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Extreme Elevation of Carbohydrate Antigen 19-9 Linked to a Simple Biliary Cyst: A Case Report

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Authors' contributions

This work was carried out in collaboration among all authors. Authors HK, FG and MD designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors NDK, BB, AHY and IK conducted the literature searches and checked the final version. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Aims: Carbohydrate antigen (CA) 19-9 is produced by epithelial cells in the pancreas, bile ducts, stomach, colon, uterus and salivary glands. It has been shown that CA 19-9 levels are also detected high in ovarian cysts, chronic renal failure, rheumatic diseases, thyroid diseases and some lung diseases, in addition to hepato-pancreatobiliary diseases. However, it is not clearly

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known whether there is a relationship between very high CA 19-9 results and the presence or severity of the disease. There is no consensus in the literature on how to proceed in cases of CA 19-9 detected in screenings or coincidentally. In this case, we present the approach to a patient who was detected to have a giant cystic lesion in the liver in screenings performed due to coincidentally high CA 19-9 levels.

Presentation of Case: In the case we present, a 56-year-old female patient was found to have extremely high CA 19-9 levels (8634 U/mL) in laboratory tests performed due to chronic abdominal pain. A giant cystic lesion was detected in the liver in the imaging studies performed afterwards. Due to the pain symptoms caused by the cyst, a hepatectomy surgery was performed that included the liver segments where the cyst was found. The pathology result was found to be a "simple biliary cyst". CA 19-9 levels decreased rapidly in the postoperative period and were observed to return to normal during follow-ups.

Discussion and Conclusion: We frequently observe that CA 19-9 is elevated in healthy individuals due to unnecessary test requests. It is known that CA 19-9 elevation associated with benign diseases has no clinical significance and does not need to be followed up. Since CA 19-9 is also known as a tumor marker, malignancy screenings or follow-up protocols are performed when high CA 19-9 levels are detected. Routine use of the CA 19-9 test as a screening tool is not recommended. However, it is beneficial to perform further examinations in patients with unexpectedly high levels.

Keywords: Biliary cyst; carbohydrate antigen 19-9; liver cyst; tumor marker.

1. INTRODUCTION

Tumor markers are produced by the tumor itself or in response to the tumor. These can be measured in the blood or body secretions. An ideal tumor marker is expected to be tumor specific. However, it is desired that it does not increase in healthy individuals or benign diseases [1].

Carbohydrate antigen 19-9 (CA 19-9), also known as Sialyl Lewis-a, is one of the most commonly used tumor markers. CA 19-9 is produced by the pancreas, ductal cells in the biliary system, stomach, colon, endometrium and epithelial cells in the salivary glands. It can be detected high in pancreatic, biliary tract, hepatocellular and gastrointestinal malignant diseases. However, it is also known to increase in pancreatitis, pancreatic cysts, liver cysts, cholestasis, and some urological, pulmonary and gynecological benign diseases [2].

We present our case, who underwent surgery with a preliminary diagnosis of biliary cystadenoma, which showed a progressive increase in blood tests and a very high CA 19-9 level, and whose pathology result revealed a simple biliary cyst.

2. PRESENTATION OF CASE

A 56-year-old female patient with no history of any abnormalities was admitted to the general surgery clinic with intermittent right upper quadrant abdominal pain for a long time. Physical examination revealed no findings other than minimal tenderness in the right upper quadrant, and routine laboratory tests were within the normal reference range. Tumor markers were also studied because of breast cancer and pancreatic cancer in the family history. CA 19-9 was measured as 3991 U/mL (0-27), alpha feto protein (AFP): 4.64 ng/mL (0-7), and carcinoembryonic agent (CEA): 3.44 µg/L (0-3.8). Abdominal ultrasonography (USG) revealed an anechoic cystic lesion measuring 70 x 50 mm in the posterior right lobe of the liver. Indirect hemagglutination test performed for possible hydatid cyst was negative. In thoracoabdominal computed tomography (CT), the cystic lesion in the liver was evaluated in favor of hydatid cyst, while abdominal magnetic resonance imaging (MRI) was evaluated as suspicious for biliary cystadenoma (Fig. 1).

The patient, whose CA 19-9 value increased to 8634 U/mL in a period of approximately six weeks, was taken to surgery with a liver resection plan. The patient was given adequate information before the surgery and an informed consent form was obtained for the surgery. A laparotomy was performed with a reverse L incision and posterior sectionectomy surgery was performed including liver segments 6 and 7 where the cyst was located. No complications were observed in the patient, who was followed up in the ward during the postoperative (PO) period. The CA 19-9 level studied at the 72nd

hour PO was determined as 2946 U/mL. The patient, whose general condition was stable, was discharged on the 5th day PO. CA 19-9 values measured on the 10th and 20th days PO were determined as 1095 U/mL and 245 U/mL, respectively (Table 1).

