CLINICAL VIGNETTE

Follicular Lymphoma of the Duodenum

Sittiporn Bencharit, MD and Michael Jean, MD

Case Presentation

A 60-year-old Korean male presented with several days of dark stool. He was on daily low dose aspirin and had a history of duodenal ulcer 3 years ago. Family history was positive for gastric cancer in his father. His hemoglobin was 13.5 at presentation. Upper endoscopy showed a 6mm clean-based gastric ulcer. Biopsies revealed a benign ulcer with a negative stain for Helicobacter pylori.

The patient was treated with daily oral proton pump inhibitor. Six weeks later, a follow up hemoglobin was 10.9. Repeat endoscopy documented complete healing of the previous gastric ulcer. However, at the second portion of the duodenum there was a cluster of white granular mucosa, less than 1 cm in size. Biopsies revealed follicular lymphoma and he had a negative bone marrow aspiration. Staging PET/CT scan revealed activity in his lung. He was treated with rituximab and had been doing very well.

Discussion

Follicular lymphoma (FL) is generally an indolent B cell lymphoproliferative disorder of transformed follicular center B cells. FL is the second most commonly diagnosed lymphoma in the United States and Western Europe.[1] The median age at diagnosis is 60, and often presents with asymptomatic lymphadenopathy. Bone marrow involvement is present in 70% of patients. Fever, night sweats, and weight loss occur in less than 20%.[1]

Primary gastrointestinal follicular lymphoma (GIFL) is an uncommon variant of FL. Due to increased recognition by endoscopists, GIFL has been established as a variant of FL by the World Health Organization.[2] Patients with primary intestinal FL generally lack systemic symptoms, in contrast to FL with secondary gastrointestinal involvement. There are no established guidelines on the optimal diagnostic strategy for patients with primary gastrointestinal FL or secondary gastrointestinal involvement of systemic FL.[3]

Misdraji et al. first reported primary FL in the duodenum in 1997.[4] Yoshino et al. subsequently reported that the second portion of the duodenum was the most common involved site.[5] Yamamoto et al. reviewed 150 previously reported cases, 43.3% were asymptomatic, while 9.3% had vague abdominal complaints. Other symptoms include abdominal pain 28.7%, nausea and vomiting 8%, tarry or bloody stool 6%.

As GIFL is most commonly found in the second portion of duodenum, it is often diagnosed at the time of upper endoscopy. The endoscopic appearance has been described as a small whitish lesion, small polypoid nodules, multiple polypoid lesions, and multiple granules. Infrequently, it can present as erosions, ulcers or mass. Jejunal and ileal involvement usually have similar endoscopic appearance. Colonic, and rectal involvement has also been reported.[6] Video capsule and small bowel enteroscopy have been used for diagnosis. CT/PET scan may not be sensitive enough to detect these small mucosal lesions. PET scan has a low sensitivity of 46.3% and false negative of 53.7%.[7]

Diagnosis of FL is based on the histology of the germinal center. The neoplastic cells consist of a mixture of centrocytes (small to medium-sized cells) and centroblasts (large cells). The clinical aggressiveness of the tumor increases with increasing numbers of centroblasts. The WHO Classification assigns grading of 1 to 3, based on the number of centroblasts per high power field. Grade I: 0-5 centroblasts/HPF, Grade II: 6-15 centroblasts/HPF, Grade III: more than 15/HPF (2). In GIFL, 95% are Grade I and II. FL cells express monoclonal immunoglobulin light chain CD 19, CD 20, CD 10, and BCL-6, and BCL-2. Immunohistochemical staining helps confirm the diagnosis of FL.

Predictors of outcome are based on FL international prognostic index (FLIPI) and tumor grade. FLIPI includes 5 prognostic factors: age>60, serum LDH>ULN, Hgb<12, Ann Arbor stage III or IV, and number of nodal sites>4. Low risk groups have 0-1 risk factors. Intermediate risk groups have 2 risk factors. High-risk groups have 3 or more risk factors.

Even though GIFL often has indolent course, all patients must be evaluated according to the guidelines for systemic FL. In addition to upper endoscopy, patients should undergo colonoscopy, video capsule endoscopy and or push enteroscopy. Bone marrow examination, PET/CT should be included in the staging of the disease.

Therapeutic options for GIFL includes 1) observation, 2) radiation, 3) chemotherapy, 4) combination radiation and chemotherapy, 5) rituximab. Treatment choices are based on risk stratification of the disease using the FLIPI and tumor grade scores.

Schmartz et al. conducted a retrospective analysis of 63 patients with primary FL of the duodenum.[8] Two untreated patients progressed to develop nodal disease. Twenty-four patients were observed: 17 of the observed patients had stable disease, while 7 had complete, spontaneous regression. Radiation therapy resulted in complete regression in 19 patients. Chemotherapy lead to complete regression in 8. Rituximab achieved complete resolution in 4 and stable disease in one.

Summary

Our patient was treated with rituximab based on his hemoglobin of 10.9 and PET/CT activity in his lung field. His repeat EGD showed complete resolution of the duodenal FL, after 4 infusions of rituximab. One author, had 2 other patients with duodenal FL. One was a 56-year-old male who was treated with rituximab, and had complete resolution for the past 5 years. Another patient is an 82-year-old female whom we elected observation only. She had spontaneous regression of her duodenal FL and had been disease free for 6 years.

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