

ORIGINAL ARTICLE

원인 불명 화농성 간농양 환자의 대장 신생물 유병률: 전향적 등록 횡단 연구

허내윤*, 홍영미^{1,2,*}, 김태오, 문영수, 양성연, 박승하, 박종하, 최준혁, 김성민, 윤기태^{1,2}, 조 몽^{1,2}, 오민경^{3,4}
인제대학교 의과대학 인제대학교 해운대백병원 내과학교실, 부산대학교 의과대학 내과학교실¹, 양산부산대학교병원 간센터², 인제대학교 의과대학 약리학교실³, 인제대학교 부산백병원 임상시험센터⁴

The Prevalence of Colonic Neoplasm in Cryptogenic Pyogenic Liver Abscess: A Prospectively Enrolled Cross-sectional Study

Nae-Yun Heo*, Young Mi Hong^{1,2,*}, Tae Oh Kim, Young Soo Moon, Sung Yeun Yang, Seung Ha Park, Jongha Park, Joon Hyuk Choi, Sung-Min Kim, Ki Tae Yoon^{1,2}, Mong Cho^{1,2}, and Minkyung Oh^{3,4}

Department of Internal Medicine, Inje University Haeundae Paik Hospital, Inje University College of Medicine, Busan, Department of Internal Medicine, Pusan National University College of Medicine, Busan¹, Liver Center, Pusan National University Yangsan Hospital, Yangsan², Department of Pharmacology, Inje University College of Medicine, Busan³, Clinical Trial Center, Inje University Busan Paik Hospital, Busan⁴, Korea

Background/Aims: Several studies suggest that pyogenic liver abscess (PLA) is associated with colon neoplasm. A colonoscopic exam for cryptogenic PLA might detect a hidden colon neoplasm, through which intestinal flora can be transmitted into the liver. However, there are no prospectively enrolled cross-sectional data for colonic neoplasm in cryptogenic PLA.

Methods: Patients with PLA were prospectively enrolled from two university hospitals. Among them, all the patients with cryptogenic PLA were recommended for colonoscopic exam to check for colonic neoplasm.

Results: One hundred eighty-three patients with PLA were enrolled in the study for 22 months. One hundred and one (55.2%) patients did not have a definite cause of liver abscess at initial evaluation. The median diameter of the largest lesion was 5.7 cm (1.0-14.0 cm), and 74.3% of the patients were treated by percutaneous abscess drainage. Ninety-one percent of the patients who had an identified pathogen yielded *Klebsiella*. Sixty-two patients underwent colonoscopic exams, and no one had a colonic cancer, one had an adenomatous polyp with high grade dysplasia (1.6%), and 27 had adenomatous polyps with low grade dysplasia (43.5%; 41.0% in male and 43.5% in female). Of fifty patients who underwent an esophagogastroduodenoscopic exam, nine had gastric ulcers, one had an esophageal ulcer, and one had hemorrhagic gastritis.

Conclusions: The prevalence of colonic neoplasm among the patients with cryptogenic PLA was not as high as that in previous studies. Further well-designed, large-scale studies are required to assess the association of the colon neoplasm and cryptogenic PLA. (Korean J Gastroenterol 2016;68:195-201)

Key Words: Liver abscess, pyogenic; Colonic neoplasms; Prevalence

INTRODUCTION

Pyogenic liver abscess (PLA) is a major intrahepatic in-

fection, and sometimes produces a fatal sepsis or septic shock. The most common route of pathogen entry is ascending cholangitis. However, a considerable proportion of PLA pa-

Received July 19, 2016. Revised September 11, 2016. Accepted September 25, 2016.

© This is an open access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Copyright © 2016. Korean Society of Gastroenterology.

교신저자: 김태오, 48108, 부산시 해운대구 해운대로 875, 인제대학교 해운대백병원 내과

Correspondence to: Tae Oh Kim, Department of Internal Medicine, Inje University Haeundae Paik Hospital, 875 Haeun-daero, Haeundae-gu, Busan 48108, Korea.

Tel: +82-51-797-1533, Fax: +82-51-797-0941, E-mail: kto0440@paik.ac.kr

*These two authors have equally contributed to this work.