The pathology result of the surgical material was reported as "simple biliary cyst" (Fig. 2).

In the patient's PO 3rd and 6th month results, CA 19-9 was measured as 21.2 U/mL and 19.3 U/mL, respectively. The patient continues to be followed up without any problems.

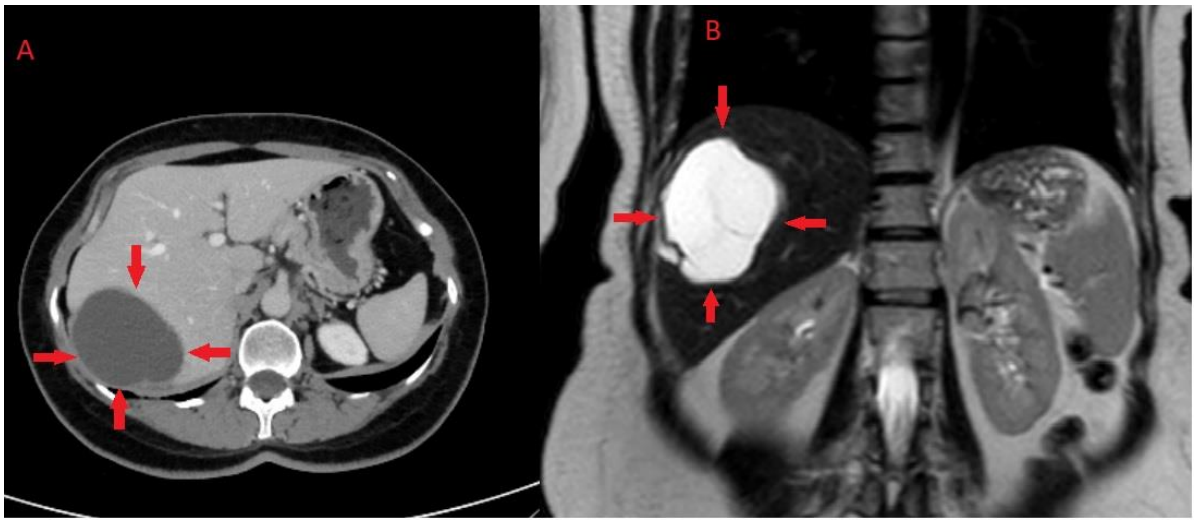

Fig. 1. Image of cystic lesion in the liver by computed tomography (A) and magnetic resonance imaging (B)

Table 1. Preoperative and postoperative CA 19-9 laboratory results

CA 19-9 U/mL (0-27)			
Preoperatif		**Postoperative**	
First Measurement	3991	Day 3	2946
2nd week control	5698	Day 10	1095
4th week control	6192	Day 20	245
5th week control	7902	Day 90	21.2
6th week control	8634	Day 180	19.3

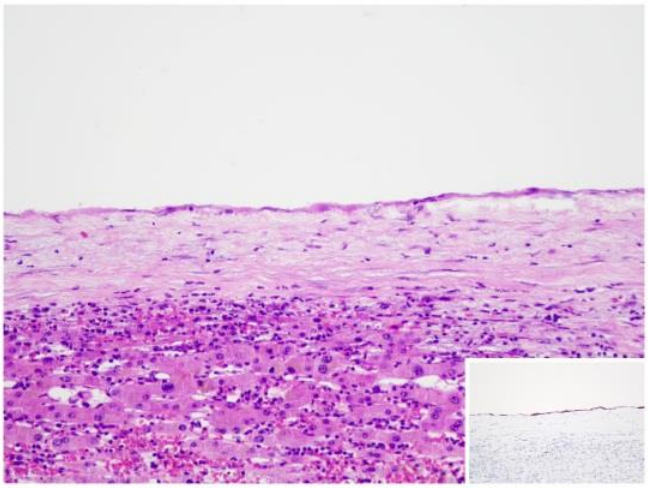

Fig. 2. Microscopic examination shows that the cyst wall was lined with a single layer of flat epithelial cells.Positive cyst epithelium with keratin (Haematoxylin and eosin, scale bar 50 µm)

