Int J Clin Exp Pathol 2021;14(10):1065-1068
www.ijcep.com /ISSN:1936-2625/IJCEP0136784

Case Report

Huge solitary necrotic nodule of the liver: a rare case report with review of literature

Xinyue Zhang, Weilan Fang, Liangtao Zeng, Fanrong Liu

Department of Pathology, The Second Affiliated Hospital of Nanchang University, Nanchang, China

Received June 27, 2021; Accepted September 6, 2021; Epub October 15, 2021; Published October 30, 2021

Abstract: Solitary necrotic nodule of the liver (SNNL) is an uncommon disease in clinical practice, and its pathogenesis is still unclear. Here, we report the case of a 35-year-old woman. After physical examination, the patient was found to have a liver neoplasm, and there were no other physical complaints. Abdominal contrast-enhanced computed tomography (CT) showed the presence of a hypodense lesion. The patient opted for surgery to eliminate the lesion. Pathologic examination revealed an isolated necrotic nodular lesion with a size of 12 cm×10 cm×10 cm. The patient had a history of hepatitis B infection. To our knowledge, this is the largest SNNL ever reported and the first case with a history of hepatitis B infection.

Keywords: Liver tumor, solitary necrotic nodule, pathology

Introduction

Solitary necrotic nodule of the liver (SNNL) is a rare lesion in the clinic. A patient with SNNL usually has no symptoms or only mild discomfort in the liver. Most patients are found to have liver nodules on physical examination and seek further treatment. At present, the pathogenesis of SNNL remains unclear. An accurate diagnosis is difficult with current medical imaging. The vast majority of cases are supported by histopathology after surgical resection. Pathologic features of SNNL are a central necrotic core surrounded by a fibrotic capsule infiltrated by inflammatory cells [1, 2].

Here, we report a case with a rare occurrence of a huge solitary necrotic nodule of the liver. The patient had a history of hepatitis B and a large SNNL lesion. Through the study of this case, we will have a more complete understanding of SNNL, and propose the hypothesis that HEPATITIS B virus may promote the enlargement of SNNL lesions, along with increasing the nodular volume.

Case report

A 39-year-old female patient without any symptoms came to the Department of Hepatobiliary Surgery with complains of a mass in the right lobe of the liver.

Ultrasound showed an oval mass with ill-defined margins and measuring 97 mm×74 mm. Abdominal contrast-enhanced computed tomography (CT) showed the presence of a hypodense lesion. In contrast-enhanced scan, uneven enhancement was observed in the arterial phase, and weakened in the portal and delayed phases. Laboratory tests verified that the patient had a history of hepatitis B, but all other tests were normal including serum carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA 19-9), and alpha-fetoprotein.

The patient underwent surgery. The specimen was sent for histopathologic examination. There was a gray-yellow mass of 12 cm×10 cm×10 cm in the liver. Microscopically, the mass was a large sheet of coagulated, denatured and necrotic tissue surrounded by multinucleated giant cells (**Figure 1**). There were several small cavities in the necrotic foci and cystic mural structures around the cavities (**Figure 2**). Local areas of lymphocyte and eosinophil aggregation were also observed in the necrotic region. The special staining results showed: PAS (+), PASM (+), acid-fast (-), Congo red (-), reticular fibers (-), and elastic fibers (-). These microscop-

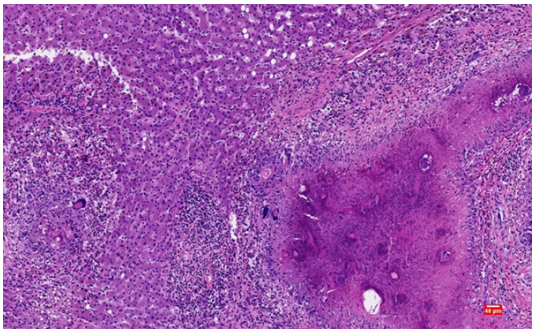

Figure 1. Multinucleated giant cells appeared at the edge of the necrotic area. (Hematoxylin and eosin staining, magnification ×100).