Financial support: None. Conflict of interest: None.

tients do not have a definite infection route into the liver, that is, cryptogenic. Although the frequency of PLA due to appendicitis has been reduced since the development of effective antibiotics and surgery, infection via a portal tract or direct transmission through the peritoneal cavity from a mucosal defect of the colon might be an entry route. A colonic neoplasm could allow infection spread due to disruption of the mucosal barrier. PLA may be associated with colonic neoplasm.¹⁻³ However, earlier research efforts were retrospectively-enrolled cross-sectional studies from Korea, or an association study using the insurance database from Taiwan. There is no study using a prospectively enrolled cross-sectional study design. Therefore, we intended to measure the prevalence of colonic neoplasm through a prospectively enrolled multi-center study in Korea.

SUBJECTS AND METHODS

1. Study subjects

Patients who were diagnosed with PLA from two university hospitals in southeast area of Korea (Inje University Haeundae Paik Hospital and Pusan University Yangsan Hospital) between January 1, 2014 and October 31, 2015 were prospectively recruited for the study. PLA was diagnosed when radiologic findings suggested PLA and abscess or blood culture yielded the pathogenic bacteria, or the abscess improved on antibiotics although culture results were negative. When the antibody to *Entamoeba histolytica* was positive, that patient was excluded from the PLA study. Cryptogenic PLA was diagnosed when the initial radiologic findings did not show a specific cause for PLA such as pyogenic cholangitis or cholecystitis due to gallstone or biliary cancer, necrotic change of liver cancer, and complicated abscess formation after loco-regional hepatocellular carcinoma including trans-arterial chemo-embolization and radio-frequency ablation. This study was approved by the Institutional Review Board of both hospitals and informed consents were acquired from the all the enrolled patients. This study was registered in the ClinicalTrials.gov (NCT0232914) at the initiation of the study.

2. Study protocol

When the patients with cryptogenic PLA were enrolled, the clinician recommended colonoscopic and/or esophago-gas-

tro-duodenoscopic evaluation within six weeks from the admission. The endoscopic work-up was not performed when the patient refused or when his or her general condition was poor for the exam. Endoscopic work-up was exempted if the patient had undergone a colonoscopic exam within one year and there were less than three colon adenomas. If the prior colonoscopy results included more than two colonic adenomas, a colonic adenoma larger than 1 cm, or pathologic findings of tubulovillous or villous adenoma or high grade dysplasia (HGD), the patients were advised to have the endoscopic exam.

3. Statistical analysis

We analyzed the categorical and continuous variables of the patients with cryptogenic PLA at baseline. For continuous variables, the median value and range were calculated. We checked the number of colonic neoplasms such as colon cancer and colonic adenoma. We checked the number of the upper gastrointestinal cancer or other mucosal defect lesions including ulcer or erosion. We compared the frequency of identified bacteria between the cryptogenic liver abscess and the abscess with known cause by chi-square test. Null hypotheses of no difference were rejected if p-values were less than 0.05. Baseline demographic and clinical characteristics were analyzed by SAS Enterprise Guide 5.1 (SAS Institute, Cary, NC, USA).

RESULTS

1. Causes of pyogenic liver abscess

During the enrollment period, 183 patients were diagnosed with PLA. Of those, 101 patients (55.2%) were classi-

Table 1. Pyogenic Liver Abscess Etiologies

Causes	Liver abscess (n=183)
Cryptogenic	101 (55.2)
Biliary ^a	71 (38.8)
Gastrointestinal ^b	2 (1.1)
Others ^c	9 (4.9)

Values are presented as n (%).

^aCholangitis due to bile duct stone or previous biliary operation.

^bOne patient had a microperforation of the stomach, the other had a stomach cancer.

^cSix patients had a post-TACE hepatic infarction, and the other three had a complicated hepatic cyst, a liver metastasis of gastric cancer, and hepatocellular carcinoma.

fied as cryptogenic, and 71 (38.8%) had a biliary causes such as cholangitis, and previous biliary operation. Only two patients were classified with gastrointestinal etiology, because one had a micro-perforation of stomach, and the other had a known stomach cancer (Table 1).