3. DISCUSSION

CA 19-9 is not a specific marker for cancer, as it can be detected in both malignant and benign pathologies. Therefore, routine CA 19-9 testing is generally not recommended. In a study in which 33,867 people were screened, CA19-9 (>37 U/mL) elevation was detected in only 572 (1.7%) individuals. Only nine of these (1.8%) showed malignancy [3]. Especially very high CA19-9 levels may cause greater concerns for clinicians. As a result of literature review, it has been observed that CA 19-9 is excessively elevated in benign etiologies in many cases. In a case with Mirizzi syndrome, after the CA 19-9 level was determined as 21 068 u/ml, many radiological examinations had to be performed to exclude possible malignancy. In this case, it was reported that CA 19-9 decreased to normal ranges after the elimination of malignancy and choledochal stent was placed with endoscopic retrograde cholangiopancreatography [4]. A similar case was reported in which the elevation of CA 19-9 due to choledocholithiasis and cholangitis decreased to the normal range after bile drainage [5]. Kim et al. reported in their study that cancer suspicion should be investigated if the initial CA 19-9 level is ≥ 80 U/mL or if there is a significant increase in CA 19-9 during the 3-month follow-up period [6]. Unnecessary screenings may be performed at CA 19-9 levels detected slightly above the normal range. As a result of processes leading up to the positron emission tomography (PET) scan, more additional tests must be performed. Duzkoylu et al. particularly emphasize the burden on the health system of performing more tests to clarify areas of moderate involvement following PET scanning [7]. In patients with elevated CA 19-9, cystic liver lesions can be detected with abdominal imaging techniques such as USG, CT and MRI. Although simple cysts are the most common cystic liver disease, it is not always possible to distinguish complicated cysts, hydatid cysts, cystadenoma and cystadenocarcinoma [8]. In the case we presented, both thoracoabdominal CT and abdominal MRI were used as a screening for possible malignancy due to the presence of very high CA 19-9. The prevalence of simple liver cysts (SHC) in the general population varies between 2.5% and 18%. It has been reported that the incidence of premalignant or neoplastic lesions in patients with symptomatic SHC can be up to 5% [8,9]. Polette et al. found in their study including 50 patients with radiological SHC that intracystic CA 19−9 value did not distinguish between simple cysts and cystic liver neoplasms. Therefore, they recommended surgical removal of the cyst wall and pathological analysis as the most effective treatment for symptomatic SHCs [9]. Budkule et al. reported that they performed a left hepatectomy in a patient with a CA 19.9 level of 212,000 u/mL to perform an R0 resection, even though no malignancy was detected in the frozen section analysis of the cyst wall during surgery [10]. Since the preliminary diagnosis of our case was evaluated as “biliary cystadenoma” in the multidisciplinary clinical council, a decision for surgical resection was made. Therefore, no intervention was required to measure intracystic CA 19-9 levels.

In recent years, laparoscopic fenestration technique has become prominent in the removal of SHCs. However, in these cases, there is an approximately 8% risk of conversion to open surgery and a 10-25% risk of recurrence during follow-up. Therefore, laparoscopic fenestration is recommended for easily accessible, superficial cysts, while open surgery is recommended for posteriorly located cysts or potentially malignant cases [11]. We preferred the open surgical approach in our case because the cystic liver lesion was in the posterior segments. In a case where a right hepatectomy was performed with a preliminary diagnosis of biliary cystadenocarcinoma with a CA 19-9 level of 68.661 U/mL, a benign cyst adenoma was detected as a result of pathology. The CA 19-9 value of the same patient decreased to 484 U/mL on the 5th day of PO [12]. Similarly, in our case, we found that the CA 19-9 levels, which increased progressively in the preoperative period, rapidly decreased in the postoperative period (Table 1). A study conducted in China found significantly elevated levels of CA19-9 in the bloodstream of patients with type 2 diabetes and suggested that CA19-9 could be used as a potential biomarker in the detection of diabetes complications [13]. Therefore, although CA 19-9 is known as a tumor marker, the clinical significance of its high detection is a comprehensive issue that should be addressed together with other patient-related factors.

4. CONCLUSION

Since the CA 19-9 test alone does not indicate the presence of a malignant or benign lesion, routine testing is not recommended. It is useful to perform radiological screening of patients with elevated CA 19-9 or to perform tumor marker studies of patients with cystic lesions in the liver.

Lesions considered premalignant or malignant should be surgically removed and the diagnosis should be confirmed with pathology.

CONSENT

"All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal."

ETHICAL APPROVAL

"All authors declare that this case report was approved by the Clinical Chief and was carried out in accordance with the ethical standards set forth in the 1964 Helsinki Declaration."

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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