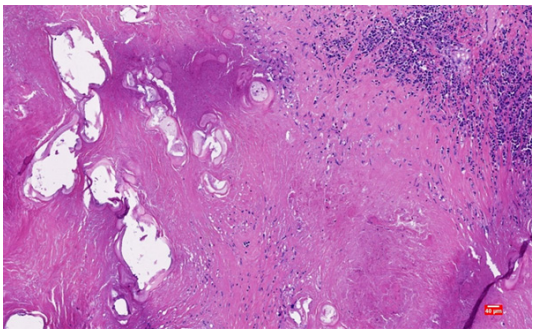

Figure 2. There were several cavities in the necrotic area, and the surrounding cavities showed cystic mural structures. (Hematoxylin and eosin staining, magnification ×100).

ic manifestations confirmed the diagnosis of SNNL and we considered it as a lesion after parasitic infection.

Discussion

Currently, only a few cases of SNNL have been reported. By conventional CT, solitary necrotic nodules usually appear as hypodense or isodense nodules. In most cases, the lesion does not show contrast enhancement, but may show enhancement in thin marginal tissue [3]. Calcification may be present in some lesions [4]. Such imaging findings make it difficult to distinguish SNNL from hepatic metastases [5]. Therefore, SNNL can be diagnosed by only pathology after surgery at present. SNN shows a significant necrotic core which may contain eosinophils, calcification, cholesterol, foam cells, and some inflammatory cells [2].

It was generally believed that SNNL was mostly a benign presence, and it was believed to be the final stage of a natural process caused by infection and degeneration [6]. However, according to recent reports, some cases of SNNL are associated with metastatic cancer, so we should consider the possibility of metastatic necrotic tumor lesions when evaluating SNNL [7]. It is important to bear in mind that "solitary" necrotic nodules may not occur in isolation [8]. In exploration of the formation mechanism of SNNLs, the sclerosis and evolution of small blood vessels [9], parasites [10], trauma, and other reasons are all hypothesized to cause its formation, and may even be caused by a combination of the above reasons [2, 11]. In the hypothesis of small-vessel sclerosis, the pathologic findings are based on the phenomena that there are some hemangiomatous parts in the lesion, which are filled with blood vessels that supply nutrients. The lesion also contains more sclerotic tissue, some of which is calcifying. Sclerosis is also a major feature [9]. The presence of "feeding vessels" and the absence of cystic spaces or other signs of parasite erosion represent the hypothesized mechanism for the evolution of sclerosis in small hemangiomas [2]. However, granulomatous tissue is similar to parasitic granulomatous and eosinophilic nematode - like material in the mechanism of parasitic infection. This microscopic appearance suggests that parasitic infection may also be responsible for SNNL [8]. In the case we reported, the necrotic area had complete coagulative necrosis with only a few inflammatory cells such as eosinophils and lymphocytes. A large number of inflammatory cells such as eosinophils and multinucleated giant cells were seen at the junction with normal liver tissue. This lesion is therefore thought to be altered by parasitic infection.

Article reports of SNNL are relatively rare in China. A total of 25 cases have been reported in the English literature (**Table 1**). Of the 25 patients reported, 20 were female and 5 were male, of whom 11 patients had clinical symptoms of abdominal pain. One patient had a history of rectal cancer and two patients had a history of gastric cancer. In one case, the SNNL lesions increased in volume over a period of 7 months. In another of these cases, however, the lesion disappeared 7 months later without surgical treatment. As we learn about the causes of SNNL, we find that patients in SNNL cases could have no clinical symptoms. After all, some cases are even identified and defined

Table 1. English literature reports of cases of Solitary necrotic nodule of the liver

