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Liver abscess caused by *Cutibacterium namnetense* after transarterial chemoembolization for hepatocellular carcinoma

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Author contributions

All authors contributed to the study conception and design. Material preparation, data

collection and analysis were performed by Eiichiro Yasutomi, Yoshihide Ueda and Yoshihiko Yano. The first draft of the manuscript was written by Eiichiro Yasutomi and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Abstract

A 72-year-old man underwent transarterial chemoembolization (TACE) for solitary hepatocellular carcinoma (HCC) located on the S6 segment. He had a history of anti-viral therapy for hepatitis C virus and was being treated for diabetes mellitus with inadequate control. On day 28 after TACE, he visited our hospital again, with complaints of fever and abdominal pain in the right upper quadrant. Blood examination showed elevated levels of white blood cells and C-reactive protein. Computed tomography showed a poorly marginated, low-density lesion measuring 9.5 × 8.0 × 4.0 cm, forming multiple small gas bubbles, located superiorly, and in contact with HCC treated by TACE. Ultrasound-guided puncture revealed whiffy and muddy pus. Gram staining of the pus showed the presence of numerous gram-positive rods, which were identified as *Cutibacterium namnetense*. He underwent percutaneous trans-hepatic abscess drainage and received antibiotics treatment. The abscess was successfully treated, and he was discharged on day 19. The incidence of liver abscess after TACE is rare, and intestinal microbiota have been reported to be the common pathogens. To the best of our knowledge, this is the first case of liver abscess caused by *Cutibacterium namnetense*.

Keywords:

Liver abscess, Transarterial chemoembolization, *Cutibacterium namnetense*

Introduction

Hepatocellular carcinoma (HCC) is the sixth commonest cancer type globally [1]. With recent developments in the therapeutic options for HCC, the 5-year survival rate of HCC in Japan has improved from 39.7% in 1994-2001 to 50.4% in 2002-2009 [2]. Among the treatment methods for HCC, transarterial chemoembolization (TACE), which is an interventional radiology procedure where chemotherapeutic and embolic agents are delivered into a tumor body, has been playing an important role in extension of prognosis through evolution of new drugs and advancing techniques [3].

However, complications associated with TACE are currently attracting attention. One of them is liver abscess, occurring in 0.1-4.5% patients [4]. The common pathogens found in liver abscess after TACE have been reported to be intestinal microbiota, concretely, *Escherichia coli*, *Enterobacter cloacae*, *Enterococcus faecalis*, and *Klebsiella pneumoniae*, among others [4, 5].

In this report, we experienced a case of liver abscess after TACE caused by *Cutibacterium namnetense* [6], a recently identified skin microbiota. This case will give us insight into the pathogenesis of liver abscess after TACE.

Case Report

A 72-year-old man was diagnosed as having recurrent HCC. From the age of 47 years, he had been visiting our hospital regularly for chronic hepatitis C. At the age of 65, he took anti-viral therapy (peg-interferon, ribavirin, and telaprevir) for hepatitis C virus (HCV) and achieved sustained virologic response. At age 66, he developed HCC for the first time. A 10 mm HCC located on S4 segment was treated by radiofrequency ablation. From the first treatment for HCC, he has had recurrence of HCC twice. The first recurrence was at age 66; intensity-modulated radiation therapy was done for a 10 mm HCC located on S8 segment. The second was at age 71; TACE was done for a 12 mm HCC located on S4 segment. In addition, he was taking medications for hypertension (telmisartan 80 mg and hydrochlorothiazide 12.5 mg, everyday) and diabetes mellitus (pioglitazone 30 mg, vildagliptin 50 mg, and metformin 250 mg, everyday). However, the control of diabetes mellitus was inadequate, and his serum hemoglobin A1c level was 8.3%. During this time, his recurrent HCC was solely located on the S6 segment, 1.6 × 1.2 × 1.0 cm in size (Fig. 1a). Blood examination at diagnosis of recurrent HCC indicated normal liver function (Table 1). Since the recurrent HCC was located on lower marginal zone of the liver and adjacent to the

intestinal tract, radiofrequency ablation was thought to be difficult to be performed safely. He refused to undergo hepatic resection. Therefore, he underwent TACE for the HCC, using epirubicin and lipiodol (Fig. 1b). The postoperative course was uneventful, and he was discharged 9 days after TACE.

