Primary Gastrointestinal Tract Lymphoma

David Reinhard Sumantri Samosir, Marcellus Simadibrata***

* Department of Internal Medicine, Eka Hospital, Tangerang
** Divison of Gastroenterology, Department of Internal Medicine, Faculty of Medicine
University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital, Jakarta

ABSTRACT

Extranodular lymphoma can be found in almost all organ. One third of the cases found in gastrointestinal (GI) tract, which is the most common form of extranodular lymphoma. All the subtypes of lymphoma may occur as primary lesion along in gastrointestinal tract, but the most common form is B-cell diffuse large cell lymphoma. Diseases that linked with GI tract lymphoma are inflammatory bowel disease, celiac disease, Helicobacter pylori, virus infection, collagen disease and ionic radiation. This report described a 40 years old man with recurrent bloody stool and colon lymphoma was blamed as the source of bleeding with its management of lymphoma.

Keywords: lymphoma, gastrointestinal tract, extranodular

INTRODUCTION

Extranodular lymphoma can be found in almost all organ. Gastrointestinal (GI) tract involvement comprises one third of all lymphoma cases, which is the commonest form of extranodular lymphoma. If tonsillar and Waldeyer ring are included, then the head and neck are the second most common sites, which comprise one fifth of all the cases.[1] Etiologies of extranodular lymphoma seem to be multifactorial which includes immune system suppression, viral and bacterial infection, pesticide exposure and other environmental factors.[2] Geographic differences indicate that the incidence of Epstein-Barr virus infection and human T-cell lymphotropic virus1-associated T-cell lymphomas is higher in Asia than in Europe and North America.[2]

All subtypes of lymphoma can occur as primary lesion of GI tract, but the most common type is B-cell diffuse large cell lymphoma subtype.[3] Histological subtype is the main predictors for prognosis in nodal and extranodal lymphoma, but the location of primary lesion is the most determining factors for aggressive extranodal lymphoma.[2] Despite for its rare occurrence, this tumor poses a threat for surgeons, oncologist, and interventional radiologist in determining optimal therapy. This report describes a 40 years old man with recurrent bloody stool, with its management

Correspondence:
David Reinhard Sumantri Samosir
Department of Internal Medicine
Eka Hospital
Central Business District Lot IX, BSD City
Tangerang 15321 Indonesia
Phone: 0818-08114909
E-mail: david_samosir@yahoo.com

CASE ILLUSTRATION

A male 44 years old, came with complaints of bloody stools since six months before hospital admission. Two months ago the patient often feels weak, loss of appetite, and looked pale. The patient weight loss of 9 kg in three months. The patient to a local hospital in Padang and underwent colonoscopy examination. Hyperemic sigmoid mucosa and descending colon were found, slight bleeding were also seen in this area. Biopsy results were diagnosed as atypical chronic colitis and not visible signs of malignant. Mesalazine 500 mg three times daily, budesonide three times daily, mebeverin HCl twice daily were prescribed for the treatment. The stools remained bloody and several transfusions have been made for the patient. Abdominal pain in right lower quadrant was also complained. There is no evident of malignancy in patient's family history. Patient sought medical attention in Cipto Mangunkusumo hospital.

Physical examination found moderate illness, conscious, blood pressure was 120/80 mmHg, heart rate was 80 times/minute, respiration rate was 18 times/minute, body temperature was 36.5^{0}C, conjunctiva was pale, while no jaundice found in sclera. No abnormality of heart and lungs in the examination, pain on palpation was found in right lower quadrant.

Laboratory result showed hemoglobin 10.9 g/dL, leukocyte 8,440/uL, platelet 336,000/uL, mean corpuscular volume 74.6 fl, mean corpuscular hemoglobin 23.1 pg, mean corpuscular hemoglobin concentration 31 g/dL, AST 21 U/L, ALT 35 u/L, random blood glucose 160 mg/dL, alkali phosphatase 133 u/L, uric acid 6.4 mg/dL, lactate dehydrogenase 244 u/L, iron serum 25 ug/dL, total iron binding capacity 195 ug/dL, ferritine 76.96 ng/mL, albumin 3 g/dL, prothrombin time (PT) 12.3 seconds (control PT: 12.6 second), activated partial thromboplastin time (APTT) 38.1 second (control APTT 36.8 second), anti tuberculosis negative, CEA 1.4 ng/mL, CA 19-9 7.8 U/mL. 3 times fecal BTA negative, anti *Helicobacter pylori* Ig G negative.