Case	Age/ gender	Location (lobe)	Clinical symptoms	Medical History	laboratory examination	Size (mm)	Therapies	Outcome
1	22/F	Right lobe (S6)	Fever	Epilepsy	hepatocyte dysfunction	10	Surgery	N0 recurrence
2	76/F	Right lobe (S6)	Normal	NA	Normal	12	Surgery	No recurrence
3	74/F	Right lobe (S8)	Normal	Rectal cancer	Normal	16	Surgery	No recurrence
4	55/M	NA	Normal	NA	NA	20	NA	NA
5	55/F	Right lobe (S8)	Abdominal pain	NA	NA	80	NA	NA
6	41/F	Right lobe (S8)	Normal	NA	NA	21	NA	NA
7	62/F	Left lobe (S3)	epigastric pain	Chronic renal failure	The count of CEA and CA199 increased slightly	80	Surgery	No recurrence
8	28/F	NA	Right abdomen pain	NA	NA	10	Surgery	NA
9	32/F	NA	Right abdomen pain	NA	NA	12	Surgery	NA
10	48/F	Right lobe (S8)	Normal	NA	The count of CEA and CA199 increased	20	Surgery	No recurrence
11	30/M	Right lobe (S5)	Right abdomen pain	NA	Leukocytosis and dysfunction of liver	70	Surgery	No recurrence
12	48/F	Right lobe (S6)	Abdominal pain	NA	Normal	15	Surgery	No recurrence
13	35/F	NA	Normal	NA	Normal	40	Surgery	No recurrence
14	46/M	NA	Normal	Type 2 diabetes	Hyperlipidemia	18	Surgery	No recurrence
15	40/F	Right lobe (S5)	Normal	NA	Normal	30	Surgery	No recurrence
16	59/F	Left lobe (S4)	Right abdomen pain	Hypertension, osteoarticular pathology and penicillin allergy	Normal	42	Surgery	No recurrence
17	52/M	Right lobe (S7)	Normal	Gastric cancer	NA	8	Surgery	No recurrence
18	30/F	Right lobe (S6)	dyspeptic symptoms	Gastric cancer	NA	15	No surgery	unchanged
19	58/F	Right lobe (S5)	Right abdomen pain	NA	NA	20	Surgery	No recurrence
20	84/F	Right lobe (S7)	Anemia	carcinoma of cecum	NA	NA	Surgery	No recurrence
21	64/F	NA	Right abdomen pain	NA	NA	NA	Surgery	NA
22	35/M	Right lobe (S6)	Normal	Fatty liver	The serum level of alanine aminotransferase rose	20	No surgery	The mass disappeared
23	33/F	Right lobe (S6)	Right abdomen pain	Normal	Normal	NA	Surgery	No recurrence
24	51/F	Right lobe (S6)	Right abdomen pain	Cervical cancer	mild transaminitis and an eosinophilia	8	Surgery	No recurrence
25	64/F	Left lobe (S3)	Normal	Diarrhea	A slightly raised white cell count	12	Surgery	No recurrence

M: Male; F: Female; NA: not available.

at autopsy [9, 10]. Most of the patients chose surgical treatment, which resulted in no recurrence of the lesion.

We reported SNNL in a patient with a history of hepatitis B and it has the largest lesion volume among the reported cases. The patient is also the only one with a history of hepatitis B reported so far. In most cases, SNNL nodules were found to be less than 20 mm in size [6]. A few lesions may be larger than 50 mm in size, but all are smaller than 100 mm. Patients with SNNL previously reported also had no history of hepatitis B. Does hepatitis B virus infection affect the size of SNNL lesions? Hepatitis B virus-encoded X protein (HBx) up-regulates special AT-rich binding protein 1 (SATB1) and promotes hepatic fibrosis through paracrine activation of stellate cells [12]. HBx also induces the production of interleukin 8 (IL-8), tumor necrosis factor α (TNF-α), and chemokine ligand 2 (CXCL-2) [13]. These three cytokines can promote inflammation. In addition to inducing the production of inflammatory factors, chronic HBV infection also promotes hepatocyte cloning. During chronic HBV infection, the number of hepatocyte clones detected using integrated HBV DNA as a specific marker was greater than the number of clones where random hepatocyte death and proliferation occurred [14].