Twenty-eight days after TACE, he visited our hospital again with complaints of fever and abdominal pain that had continued for several days. He looked very ill. His body temperature was 38.3□, and he had moderate tenderness in the right upper quadrant. Blood examination showed elevated levels of white blood cells and C-reactive protein (Table 1). Computed tomography (CT) showed a poorly marginated, low-density lesion measuring 9.5 × 8.0 × 4.0 cm, located in contact with HCC treated by TACE and spreading superiorly (Fig. 2). Within the lesion, multiple small gas bubbles were recognized. These findings together with the clinical course gave a strong suspicion of liver abscess. Therefore, an ultrasound-guided puncture was conducted, which revealed whiffy and muddy pus, suggesting that the abscess was formed through bacterial infection (Fig. 3a). Gram staining of the pus showed the presence of numerous gram-positive rods (Fig. 3b). *Cutibacterium namnetense* was identified by anaerobic culture and 16S ribosomal RNA gene amplicon sequencing. The sequence of 16S ribosomal RNA gene, which was determined after polymerase chain reaction from the

bacterial DNA by the methods described in a previous report [7], was matched with *Cutibacterium namnetense* (accession number: LWHO01000015). He was started on vancomycin (1500 mg/day intravenously). However, CT on day 7 did not show any improvement of the abscess. Therefore, on day 8, he underwent percutaneous trans-hepatic abscess drainage with a size 7 French pigtail catheter. Based on the bacterial susceptibility, antibiotics were switched to intravenous ampicillin 8 g/day from day 10 to day 14, then oral amoxicillin 1500 mg/day from day 15 onwards. His symptoms and laboratory data improved rapidly, and CT on day 14 showed prominent reduction of the abscess (Fig. 4a). He was discharged on day 19. He continued to take amoxicillin for 118 days in total, until C-reactive protein was normalized. For diabetes mellitus, he started to take canagliflozin (100mg, everyday), and his serum hemoglobin A1c level was improved to 6.3%. CT 6 months after discharge showed complete remission of the abscess (Fig. 4b), indicating efficacy of the treatment. He continues to receive medical check-up regularly without fever or abdominal pain.

Discussion

This is the first report that describes *Cutibacterium namnetense* as a pathogen found in liver abscess. This case suggests two important things. First, the mechanism of liver abscess formation after TACE is somehow different from traditional bacterial liver abscess formation. Recent developments in therapeutic instrument and techniques have made it possible to proceed with "selective TACE" by identifying feeding arteries to the tumor and treat it at a pinpoint [8]. Owing to selective TACE, control of each nodule has drastically improved [9]. However, it enhances the risk of liver abscess when embolization causes arterial stasis or remarkable visualization of portal veins during TACE [10]. In the present case, HCC was embolized selectively with visualization of portal vein, which would become the cause of liver abscess formation. The possible underlying mechanisms of liver abscess formation after TACE are ischemic destruction of the intrahepatic bile duct due to peribiliary arterial occlusion and immunosuppressant effect of chemotherapeutic agents [11], which are superimposed by bacterial infection [12]. The main pathway through which pathogenic bacteria reach the site, treated with TACE is through the bile duct from gastrointestinal tract [10, 13]. It is supported by the fact that in most cases, pathogens found in the liver abscess after TACE are *Escherichia*