Electrocardiography (ECG) reading was within normal limit, thoracal radiology was suspected lymph nodes enlargement in left thoracal plexus, abdominal CT-scan found caecal tumor, with ulcerative colitis as the differential diagnosis. Follow through examination profound colon carcinoma at ascendence colon-caecum which was also infiltrate terminal ileum. Conclusion from colonoscopy was caecal colon cancer and grade II internal hemorrhoid. Biopsy identified suspect of malignant non-Hodgkin lymphoma, classified as monocytoid/marginal zone B cell lymphoma subtype. Esophagogastroduodenoscopy was normal.

The patient was planned to have right hemi-colectomy for tumor resection and ileo anastomoses transversustomy. Microscopic pathology showed malignant lymphoma, perhaps subtype of anaplastic large cell lymphoma (ALCL). Immuno-histochemical test result found positive reaction of CD 20 and negative reaction of CD 3, CD 10, and CD 38, these findings was concluded to be associated with malignant large B cell lymphoma. No abnormality was found in bone marrow preparation. From bone marrow aspiration, histological associated with hypocellularity but no malignancy was observed. Post-surgery abdominal CT-scan did not find lymph nodes enlargement and no intraabdominal mass was found. Thoracal CT-scan exhibits segmental pneumonia in inferior lobe of both lungs with fibrotic component and minimal parapneumonic effusion (tuberculosis suspect) and there was neither metastatic sign nor lymph nodes enlargement. CHOP chemotherapy was planned for the patient for 6-8 cycles.

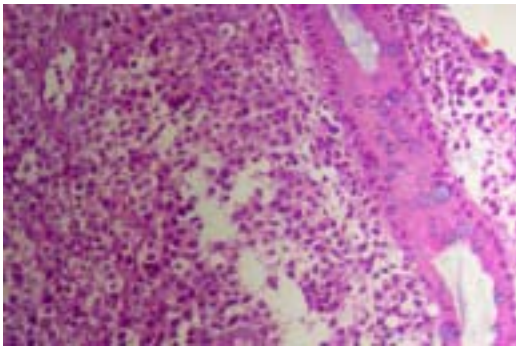

Figure 1. Based on microscopic examination of the biopsy, suspected of malignant non-Hodgkin lymphoma, subtype monocytoid/marginal zone B cell lymphoma

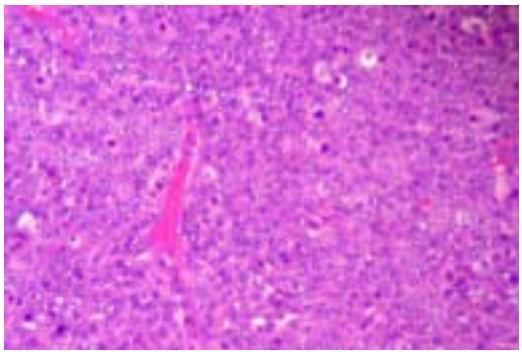

Figure 2. Malignant lymphoma was observed of post operative histopathology results

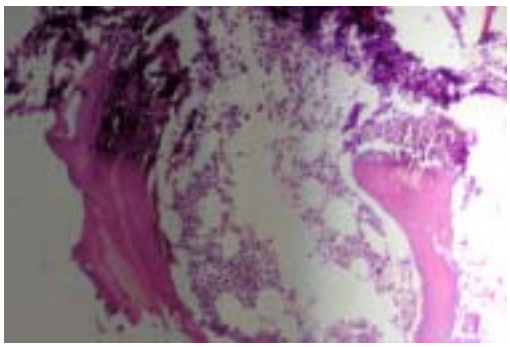

Figure 3. Result of bone marrow biopsy showed hypocellularity of the bone marrow was apparent. There was not appear of malignant tumor cell