We still need to further explore the occurrence and growth mechanism of SNNL. We followed up on the patient in the report. Three months after the operation, the patient was healthy and had no recurrence. Certainly, longer follow-up time is required.

Acknowledgements

The study was supported by the grants from the National Natural Science Foundation of China (Grant number: 81960521).

Informed consent was obtained from the patient described in this study.

Disclosure of conflict of interest

None.

Address correspondence to: Fanrong Liu, Department of Pathology, The Second Affiliated Hospital of Nanchang University, No. 1, Minde Road, Donghu District, Nanchang, China. E-mail: liufanrong@163.com

References

[1] Colagrande S, Politi LS, Messerini L, Mascalchi M and Villari N. Solitary necrotic nodule of the liver: imaging and correlation with pathologic features. Abdom Imaging 2003; 28: 41-44.

[2] Patti R, Cabibi D, Sparacello M, Di Vita G and Montalto G. Solitary necrotic nodule of the liver: different pathological findings express a different histogenesis. Case Rep Gastroenterol 2008; 2: 149-154.

[3] Wang LX, Liu K, Lin GW and Zhai RY. Solitary necrotic nodules of the liver: histology and diagnosis with CT and MRI. Hepat Mon 2012; 12: e6212.

[4] Colagrande S, Paolucci ML, Messerini L, Schima W, Stadler A, Bartolotta TV, Vanzulli A and Brancatelli G. Solitary necrotic nodules of the liver: cross-sectional imaging findings and follow-up in nine patients. AJR Am J Roentgenol 2008; 191: 1122-1128.

[5] Hwang JY, Lee JE and Jung MJ. A challenging case of solitary necrotic nodules of the liver mimicking hepatic metastases: CT, MRI, and PET-CT findings. J Belg Soc Radiol 2020; 104: 16.

[6] Zhou Y, Li B, Xu F, Wang B, Li D, Liu P and Yang J. Clinical features of solitary necrotic nodule of the liver. Hepatobiliary Pancreat Dis Int 2008; 7: 485-489.

[7] Deniz K and Coban G. Solitary necrotic nodule of the liver: always benign? J Gastrointest Surg 2010; 14: 536-540.

[8] Kondi-Pafiti AI, Grapsa DS, Kairi-Vasilatou ED, Voros DK and Smyrniotis VE. "Solitary" necrotic nodule of the liver: an enigmatic entity mimicking malignancy. Int J Gastrointest Cancer 2006; 37: 74-78.

[9] Berry CL. Solitary "necrotic nodule" of the liver: a probable pathogenesis. J Clin Pathol 1985; 38: 1278-1280.

[10] Tsui W, Yuen R, Chow L and Tse C. Solitary necrotic nodule of the liver: parasitic origin? J Clin Pathol 1992; 45: 975-978.

[11] Wang HQ, Wu ZS and Li DW. Solitary necrotic nodule of the liver: a report of two cases and review of the literature. Case Reports Hepatol 2011; 2011: 845406.

[12] Gong J, Tu W, Han J, He J, Liu J, Han P, Wang Y, Li M, Liu M, Liao J and Tian D. Hepatic SATB1 induces paracrine activation of hepatic stellate cells and is upregulated by HBx. Sci Rep 2016; 6: 37717.

[13] Wang L, He T, Wan B, Wang X and Zhang L. Orexin A ameliorates HBV X protein-induced cytotoxicity and inflammatory response in human hepatocytes. Artif Cells Nanomed Biotechnol 2019; 47: 2003-2009.

[14] Mason WS, Jilbert AR and Litwin S. Hepatitis B virus DNA integration and clonal expansion of hepatocytes in the chronically infected Liver. Viruses 2021; 13: 210.