coli, *Enterobacter cloacae*, *Enterococcus faecalis*, and *Klebsiella pneumoniae* [4, 5]. Moreover, many reports demonstrated that a history of biliary procedures such as bilioenteric anastomosis, endoscopic papillotomy, and percutaneous transhepatic biliary drainage can be risk factors for liver abscess formation after TACE [4, 5, 10, 11, 13], although the present case had no history of biliary procedure. However, it has been previously reported that bloodstream infections occur at a rate of 0.69% after interventional therapy, and the most common pathogen is Coagulase-negative *Staphylococcus*, which accounts for 30.57% of all bloodstream infections [14]. A study about the microorganisms causing liver abscess after TACE identified *Staphylococcus epidermidis* in about 9.5% of the cases [5]. These reports clearly indicate that skin indigenous bacteria can enter into the bloodstream during TACE, infect the site where "high-risk procedures" have been conducted, and form abscess. This infection route and pathogens are not similar to those of traditional liver abscess, which in most cases is thought to be developed via the bile duct [15, 16] or by portal vein through bacterial translocation from the intestine [16]. Although there has been no consensus about the preventive use of antibiotics in the perioperative period of TACE [4, 5, 10], we have to pay sufficient attention to liver abscess after TACE. Moreover, the patient in this report had poorly controlled diabetes mellitus. Diabetes mellitus is a risk factor for both onset

[15, 17] and severer complications [18] of bacterial liver abscess. Similarly, previous studies have reported that around 40% of patients had a history of diabetes mellitus in cases of liver abscess after TACE, although the sample size was small [5, 10]. In addition, diabetes mellitus is reported to increase the incidence of HCC after HCV has been eradicated by an interferon-based regimen [19]. Control of diabetes mellitus is quite important in reducing the occurrence of HCC and complications associated with the treatment.

Second, this report showed that *Cutibacterium namnetense* can be a cause of liver abscess. For *Cutibacterium* (previously termed *Propionibacterium*), a group of *Actinobacteria*, only five species have been identified, *Cutibacterium acnes, Cutibacterium avidum, Cutibacterium granulosum, Cutibacterium namnetense, and Cutibacterium modestum* [20]. Among them, *Cutibacterium namnetense* has been recently identified as an indigenous skin bacterium. It was reported for the first time in 2016 as bacteria isolated from the surgical sample of an open tibial fracture [6]. Until now, little has been understood regarding the pathogenicity of *Cutibacterium namnetense*, except that it causes superinfection of the bone, after treatment for *Staphylococcus aureus* [21]. Although liver abscess caused by *Cutibacterium namnetense* has not been reported, physicians must consider its pathogenicity, especially

after percutaneous procedures.

In conclusion, we experienced a case of liver abscess after TACE caused by *Cutibacterium namnetense*. This case is highly suggestive in terms of the pathogenesis of liver abscess after TACE and the pathogenicity of this bacterium.

References

1. Fan G, Wei X, Xu X. Is the era of sorafenib over? A review of the literature. Ther Adv Med Oncol. 2020; doi:10.1177/1758835920927602.

2. Kudo M, Izumi N, Kubo S, et al. Report of the 20th Nationwide follow-up survey of primary liver cancer in Japan. Hepatol Res. 2020; 50:15–46.

3. de Baere T, Arai Y, Lencioni R, et al. Treatment of Liver Tumors with Lipiodol TACE: Technical Recommendations from Experts Opinion. Cardiovasc Intervent Radiol. 2016; 39:334-343.

4. Arslan M, Degirmencioglu S. Liver abscesses after transcatheter arterial embolization. J Int Med Res. 2019; 47:1124-1130.

5. Lv WF, Lu D, He YS, et al. Liver Abscess Formation Following Transarterial Chemoembolization: Clinical Features, Risk Factors, Bacteria Spectrum, and Percutaneous Catheter Drainage. Medicine (Baltimore). 2016; 95:e3503.

6. Aubin GG, Bémer P, Kambarev S, et al. *Propionibacterium namnetense* sp. nov., isolated from a human bone infection. Int J Syst Evol Microbiol. 2016; 66:3393-3399.

