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Short Communication

An Unusual Autopsy Case of Pyogenic Liver Abscess Caused by Periodontal Bacteria

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SUMMARY: Pyogenic liver abscess (PLA) formation is thought to originate from the transmission of infection via three major routes including the biliary tract, portal vein and hepatic artery. However, about 50% of PLA cases are considered to be cryptogenic. Here we report an unusual autopsy case of PLA associated with periodontopathic bacterial infection. A 59-year-old female suddenly developed cardiopulmonary arrest and died. Despite macroscopic and microscopic examinations, the infectious routes and source of infection were unidentified, and the case appeared to be cryptogenic. Since this patient had suffered severe periodontitis for a long period of time, we investigated the involvement of periodontal infection in PLA formation by performing immunohistochemical analyses. We identified several periodontopathic bacterial species in the PLA of this patient, including *Fusobacterium nucleatum*, *Treponema denticola*, *Prevotella intermedia* and *Porphyromonas gingivalis*. Thus, we demonstrate here that periodontal infection is a potential source of infection in the formation of PLA.

Pyogenic liver abscess (PLA) formation is recognized as a life-threatening disease. In the pre-antibiotic era, the mortality rate from PLA was close to 100%, but advances in radiological diagnosis and antibiotic therapy have lead to a remarkable improvement in the mortality rate, which in recent decades has been reported to range from 2 to 30% (1-5). The most frequently isolated microorganisms in the blood or liver aspirate cultures of PLA cases include *Klebsiella pneumoniae* followed by *Escherichia coli*, whereas the lesions in only 40% of PLA cases harbor these bacteria (3-8). PLA formation is thought to originate from the transmission of infection via three major routes including the biliary tract, portal vein and hepatic artery. However, even in recent years, about 50% of PLA cases are considered to be cryptogenic (6-10). Several reports suggest that oral infectious diseases such as periodontitis are a potential source of infection in PLA (11-13). Here, we report an autopsy case of PLA with periodontopathic bacterial infection, which had been originally diagnosed as cryptogenic.

A 59-year-old female who had suffered a fever and abdominal pain in the lateral region for about 20 days suddenly developed cardiopulmonary arrest and died soon after admission. Postmortem abdominal computed tomography (CT) demonstrated the presence of a large loculated hypodense lesion in the right lobe of the liver (Fig. 1A). There was no evidence of dilated biliary tracts in the CT image. Laboratory blood tests revealed that the levels of C-reactive protein (CRP), aspartate transaminase (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), γGT and ammonia were markedly elevated. Total bilirubin, urea nitrogen and creatinine were also elevated and the prothrombin time (PT) was elongated (Table 1). Malodorous turbid purulent fluid was obtained by liver puncture. We identified *Prevotella melaninogenica*, *Fusobacterium varium* and *Bacteroides vulgatus* by closed pus culture as the predominant bacterial species in the purulent material obtained from the liver. We performed an autopsy to make a definite diagnosis and to identify the infectious routes of her liver abscess. A large multilocular abscess measuring 10 × 7 × 6 cm was observed in the right lobe of the liver (Fig. 1B), and

Table 1. Laboratory data on admission

Leukocyte count (50-80 × $10^2/\mu$l)	56 × 10^2
Erythrocyte count (380-480 × $10^4/\mu$l)	386 × 10^4
Hemoglobin (12.0-16.5 g/dl)	10.6
Hematocrit value (35.0-46.0%)	34.8
Platelet (12.0-28.0 × $10^4/\mu$l)	5.5 × 10^4
PT (70-130%)	32.3
Fibrinogen (220-470 mg/dl)	144
CRP (< 0.3 mg/dl)	42.2
NH_3 (9-33 μmol/l)	214
Total bilirubin (0.2-1.2 mg/dl)	1.3
Direct bilirubin (0.1-0.4 mg/dl)	0.7
AST (10-35 U/l)	606
ALT (5-35 U/l)	360
LDH (120-230 U/l)	840
ALP (100-340 U/l)	790
γGT (<73 U/l)	127
Urea nitrogen (8-20 mg/dl)	50
Creatinine (0.5-1.2 mg/dl)	1.73
Amylase (40-130 U/l)	30

PT, prothrombin time; CRP, C-reactive protein; AST, aspartate transaminase; ALT, alanine trans-aminase; LDH, lactate dehydrogenase; ALP, alkaline phosphatase; γGT, γ-glutamyl transpeptidase.