2. Baseline characteristics of patients with cryptogenic pyogenic liver abscess

One hundred and one patients with cryptogenic PLA included 47 from Inje University Haeundae Paik Hospital and 54 from Pusan National University Yangsan Hospital. The median age was 62 years (20-94 years), and men were 63.4% of the patients. The initial presenting symptoms were fever (78.2%), abdominal or right flank pain (43.6%), chilling (38.6%), weakness (19.8%), myalgia (18.8%), anorexia (18.8%), nausea (14.9%), vomiting (14.9%), cough (8.9%), headache (7.9%), dizziness (7.9%), dyspnea (6.9%), dyspepsia (6.9%), diarrhea (5.0%), weight loss (5.0%), altered mental status (3.0%), sputum (2.0%), chest pain (2.0%), and sore throat (1.0%), jaundice (1.0%), dysuria (1.0%), hematuria (1.0%), and melena (1.0%). White blood cell count was 13,190/mm³ (1,950-36,480/mm³). The median AST was 63 IU/L (15-4,336 IU/L) and ALT level 66 IU/L (11-1,685 IU/L). The median albumin level was slightly decreased to 3.2 g/dL (2.0-4.6 g/dL). The median C-reactive protein level was 17.8 mg/dL (0.5-40.9 mg/dL). Hepatitis B surface antigen was positive in 6.1%, and diabetes mellitus (DM) was found in 37.6%. One patient was taking methotrexate and leflunomide for rheumatoid arthritis. Three patients had a history of cancer (one with stomach and prostate cancer, one with colon cancer, and one with thyroid cancer). One patient currently had pancreas cancer. No study subject was undergoing chemotherapy at admission. The number of abscess pockets was 1 in 74.3%, 2 in 17.8%, 3 in 4.0% and ≥ 4 in 4.0%. The median value of maximal diameter of the largest lesion was 5.7 cm (1.0-14.0 cm). Percutaneous drainage was performed in 74.3%, and none received surgical drainage (Table 2).

3. Colonoscopic evaluation for the patients with cryptogenic pyogenic liver abscess

Among 101 patients with cryptogenic PLA, 62 patients had a colonoscopic evaluation. The colonoscopic examination were not performed because of refusal (11), poor general

condition (11), recent colonoscopy (8), unknown (8), and economic problem (1). Among 62 patients who had a colonoscopic evaluation, 27 (43.5%) patients showed normal findings, 12 (19.4%) did diverticulosis, 27 (43.5%) did adenomatous polyp with low grade dysplasia (LGD), 1 (1.6%) did adenomatous polyp with HGD. There were no cases of colon cancer (Fig. 1). Among the patients with adenomatous polyps, the median number of polyps was 2 (range, 1-5), and the size of the largest was median 4 mm (range, 2-15 mm).

Table 2. Baseline Characteristics of Patients with Cryptogenic Pyogenic Liver Abscess

Characteristic	Cryptogenic liver abscess (n=101)
Age (yr)	62 (20-94)
Male	64 (63.4)
White blood cell (/mm ³)	13,190 (1,950-36,480)
Hemoglobin (g/dL)	12.3 (8.4-16.6)
Platelet (/mm ³)	170,000 (9,000-759,000)
AST (IU/L)	63 (15-4,336)
ALT (IU/L)	66 (11-1,685)
ALP (IU/L)	
Hospital 1 ^a	331 (120-2,201)
Hospital 2, phase I ^b	457 (181-2,093)
Hospital 2, phase II ^b	172 (37-1,293)
GGT (IU/L)	100 (17-831)
Total bilirubin (mg/dL)	1.0 (0.2-6.6)
Albumin (g/dL)	3.2 (2.0-4.6)
Creatinine (mg/dL)	0.89 (0.40-5.65)
Glucose (mg/dL)	132 (74-503)
PT INR	1.19 (0.95-3.22)
CRP (mg/dL)	17.8 (0.5-40.9)
HBsAg ^c (%)	6 (6.1)
Anti-HCV ^c (%)	0
Anti-HIV ^c (%)	0
Diabetes mellitus	38 (37.6)
Immune suppressant use	1 (1.0)
Colonoscopic procedure within 1 month	1 (1.0)
Number of abscess pockets	
1	75 (74.3)
2	18 (17.8)
3	4 (4.0)
≥ 4	4 (4.0)
Maximal diameter of largest lesion (cm)	5.7 (1.0-14.0)
Percutaneous drainage use	75 (74.3)

Values are presented as median (range) or n (%).