7. Masaki T, Ohkusu K, Hata H, et al. *Mycobacterium kumamotonense* Sp. Nov.

Recovered from Clinical Specimen and the First Isolation Report of *Mycobacterium arupense* in Japan: Novel Slowly Growing, Nonchromogenic Clinical Isolates Related to *Mycobacterium terrae* Complex. Microbiol Immunol. 2006; 50: 889–897.

8. Miyayama S, Yamashiro M, Hashimoto M, et al. Identification of small hepatocellular carcinoma and tumor-feeding branches with cone-beam CT guidance technology during transcatheter arterial chemoembolization. J Vasc Interv Radiol. 2013; 24:501–508.

9. Golfieri R, Cappelli A, Cucchetti A, et al. Efficacy of selective transarterial chemoembolization in inducing tumor necrosis in small (<5 cm) hepatocellular carcinomas. Hepatology. 2011; 53:1580–1589.

10. Woo S, Chung JW, Hur S, et al. Liver abscess after transarterial chemoembolization in patients with bilioenteric anastomosis: frequency and risk factors. AJR. 2013; 200:1370-1377.

11. Sun Z, Li G, Ai X, et al. Hepatic and biliary damage after transarterial chemoembolization for malignant hepatic tumors: incidence, diagnosis, treatment, outcome and mechanism. Crit Rev Oncol Hematol. 2011; 79:164-174.

12. Xia J, Ren Z, Ye S, et al. Study of severe and rare complications of transarterial

chemoembolization (TACE) for liver cancer. Eur J Radiol. 2006; 59:407-412.

13. Son DJ, Hong JY, Kim KH, et al. Liver abscess caused by *Clostridium haemolyticum* infection after transarterial chemoembolization for hepatocellular carcinoma: A case report. Medicine (Baltimore). 2018; 97.e0688.

14. Bai Y, Zheng Z, Du M, et al. Bloodstream Infection and Its Clinical Characteristics and Relevant Factors Associated with Interventional Therapy in a Large Tertiary Hospital: A Six Years Surveillance Study. Biomed Res Int. 2019; doi:10.1155/2019/8190475.

15. Kaplan GG, Gregson DB, Laupland KB. Population-based study of the epidemiology of and the risk factors for pyogenic liver abscess. Clin Gastroenterol Hepatol. 2004; 2:1032–1038.

16. Ahmed Z, Bansal SK, Dhillon S. Pyogenic liver abscess caused by *Fusobacterium* in a 21-year-old immunocompetent male. World J Gastroenterol. 2015; 21:3731–3735.

17. Wang WJ, Tao Z, Wu HL. Etiology and clinical manifestations of bacterial liver abscess: A study of 102 cases. Medicine (Baltimore). 2018; 97.e12326.

18. Li W, Chen H, Wu S, et al. A comparison of pyogenic liver abscess in patients with or without diabetes: a retrospective study of 246 cases. BMC Gastroenterol.

2018; doi:10.1186/s12876-018-0875-y.

19. Hung CH, Lee CM, Wang JH, et al. Impact of diabetes mellitus on incidence of hepatocellular carcinoma in chronic hepatitis C patients treated with interferon-based antiviral therapy. Int J Cancer. 2011; 128:2344-2352.

20. Dekio I, Sakamoto M, Suzuki T, et al. *Cutibacterium modestum* sp. nov., isolated from meibum of human meibomian glands, and emended descriptions of *Cutibacterium granulosum* and *Cutibacterium namnetense*. Int J Syst Evol Microbiol. 2020; 70:2457-2462.

21. Corvec S, Guillouzouic A, Aubin GG, et al. Rifampin-Resistant *Cutibacterium* (formerly *Propionibacterium*) *namnetense* Superinfection after *Staphylococcus aureus* Bone Infection Treatment. J Bone Jt Infect. 2018; 3:255-257.