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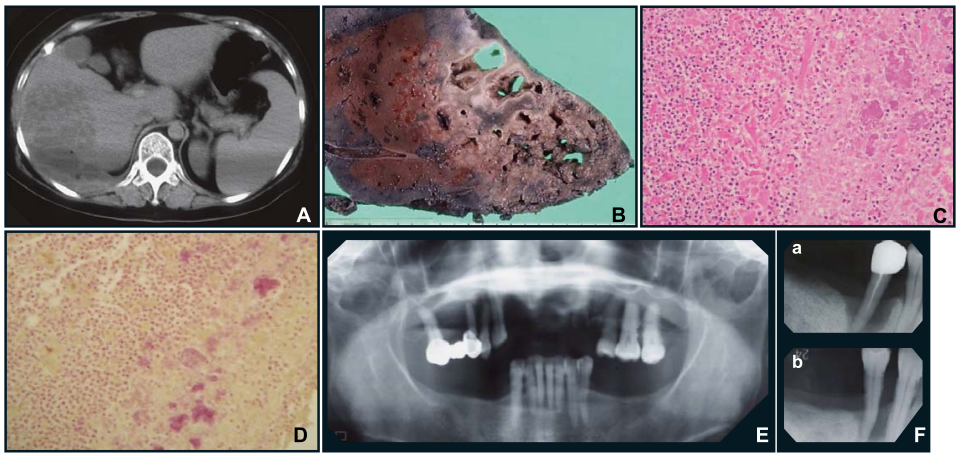

Fig. 1. (A) Enhanced abdominal computed tomography showing a large loculated hypodense lesion in the right lobe of the liver. (B) Cross-section of the liver. There was a large multilocular abscess in the right lobe. (C) Representative histological section of the liver with abscess formation. Most parts were composed of necrotic tissues with massive infiltration of inflammatory cells and bacterial colonies. (D) Gram-stained histological section showing that most of bacterial colonies were composed of Gram-negative bacilli. (E) Oral panoramic radiograph at 3 years prior to death. Severe periodontal lesions were found in the upper right premolar and upper left molar regions. The left incisor remained as a stump. (F) Previous oral radiographs in the lower right premolar region ([a] 14 years prior to death, [b] 11 years prior to death). Most teeth were missing due to periodontal disease.

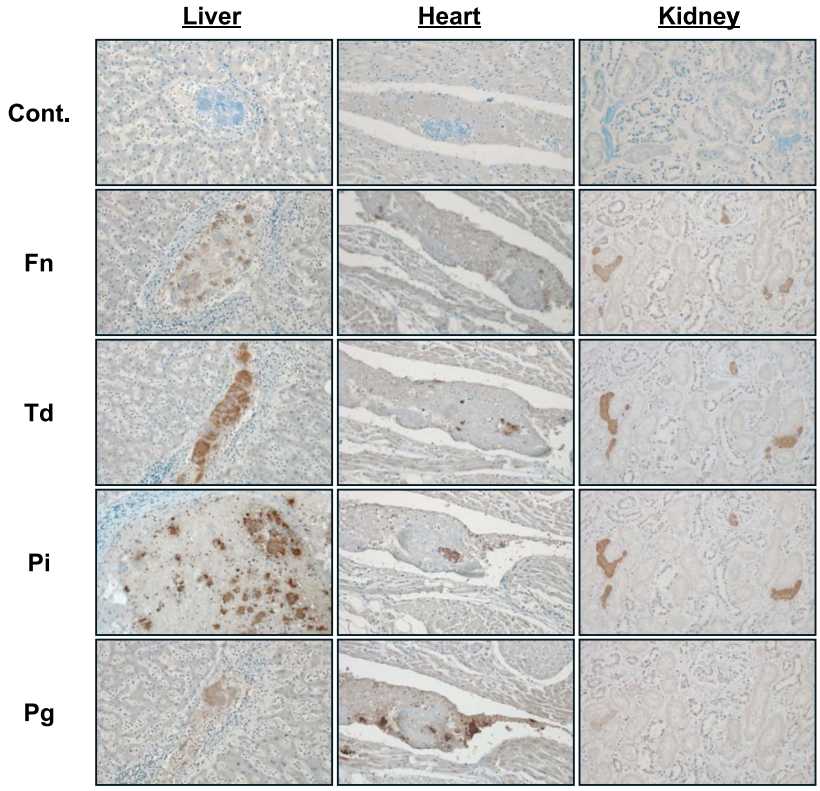

Fig. 2. Immunohistochemical analysis of the liver, the heart (around the tricuspidal valve) and the kidney sections by using the antisera against periodontopathic bacteria, including *Fusobacterium nucleatum* (Fn), *Treponema denticola* (Td), *Prevotella intermedia* (Pi) and *Porphyromonas gingivalis* (Pg). Cont. indicates negative control staining. The bacterial colonies in the infective thrombus and vessels were positive at distinct levels among the organs.