^aHospital 1 is Inje University Haeundae Paik Hospital, in which the reference range of ALP is 104-338 IU/L.

^bHospital 2 is Pusan National University Yangsan Hospital, in which the reference range of ALP was changed into phase I (95-280 IU/L) and II (30-120 IU/L) before and after March 1, 2015, respectively.

^cMissing data is 3, 3, and 8 in HBsAg, anti-HCV, and anti-HIV, respectively.

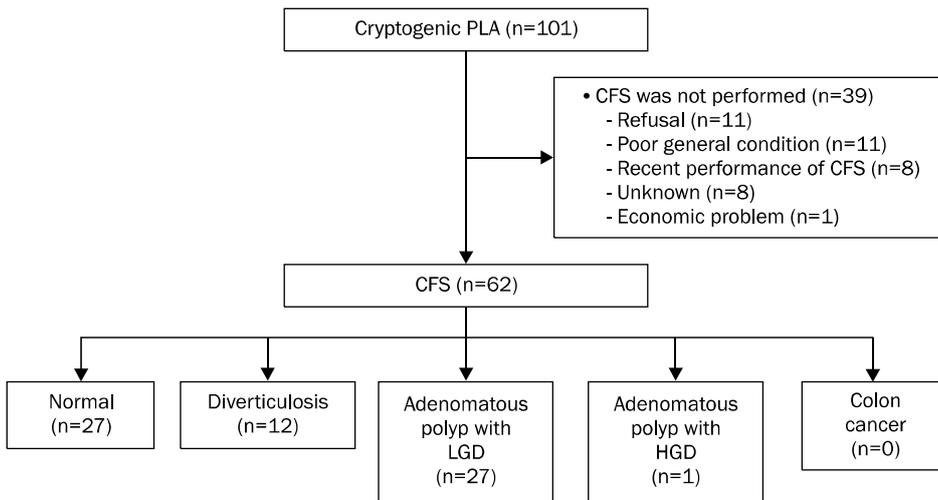


Fig. 1. Colonoscopic findings for the patients with cryptogenic pyogenic liver abscess. PLA, pyogenic liver abscess; CFS, colonoscopy; LGD, low grade dysplasia; HGD, high grade dysplasia.

Table 3. Esophago-gastro-duodenoscopic Findings for Cryptogenic Pyogenic Liver Abscess Patients

Endoscopic finding	Patient (n=50)
Normal	10 (20.0)
Gastric ulcer	9 (18.0)
Atrophic gastritis±intestinal metaplasia	20 (40.0)
Erosive gastritis	4 (8.0)
Erythematous gastritis	6 (12.0)
Gastric polyp or adenoma	3 (6.0)
Hemorrhagic gastritis	1 (2.0)
Ampullary adenoma	1 (2.0)
Esophageal ulcer	1 (2.0)
Reflux esophagitis, LA-A	1 (2.0)

Values are presented as n (%). Three cases had atrophic gastritis with erosive gastritis, and one had atrophic gastritis with non-specific esophageal ulcer.

The frequency by size was 22.6% at < 5 mm, 14.5% at 5-9 mm, and 6.5% at ≥ 10 mm. All histologic findings were tubular adenoma. In the case of adenomatous polyp with HGD, there was one adenomatous polyp, the size was 15 mm, and it was pedunculated type.

After excluding the cases with DM and immunosuppressant use, 63 immunocompetent patients were identified. Among them, 42 had a colonoscopic evaluation, 18 patients (42.9%) had an adenomatous polyp with LGD, and no one had an adenomatous polyp with HGD or colon cancer.

4. Esophago-gastro-duodenoscopic evaluation for patients with cryptogenic pyogenic liver abscess

Among 101 patients with cryptogenic PLA, 50 patients had an esophago-gastro-duodenoscopic evaluation. This exam was optional according to the opinion of the clinician. Among

Table 4. Causative Bacteria of Cryptogenic Pyogenic Liver Abscess (PLA)