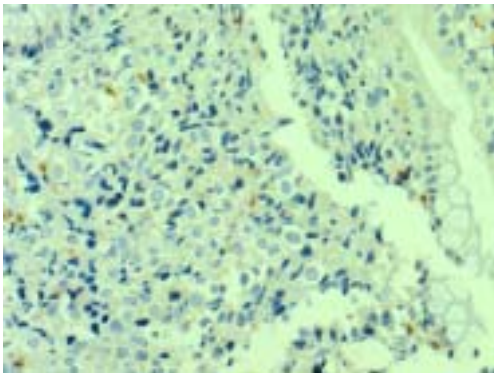

Figure 4. Immunohistochemical showed CD 20 positive, malignancy in diffuse large B-cell cell lymphoma

DISCUSSION

GI tract is the most common extranodal site from non-Hodgkin lymphoma. Hospital based and population based publication suggested that non-Hodgkin lymphoma approximately occur in 4-20% (with average of 12-13%) of all non-Hodgkin lymphoma cases and comprised 30-40% of all extranodal cases.[1] In Europe, the most common location is gaster (approximately 50-60%), small bowel (+ 30%), and large bowel (+ 10%).[1,4] In Middle Asia most of primary GI tract lymphoma occurs in small bowel and gaster.[4] In Indonesia the prevalence of GI tract lymphoma is still unknown. In this case, there was only one extranodal location have been found and was not found in other location. The diagnosis of primary GI tract lymphoma was established by the presence of lymphoproliferative neoplasm from histological examination without any palpable adenopathy and hepatosplenomegaly and no prove of lymphoma in thoracal X-ray nor in CT-scan, peripheral blood smear, or bone marrow aspiration and biopsy.[5]

In this case, it was not clear whether this lymphoma was the progression of colitis or not. Cohort study based on population and patient suggested that the risk of lymphoma in inflammatory bowel disease is low with absolute risk as low as 0.03% per person-year. Data taken from the hospital has suggested that severe inflammatory bowel disease (IBD) patients have higher possibility to suffer lymphoma, although population based study did not find any increase of risk of lymphoma in IBD patients.[6] Patients with celiac disease increase the risk of intestinal lymphoma up to 200 fold, this condition described as enteropathy-associated T-cell lymphoma.[1,7] Other causes that has been linked with GI tract lymphoma are virus, collagen disease, and ionic radiation.[3] Just like stomach mucosa-associated lympholid tissue (MALT) disease, there is obvious relation between bowel MALT and *Helicobacter pylori* infection.[7] MALT can occur in almost every organ as response of persistent stimulation like chronic infections or autoimmune process. In uncontrolled proliferation of lymphoid, malignant clones could be generated and continue to progress to form MALT lymphoma.[8] Other diseases that associated with non-Hodgkin lymphoma are Sjogren syndrome, rheumatoid arthritis; Epstein-Barr virus infection is linked with Burkitt lymphoma; primary effusion lymphoma is related with a human herpes virus infection,[8] and *Chlamydia psittaci* infection is linked with ocular adnexal lymphomas.[9] Prevalence of non-Hodgkin lymphoma increased in immunocompromised patient. Non-Hodgkin lymphoma which related with AIDS have specific characteristic: usually spread to other location, commonly extranodal, and all extranodal location could be involved (central nervous system, bone marrow, gastrointestinal, and atypical location like anus and rectum, oral cavity, and heart) and the prognosis is very poor.[10]

Primary lymphoma in this case was occured in caecum area. It was already mentioned that common sites of large bowel lymphoma are caecum and rectum.[1,5,11] CT-scan could not distinguished between lymphoma and adenocarcinoma of colon.[11]

The type of lymphoma in this patient was malignant B cell diffuse large cell lymphoma, it was proven by histology and immunohistochemical examination. Almost primary intestinal lymphoma was B cell origin and most of B cells are high degree tumors.[7] Fifty until seventy percents of GI tract lymphomas are aggressive types and prognostically not preferable, which are diffuse large cell and immunoblastic lymphoma.[5]

Based on tumor node metastasis (TNM) classification, this patient was on stage I_E-B, in which there was only local involvement in one extralymphatic organ and there was prodromal symptoms like weight loss. It is important to seek the spread of all primary GI tract non-Hodgkin lymphoma in purpose of choosing the therapy, whether it would be surgery or chemotherapy.[5]

