strategy seems...
to be appropriate for cases with primary gastrointestinal follicular lymphoma unless they have symptoms including B symptoms (fever, night sweating, and weight loss), hematopoietic impairment, bulky disease, vital organ compression, ascites, pleural effusion, or rapid lymphoma progression (11). In the present case, surgical resection was performed as the initial therapeutic modality for the duodenal follicular lymphoma. According to recent understanding of primary gastrointestinal follicular lymphoma as described above, resection does not appear to be justified, except in cases with symptoms related to bulky tumors such as ileus. However, patients who underwent resection have been reported in the literature (4, 5, 8, 14, 15). In these patients, postoperative surveillance should be carried out for more than 10 years.

In the present case, no treatment was initiated when recurrence of follicular lymphoma was diagnosed, because the patient lacked systemic symptoms. Although the lymph nodes were slightly enlarged and prominent intestinal lesions appeared during the two-year follow-up period, there were no systemic symptoms related to the lymphoma. Thus, we believe that the watch and wait strategy was an acceptable management for this patient.

In conclusion, we presented a case of primary follicular lymphoma of the duodenum relapsing 11 years after resection. A relapse more than 10 years after complete remission is probably rare, but it can occur. Patients with primary gastrointestinal follicular lymphomas should be followed up for over 10 years, and the patient data should be collected to establish an evidence-based standard of care.

The authors state that they have no Conflict of Interest (COI).

References