Bacteria	Cryptogenic PLA (n=101)	PLA with known cause (n=82)
No growth	31 (30.7)	33 (40.2)
<i>Klebsiella</i> ^a	63 (62.4)	22 (26.8)
<i>Streptococcus</i>	3 ^b (2.9)	6 ^c (7.3)
<i>Escherichia coli</i>	1 (1.0)	14 (17.1)
<i>Enterobacter</i>	1 (1.0)	4 (4.9)
<i>Pseudomonas</i>	1 (1.0)	
<i>Gemella morbillorum</i>	1 (1.0)	
<i>Enterococcus</i>		16 (19.5)
<i>Proteus</i>		2 (2.4)
<i>Citrobacter</i>		2 (2.4)
<i>Serratia</i>		1 (1.2)
<i>Providentia</i>		1 (1.2)
<i>Shewanella</i>		1 (1.2)

Among the patients with PLA with known cause, 8 had 2 pathogens, 5 had 3 pathogens, 1 had 4 pathogens.

^aOne patient presented *Klebsiella oxytoca*, and those remaining had *K. pneumoniae*.

^bThis group included *Streptococcus gordonii*, *S. sanguis*, and *S. constellatus* ssp. *pharyngis*.

^cThis group included *S. anginosus*, *S. sanguinis*, *S. intermedius*, and viridans streptococci.

them, 10 patients were normal, nine had gastric ulcer (three active, two healing, four scars), 20 had atrophic gastritis with or without intestinal metaplasia, four had erosive gastritis, six had erythematous gastritis, three had gastric polyp or adenoma. Other presentations were hemorrhagic gastritis with gastric antral vascular ectasia, a non-specific esophageal ulcer in healing stage, reflux esophagitis (LA classification A), and ampullary adenoma (Table 3).

5. Pathogens for the pyogenic liver abscess

Among the 101 patients with cryptogenic PLA, 30.7% of the patients presented no growth in culture and *Klebsiella* was found in 62.4%. Among the patients with PLA with known cause, 40.2% of the patients presented no growth in culture, *Klebsiella* was found in 26.8%, *Enterococcus* was in 19.5%, and *Escherichia coli* 17.1%.

All patients with cryptogenic PLA had a single pathogen. However, 14 (17.1%) of the patients with PLA with known cause had multiple pathogens. When the causal bacterial culture results were classified as no growth, *Klebsiella*, and non-*Klebsiella* bacteria, *Klebsiella* was significantly more frequently identified in cryptogenic PLA compared to the PLA with known cause (62.4% vs. 26.8%; $p < 0.01$) (Table 4).

Among 70 patients of cryptogenic PLA in which causative bacteria were identified, 44 cases had their pathogen in abscess, 13 in blood, 10 in abscess and blood, and three in others (one in abscess, blood and urine, one in blood and urine, one in urine). Among 48 patients with PLA with known cause, in which causative bacteria were identified, 24 cases had their pathogen in abscess, eight in blood, 10 in abscess and blood, six in others (four in bile, one in ascites, and one in abscess, blood and urine).

DISCUSSION

In this prospectively enrolled cross-sectional study, there was no one who had a colon cancer among 62 patients with cryptogenic PLA who had colonoscopic evaluation. Initially, we selected sample size for this study considering the estimated prevalence of colon neoplasm might be 20%,^{1,2} and the estimated standard error $\pm 10\%$ in 95% confidence level. Therefore, our result suggests that the prevalence of colon neoplasm in the patients with cryptogenic PLA is less than 10%.

In the past, most cases of PLA were a consequence of appendicitis complicated by pylephlebitis in a young patient. This presentation is uncommon today as a result of earlier diagnosis and effective antibiotic therapy. Most cases now are cryptogenic or occur in older patients with underlying biliary tract disease.⁴ Although most causes of PLA are associated with the biliary disease such as cholangitis or previous biliary operation, another important infection route is via portal flow