Figure Legends

Fig. 1 CT at diagnosis and after TACE procedure for the recurrent HCC. CT showed a well-circumscribed HCC measuring 1.6 × 1.2 × 1.0 cm, located on the S6 segment. The lesion was clearly enhanced in the arterial phase (a). In non-contrast CT after the TACE procedure, complete accumulation of lipiodol into the HCC was achieved (b).

Fig. 2 CT at diagnosis of liver abscess. CT showed a poorly-marginated abscess measuring 9.5 × 8.0 × 4.0 cm, forming multiple small gas bubbles (a). The abscess were located superiorly and in contact with HCC treated by TACE where was filled with lipiodol (high density area) (b).

Fig. 3 Macroscopic and microscopic findings of the abscess. The punctured fluid was whiffy and muddy pus, suggesting that the abscess was developed through bacterial infection (a). Gram staining of the pus showed a lot of gram-positive rods (b).

Fig. 4 CT during and after the treatment for liver abscess. CT on day 14 of the treatment showed a prominent reduction of the abscess compared with those at diagnosis of liver abscess (a). Enhanced CT of 6 months after discharge did not show liver abscess (b).

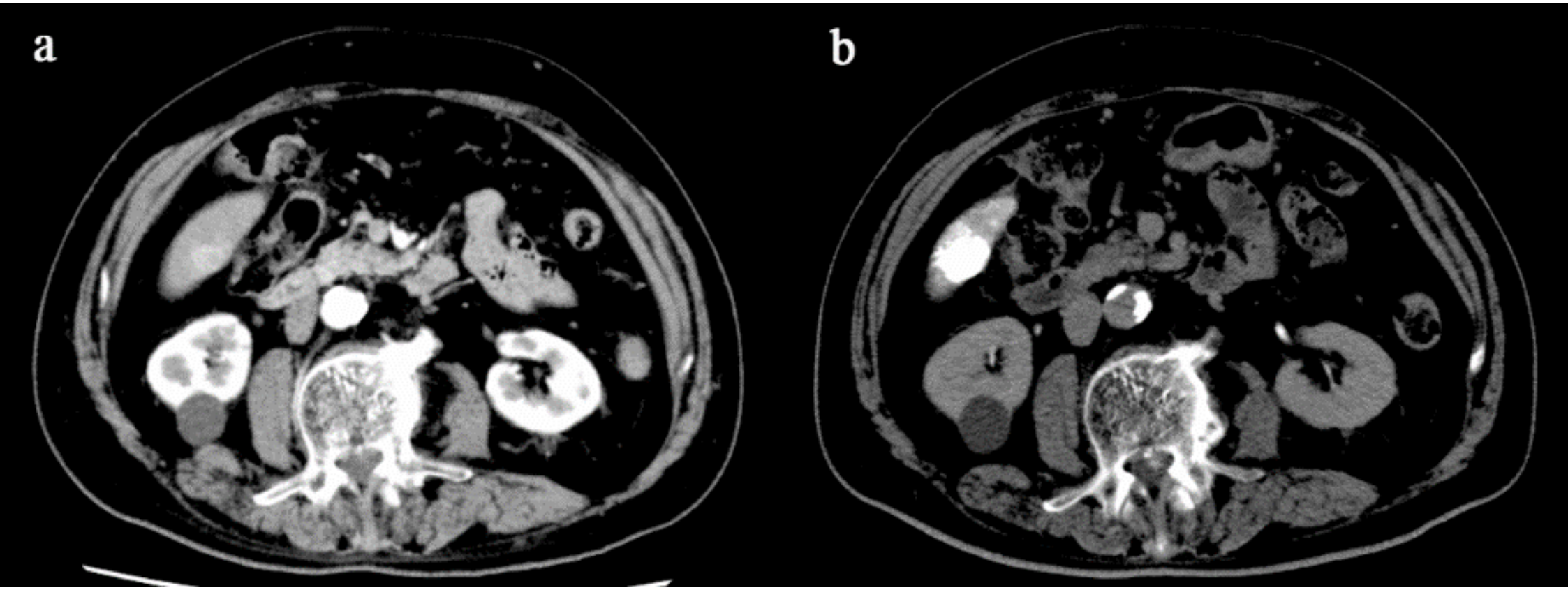

Figure 1