was filled with thick gray-brown pus. The cavity of the right atrium and the pulmonary arteries over an extensive region in both lungs were filled with thrombi. Histological examination revealed that most of the liver abscess consisted of necrotic tissue with massive infiltration of inflammatory cells composed primarily of neutrophils and numerous bacterial colonies (Fig. 1C). However, there was no typical histopathological evidence of suppurative pylephlebitis in the portal area around the abscess. Infected thrombus formation was observed in hepatic veins of various sizes throughout the liver, but not in the hepatic portal vein. In addition, a notable number of infected thrombi with bacterial colonies were observed within pulmonary arteries, splenic and cystic capillary vessels and within capillary vessels of the glomeruli and interstitial tissues of the kidneys. Gram staining revealed that most bacterial colonies were composed of Gram-negative bacilli (Fig. 1D).

This patient had a history of hysterectomy and bilateral ovariectomy based on the diagnosis of mucous cystic adenocarcinoma of the ovary 24 years ago. Ten years after the operation, she underwent another operation for the purpose of curettage and extirpation of the fistula between the vagina and appendix. Considering this medical history, bacteria originating from the portal region were initially thought to be the most likely infectious route. However, we found no evidence of infection in the portal region or evidence of suppurative pylephlebitis in the portal area around the abscess by histopathological examination. Moreover, the involvement of portal infection in abscess formation is unlikely because of the 14-year year time lag. Based on these reasons, we considered 'portal vein seeding' an unlikely explanation for the infectious route in this case of PLA. We were also unable to identify focal lesions as an obvious source of infection in any organs within the intraperitoneal and chest cavity, despite repeated and extensive investigations, and obstructed and/or constricted sections of the extrahepatic biliary ducts. Since we also rejected biliary origin and hepatic artery seeding as routes of infection for abscess formation, we diagnosed this case as cryptogenic PLA.

In this case, we detected *P. melaninogenica* in the purulent material from the liver abscess. This bacterial strain is the most frequently detected bacteria in periodontal abscesses among *Prevotella* spp. (14). This patient had suffered chronic severe periodontitis with deep periodontal pocket formation in many teeth and had received several anti-inflammatory treatments as well as undergoing tooth extractions (Figs. 1E-F). She received continuous periodontal therapy for several years, but had stopped receiving this treatment 3 years before she died, before the course of therapy had been completed. These facts led us to hypothesize that periodontal infection could have been the source of infection for PLA formation. This notion is consistent with previous reports of the periodontal bacteria *Fusobacterium nucleatum* and *Streptococcus intermedius* as a possible source of infection in the development of PLA (11-13). Furthermore, *Prevotella* and *Porphyromonas* spp. have been isolated in clinical specimens from patients with PLA (15,16). To assess the implication of periodontal infection in the pathogenesis of PLA, we performed immunohistochemical analyses using antisera against several species of anaerobic Gram-negative periodontopathic bacteria (17). We positively identified *F. nucleatum*, *Treponema denticola*, *Prevotella intermedia* and *Porphyromonas gingivalis* in the bacterial colonies within the infected thrombi and vessels at varying intensity among different organs (Fig. 2). Our report is the first to demonstrate the existence of *F. nucleatum* as well as other periodontopathic bacteria, including *P. intermedia*, *P. gingivalis* and *T. denticola*, in many organs and the thrombus of a patient with PLA by immunohistochemical staining.

Taken together, our results suggest that the infectious route of this case consisted of periodontopathic bacteria being carried into the heart from periodontal lesions through the venous circulation followed by intra-arterial spreading into the liver. This route of infection is supported by the fact that the association between periodontopathic bacteria and bacterial endocarditis is well-established (18-22). However, it is not clear why the abscess in this case formed only in the liver and not in other organs.

In summary, our findings demonstrate the importance of considering periodontal infection as a potential source of infection in the formation of PLA. Additionally, periodontopathic microorganisms that have the potential to cause abscess formation may include *T. denticola*, *P. intermedia* and *P. gingivalis* in addition to *F. nucleatum* and *S. intermedius*. To confirm the role of periodontal bacterial infection in PLA formation, a large number of cryptogenic PLA patients would need to be examined.

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