or peritoneal spreading of the pathogen from gastrointestinal tract due to diverticulitis, appendicitis, penetrating peptic ulcer, inflammatory bowel disease, intestinal tuberculosis, or peritonitis.⁴⁻⁹ In addition, PLA has been reported as the initial manifestation of silent colon cancer and advanced colonic polyps. A retrospectively enrolled cross-sectional study in a hospital in Korea found that 81 among 230 patients with PLA were cryptogenic, of whom 37 underwent colonoscopy, with the result that eight were diagnosed with colon cancer ($n=6$) and laterally-spreading tumor with HGD ($n=2$).¹ Another retrospectively enrolled cross-sectional multi-center study in Korea examined 121 patients with cryptogenic PLA by colonoscopy, of whom 12 had adenocarcinoma and eight had adenoma with HGD.² These studies found that when the patients with cryptogenic PLA had colonoscopy, the prevalence of colon cancer was 10-16%, and that of advanced colonic neoplasm (cancer, HGD) was 17-22%. The National Cancer Information Center in Korea estimates the incidence of colon cancer in age ≥ 65 years at 241.4 per 100,000 persons in 2013, which means that 0.24% of the general population over 65 years were diagnosed as colon cancer during that year.¹⁰ Thus, both of the cross-sectional studies found a much higher prevalence of colon cancer among the patients with cryptogenic PLA compared with the general population. A population-based cohort study in Taiwan reported that the hazard of colorectal cancer during a five year period was 3.36 times greater for patients with cryptogenic PLA than for the control group, and this risk was higher in the patients with DM. They found 274 patients who were diagnosed as cryptogenic PLA between 2001 and 2003 using the longitudinal database from Taiwan National Health Insurance program. Among them, 15 patients (5.45%) had colorectal cancer during a five year observation period.³ Another cohort study in Taiwan that enrolled patients with PLA from 2000 to 2007 showed that the risk of colorectal cancer was higher in the patients with PLA than in controls even after adjusting for biliary diseases (hazard ratio, 5.50; 95% CI, 4.83-6.25).¹¹

Although these population-based cohort studies in Taiwan suggested an association between the PLA and colon cancer, this risk of colon cancer may not be as high as those of the cross-sectional studies in Korea considering our result. We think that there may be selection bias in the retrospectively enrolled cross-sectional study compared with our pro-

spectively enrolled study. For example, in a retrospective cross-sectional study in Korea, the frequency of DM was 67% in colon-origin abscess group, which is higher than that of general population.¹ DM raises the risk not only of liver abscess but also colon cancer. Thus, it might be confounding the association between PLA and colon cancer in the retrospective study. In order to adjust for confounding factors and confirm the association between PLA and colon cancer in Koreans, we need to perform a larger population study.

An epidemiologic study of asymptomatic Korean men and women found the prevalence of adenomatous polyp in 60 years old was 43% in male and 30% in female.¹² Compared with this study results, the frequency of adenomatous polyp with LGD was similar in males (41%), but higher in females (48%) among the patients with cryptogenic PLA in our study.

In our study, 49.5% of the patients with cryptogenic PLA had an esophago-gastro-duodenoscopy. Among them, 20.0% had gastric or esophageal ulcers. *Klebsiella pneumoniae* is normal flora in the colon, but sometimes it colonizes the oropharynx without infection. When an esophageal or gastric mucosal defect occurs, the colonized bacteria may gain access to the liver. There are several case reports that liver abscess occurred with gastric cancer, penetrating gastric ulcer or phlegmonous gastritis, stromal tumor of the stomach.¹³⁻¹⁵ On the other hand, these gastric ulcers might be result from physiologic stress such as septic condition and pain related to percutaneous drainage. We cannot confirm the association between PLA and the esophageal or gastric ulcer, but it is necessary to find the association through further study.

In our study, we could not detect the benign ulcerative lesion from inflammatory bowel disease such as ulcerative colitis and Crohn's disease among patients with cryptogenic PLA. It could be that the frequency of these diseases was less frequent than that of colon cancer in the patients of this age; thus it may require a large sample size to find inflammatory bowel disease among the study population. A recent nationwide cohort study in Taiwan showed an association between PLA and inflammatory bowel disease, especially ulcerative colitis.¹⁶

This study has a few limitations. First, although this study intended to enroll all patients with cryptogenic PLA and tried to perform the colonoscopic evaluation, there were a large proportion (38.6%) of subjects who did not receive it. Some of them may have a hidden colon cancer. More half of them

were due to the refusal to exam and poor general condition. None of them had an overt colon cancer on initial abdominal-pelvic computed tomography. Eight patients had an earlier colonoscopic evaluation within one year, with no colon cancer diagnosis, so they are unlikely to have a newly detected colon cancer at this admission. Second, some of the patients had a colonoscopic evaluation over six weeks after the diagnosis of cryptogenic PLA. Therefore, some ulcerative lesions with inflammation might be healed at the exam. Nevertheless, this fact should not influence the risk of colon neoplasm. Third, the sample size might be too small to detect the prevalence of colon neoplasm in cryptogenic PLA although it might be higher than the prevalence of the general population. Fourth, there is a possibility that we might not detect a minimal sized colon cancer at initial admission through radiologic or colonoscopic evaluation, which could be revealed by serial exams after the diagnosis of PLA. This problem should be solved by a study using big data from the nation-wide database with serial exams.

