

Letter to the Editor

## Simple cholangitis induces extremely and recurrently elevated serum carbohydrate antigen 19-9 level

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To the Editor:

The carbohydrate antigen 19-9 (CA19-9) is a tumor marker which is usually used in biliary and pancreatic malignancies [1]. However, the specificity of CA19-9 can be reduced by biliary inflammation and other benign diseases [2]. Generally, the level of CA19-9 in benign diseases is less than 100 U/mL, whereas the serum level of CA19-9 can rise to 500 U/mL or even higher than 1000 U/mL in some cases with chronic pancreatitis [3]. Marrelli et al. [4] reported that CA19-9 may be elevated in 61% of benign cases. Moreover, the level of CA19-9 may rise to over 1000 U/mL in patients with choledocholithiasis. Sheen-Chen et al. [5] reported a case of acute cholangitis with extremely elevated serum CA19-9 (5673.8 U/mL). After one month of treatment, the level of CA19-9 returned to normal (10.4 U/mL). We reported here a patient with simple cholangitis who had recurrent elevations of CA19-9 which is rare in previous studies.

A 90-year-old woman was admitted to our hospital due to symptoms of jaundice, darkened urine, fever (around 38 °C) and abdominal pain. She complained of recurrent abdominal pain for one year. The physical examination revealed scleral icterus, jaundice and epigastric tenderness. The laboratory indices were as following: white blood cells (WBC)  $10.5 \times 10^9/L$ , total bilirubin (TBil) 72  $\mu\text{mol/L}$ , direct bilirubin (DBil) 39  $\mu\text{mol/L}$ , and serum CA19-9 21045 U/mL (normal range: 0–37 U/mL). Abdominal computerized tomography (CT) and magnetic resonance cholangiopancreatography (MRCP) showed multiple stones in the common bile duct and gallbladder (Fig. 1). Emergency ERCP was required to relieve the obstruction of the bile duct, while a cholecystectomy and exploration of the common bile duct was necessary after the infection was treated. However, the patient and her family rejected the suggestion of surgery and ERCP because of elderly age and high surgical risk. Therefore, the patient received antibiotics, liver-protecting therapy and symptomatic treatment. The level of CA19-9 fell to 2955 U/mL and symptoms were relieved after one week. One month later, CA 19-9 fell within the normal range.

Six months later, the patient came back with the same symptoms (jaundice, darkened urine, fever and abdominal pain). The laboratory indices were: WBC  $16.5 \times 10^9/L$ , TBil 100  $\mu\text{mol/L}$ , DBil 43  $\mu\text{mol/L}$ , and serum CA19-9 8276 U/mL. The radiological images showed the same as the last visit. The patient and her family chose the conservative treatment, and her symptoms were relieved thereafter. Subsequently, the level of CA19-9 fell to 72.59 U/mL one week later, and to normal range one month later.

One year later, the patient visited us for the third time with the same complains (fever, fatigue and abdominal pain). The laboratory indices were: WBC  $12.6 \times 10^9/L$ , TBil 12  $\mu\text{mol/L}$ , DBil 5  $\mu\text{mol/L}$ , and serum CA19-9 28.6 U/mL. The images indicated cholecystitis and multiple stones in the common bile duct. The patient received antibiotics and symptomatic treatment. She was discharged 5 days later after her symptoms were relieved.