After tumor resection, this patient was given CHOP regimens, which consist of cyclophosphamid 750 mg/m^2, doxorubicin 50 mg/m^2, vincristine 1.4 mg/m^2 and prednison 100 mg/m^2, this regimen was planned for 6-8 cycles with 3 weeks interval. Curative tumor resection increase the 5-years survival rate up to more than 75%.[12] Gastrointestinal lymphoma is more radiosensitive and more responsive to chemotherapy compared with adenocarcinoma.[12] The risk of radiation complication like perforation and bleeding and also chemotherapy adverse reaction like bone marrow suppression would be decreased if they were done after surgical resection.[12] In GI tract lymphoma, adjuvant chemotherapy after surgical resection would also reduce the recurrency and increase survival rate.[12,13,14] Although few randomized study that compares surgical resection as single therapy and adjuvant chemotherapy, recently the combination of modalities are the choice of therapy for primary intestinal lymphoma.[1]

The prognosis of this patient was good since patient classified as grade $I_{E,}$ which has long term survival rate of approximate 60-80%.[5] The only important prognostic factor of intestinal lymphoma in western countries are clinical grading, in which 5-years survival rate is around 40-50 % for grade I-II and less than 10% in more severe grade.[4]

REFERENCES

1. Zucca E, Roggero E, Bertoni F, Cavalli F. Primary extranodal non-Hodgkins's lymphomas. Part 1 Gastrointestinal, cutaneous and genitourinary lymphomas. Ann Oncol 1997;8;727-37.
2. Zucca E. Extranodal lymphoma: a reappraisal. Ann Oncol. 2008;19(Suppl 4):iv77-80.
3. Velasco MR, Concepcion L, Jones DV. Primary gastric and intestinal lymphomas. In: Kelsen DP, Daly JM, Kern SE, Levin B, Tepper JE, eds. Gastroentestinal Oncology. Principles and Practice. 1st ed. Philadelphia: Lippincott Williams & Wilkins 2002.p.899-919.
4. Zinzani PL, Magagnoli M, Pagliani G, Bendandi M, Gherlinzoni F, Merla E, et al. Primary intestinal lymphoma: clinical and therapeutic features of 32 patients. Hematologica 1997;82:305-8.
5. Haber DA, Mayer RJ. Primary gastrointestinal lymphoma. Semin Oncol 1988;15:154-69.
6. Aithal GP, Mansfield JC. The risk of lymphoma associated with inflammatory bowel disease and immunosuppressive treatment. Aliment Pharmacol Ther 2001;15:1101-8.
7. Ibrahim EM, Ezzat AA, El-weshi An, Martin JM, Khafaga YM, Al Rabih W, et al. Primary intestinal diffuse large B-cell non-Hodgkin's lymphoma: clinical features, management, and prognosis of 66 patients. Ann Oncol 2001;12:53-8.
8. Cohen SM, Petryk M, Varma M, Kozuch PS, Ames ED, Grossbard ML. Non-Hodgkin's lymphoma of mucosa-associated lymphoid tissue. Oncologist 2006;11:1100-17.
9. Ansell SM, Armitage J. Non-Hodgkin lymphoma: diagnosis and treatment. Mayo Clin Proc 2005;80:1087-97.
10. Muller AM, Ihorst G, Mertelsmann R, Engelhardt M. Epidemiology of non-Hodgkin's lymphoma (NHL): trends, geographic distribution and etiology. Ann Hematol 2005;84:1-12.
11. Lupescu IG, Grasu M, Goldis G, Pola G, Gheorghe C, Vasilescu C, et al. Computer tomographic evaluation of digestive tract non-Hodgkin lymphomas. J Gastrointest Liver Dis 2007;16:315-9.
12. Talamonti MS, Dawes LG, Joehl RJ, Nahrwold DL. Gastrointestinal lymphoma. A case for primary surgical resection. Arch Surg 1990;125:972-7.
13. Atalay C, Kanlioz M, Demir S, Pak I, Altinok M. Primary gastrointestinal tract lymphomas. Acta Chir Belg 2003;103:616-20.
14. Amer MH, El-Akkad S. Gastrointestinal lymphoma in adults: clinical features and management of 300 cases. Gastroenterol 1994;106:846-58.