In summary, we could not find colon cancer in 62 sequential patients who had a cryptogenic PLA by colonoscopic evaluation. This result suggests that the prevalence of colon cancer is not as high as that of the previous studies. Apparently a large sample size is required to detect the putative association of cryptogenic PLA and colon neoplasm.

ACKNOWLEDGEMENTS

The authors thank Drs. So Jeong Heo and Ju Won Lee for their help in data collection.

REFERENCES

1. Jeong SW, Jang JY, Lee TH, et al. Cryptogenic pyogenic liver abscess as the herald of colon cancer. *J Gastroenterol Hepatol* 2012;27:248-255.
2. Koo HC, Kim YS, Kim SG, et al. Should colonoscopy be performed in patients with cryptogenic liver abscess? *Clin Res Hepatol Gastroenterol* 2013;37:86-92.
3. Lai HC, Lin HC. Cryptogenic pyogenic liver abscess as a sign of colorectal cancer: a population-based 5-year follow-up study. *Liver Int* 2010;30:1387-1393.
4. Kim AY, Chung RT. Bacterial, parasitic, and fungal infections of the liver, including liver abscess. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's gastrointestinal and liver disease*. 10th ed. Philadelphia, PA: Saunders, 2016:1374-1392.

5. Antia FP, Marker F. Hepatic abscess secondary to duodenal ulcer. *Lancet* 1955;268:649-650.
6. Heo NY, Park SH, Park J, et al. Pyogenic liver abscess with complicating intestinal tuberculosis. *J Med Cases* 2013;3:370-372.
7. Knowels R, Rinaldo JA. Pyogenic liver abscess probably secondary to sigmoid diverticulitis: report of two cases. *Gastroenterology* 1960;38:262-266.
8. Margalit M, Elinav H, Ilan Y, Shalit M. Liver abscess in inflammatory bowel disease: report of two cases and review of the literature. *J Gastroenterol Hepatol* 2004;19:1338-1342.
9. Song J, Swekla M, Colorado P, Reddy R, Hoffmann S, Fine S. Liver abscess and diarrhea as initial manifestations of ulcerative colitis: case report and review of the literature. *Dig Dis Sci* 2003;48:417-421.
10. Cancer incidence according to the age group. [Internet]. Goyang: National Cancer Information Center; [updated 2015 Dec 23; cited 2016 Jul 17]. Available from: http://www.cancer.go.kr/mbs/cancer/subview.jsp?id=cancer_040103000000.
11. Lai HC, Lin CC, Cheng KS, et al. Increased incidence of gastrointestinal cancers among patients with pyogenic liver abscess: a population-based cohort study. *Gastroenterology* 2014;146:129-137.e1.
12. Yang MH, Rampal S, Sung J, et al. The prevalence of colorectal adenomas in asymptomatic Korean men and women. *Cancer Epidemiol Biomarkers Prev* 2014;23:499-507.
13. Jung HG, Kim DH, Lee CH. A case of subcapsular liver abscess secondary to perforating ulcer of gastric cancer. *Korean J Gastroenterol* 2010;56:109-113.
14. Okuno M, Adachi S, Nakamura N, et al. A case of advanced gastric cancer with liver abscesses. *Nihon Shokakibyō Gakkai Zasshi* 2013;110:869-874.
15. Sakata T, Narita M, Ohtani N, et al. A case of phlegmonous gastritis with multiple liver and splenic abscesses. *Nihon Shokakibyō Gakkai Zasshi* 2011;108:50-58.
16. Lin JN, Lin CL, Lin MC, Lai CH, Lin HH, Kao CH. Pyogenic liver abscess in patients with inflammatory bowel disease: a nationwide cohort study. *Liver Int* 2016;36:136-144.