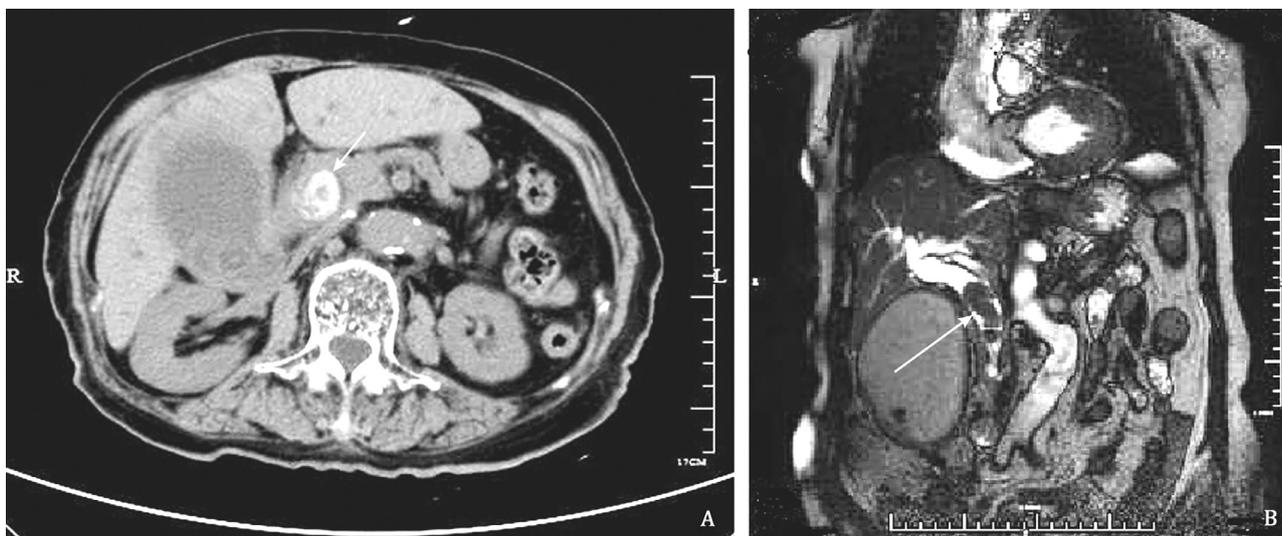
Six months after the discharge, the patient died at home with no clear cause. The patient's family provided a written informed consent to allow us to disclose details of the medical record.

CA19-9 levels are commonly used in the detection of malignant diseases, such as pancreatic cancer, biliary cancer and intrahepatic cholangiocarcinoma [6]. Liu et al. reported an elevation of CA19-9 levels in 70%–90% pancreatic-biliary adenocarcinoma with obstructive jaundice [7]. However, elevated levels of CA19-9 can also be found in patients with benign obstructive jaundice, such as choledocholithiasis, cholangitis and Mirizzi syndrome [8]. In our case and some other reports, extremely elevated levels of CA19-9 could be detected in benign diseases. Morinaga et al. [9] reported an extremely elevated level of CA19-9 (>12,000 U/mL) in a patient with multicystic biliary hamartoma, and the level of CA 19-9 was reduced to normal range 5 months later.

The mechanism behind the elevation in levels of CA19-9 in cases of benign diseases is not clear, the possible explanations are: (1) the increased biliary pressure may induce the bile duct cells to produce more CA19-9; (2) the obstruction and inflammation of bile duct may increase the generation of CA19-9; (3) obstruction and the increased biliary pressure may cause a certain amount of CA19-9 reflux into the circulation; (4) the inflammatory cytokines, which were produced in cholangitis, may also be involved [10]. Morris-Stiff et al. demonstrated that the level of CA19-9 directly correlates with the serum bilirubin in benign diseases [11]. Other

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**Fig. 1.** **A:** The abdominal CT scan showed the multiple stones (arrow) in the common bile duct and the enlarged gallbladder. **B:** The magnetic resonance cholangiopancreatography images showed multiple stones (arrow) in the common bile.

reports showed that the elevation of CA19-9 is related to biliary inflammation [1,5]. Thus, the extremely elevated levels of CA19-9 are related to the inflammation and obstruction of the bile duct.

Our patient had recurrent elevation of CA19-9, and the mechanisms might be the biliary inflammation and obstruction. The patient came to our hospital for three times. At the first two times, the levels of CA19-9, WBC and total bilirubin recurrently rose simultaneously. Also, no malignant diseases were found in the CT scan or MRCP. However, at the third time the patient was admitted, the level of WBC increased while the levels of CA19-9 and TBil were normal. It is possible that the temporary obstruction of the common bile duct induced the cholangitis. As the obstruction was immediately relieved, the CA19-9 produced in the bile duct did not enter the circulation. Therefore, the patient exhibited symptoms of inflammation without any elevation of serum CA19-9. The elevated level of CA19-9 alone is insufficient to distinguish between benign and malignant diseases. A dynamic change of CA19-9 is necessary for the differential diagnosis of malignant and benign as the level of CA19-9 was decreased back to normal after conservative treatment.

In conclusion, extremely high serum level of CA19-9 is not a specific marker of malignancy, and benign diseases may also cause a significant elevation of serum CA19-9 due to inflammation and obstruction of the common bile duct. The dynamic change is helpful in differential diagnosis.

#### Contributors

WYQ and YHJ designed the research. XDL analyzed the data and wrote the paper. XC, ZQF and CML collected the patient's clinical data. All authors contributed to the design and interpretation of the study and to further drafts. YHJ is the guarantor.

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#### Ethical approval

Consent was obtained from relatives of the patient for publication of this report and any accompanying images.

#### Competing interest

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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