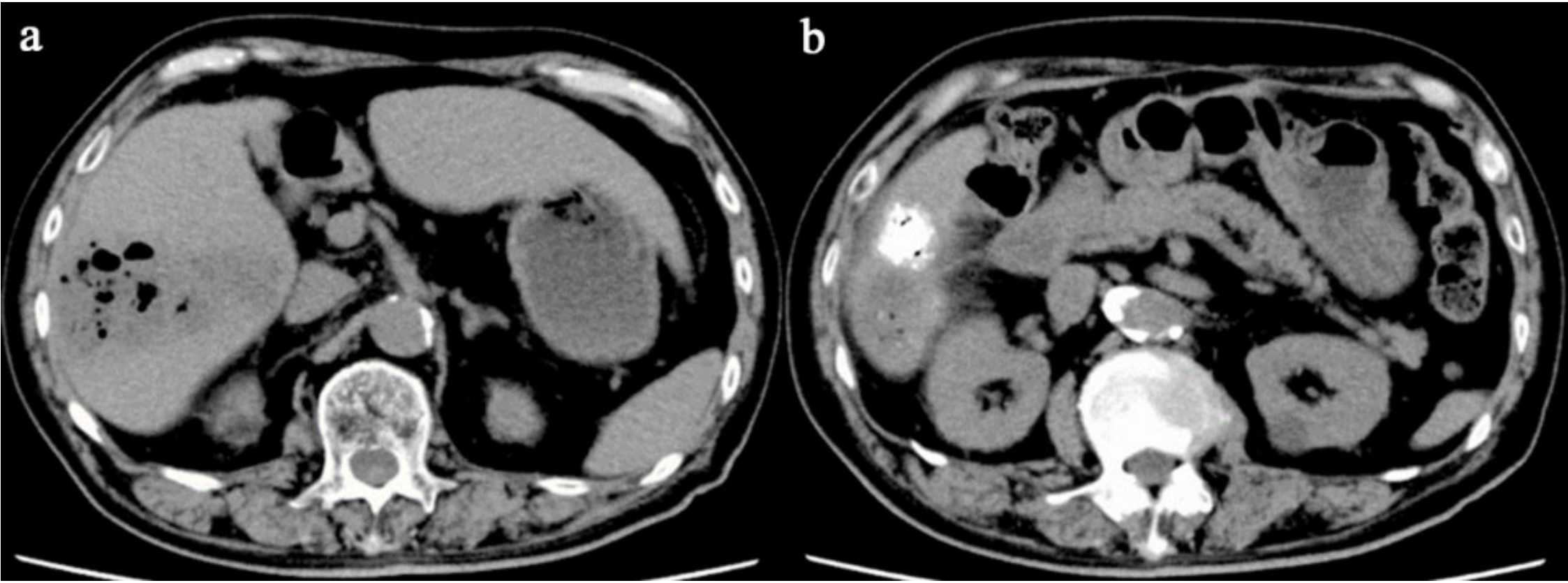

Figure 2

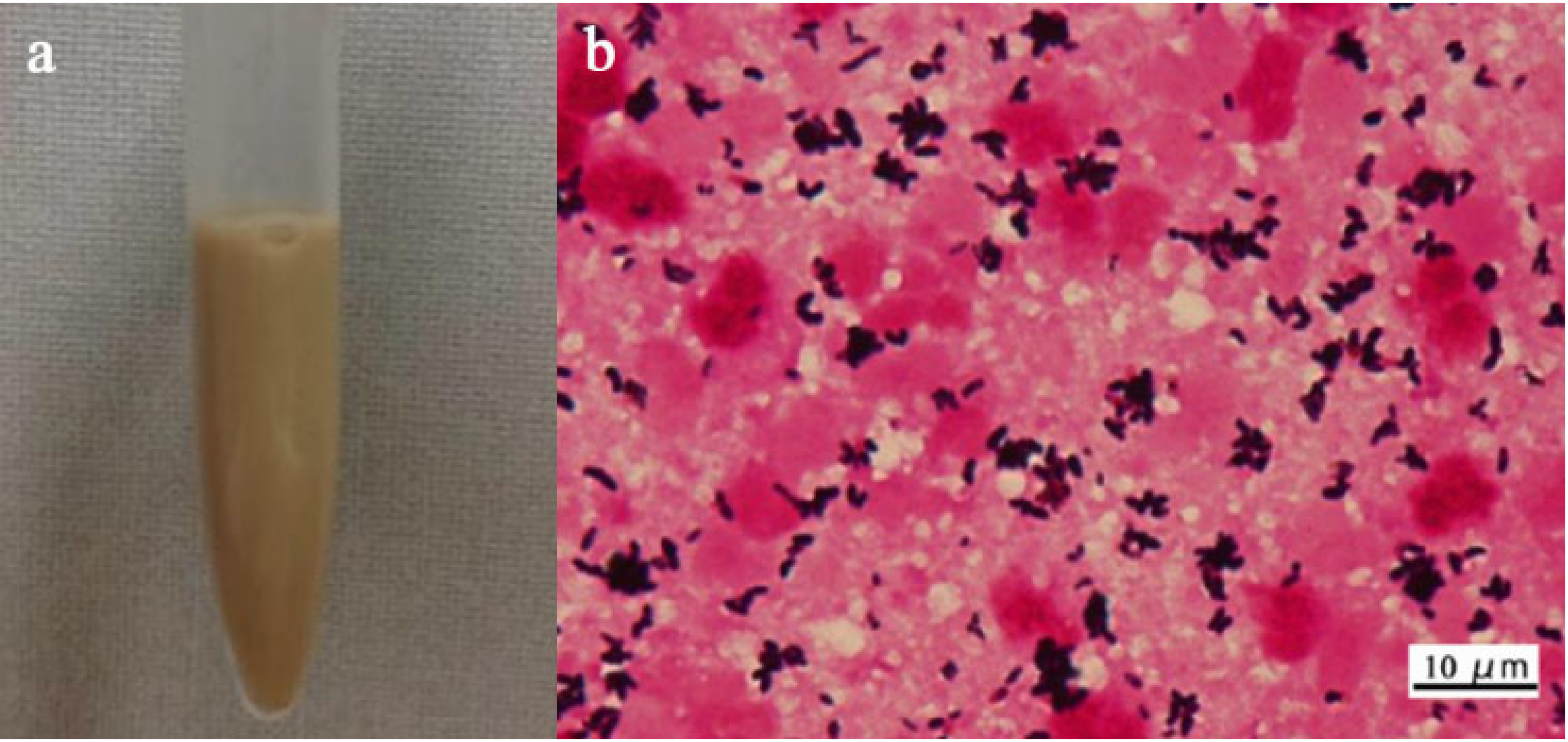

Figure 3

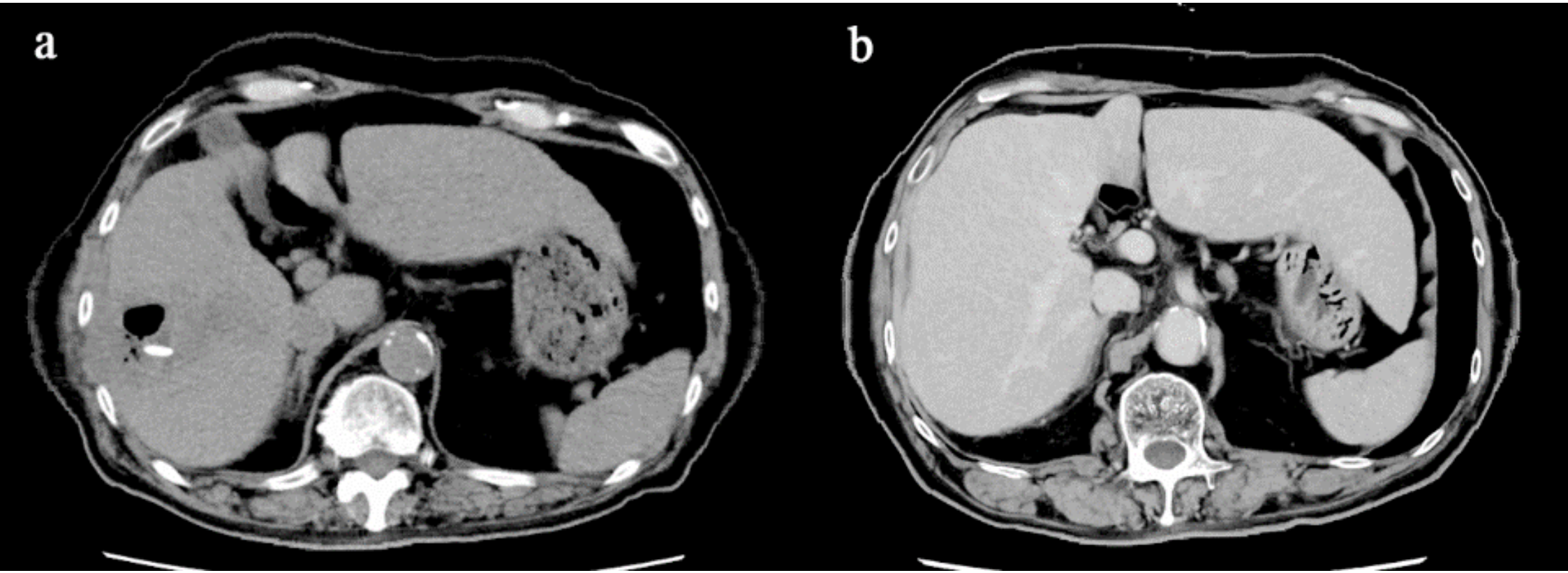

Figure 4

Table 1 Laboratory data at pre-TACE.

	pre-TACE	Diagnosis of liver abscess	
Complete blood count			
White blood cells	7.2×10^3	13.3×10^3	/μL
Neutrophil	65.9	86.0	%
Monocyte	8.3	6.0	%
Lymphocyte	24.4	8.0	%
Eosinophil	1.0	0.0	%
Basophil	0.4	0.0	%
Red blood cells	4.14×10^6	3.80×10^6	/μL
Hemoglobin	13.6	12.3	g/dL
Hematocrit	39.5	35.1	%
Platelet	20.9×10^4	48.3×10^4	/μL
Coagulation test			
Prothrombin time	108.2	80.4	%
Activated partial thromboplastin time	30.4	29.4	sec
Biochemical test			
Aspartate aminotransferase	19	22	U/L
Alanine aminotransferase	23	37	U/L
γ-glutamyl transpeptidase	69	389	U/L
Alkaline phosphatase	397	1219	U/L
Lactate dehydrogenase	186	166	U/L
Cholinesterase	262	96	U/L
Sodium	137	129	mmol/L
Potassium	4.4	4.4	mmol/L
Chloride	103	96	mmol/L
Blood urea nitrogen	20.9	15.5	mg/dL
Creatinine	1.09	1.11	mg/dL
estimated glomerular filtration rate	51.7	50.7	mL/min/1.73m^2
Uric acid	4.5	3.6	mg/dL
Total protein	7.1	6.5	g/dL

Albumin	4.5	2.7	g/dL
Total-bilirubin	0.8	1.2	mg/dL
Direct-bilirubin	0.1	0.5	mg/dL
C-reactive protein	0.12	10.62	mg/dL