Huge Splenic Cyst with High Level of CA 19-9: the Rule or the Exception?

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Splenic cysts are rare entities; most are asymptomatic and are discovered incidentally. Symptomatic and large non-parasitic splenic cysts are generally treated surgically [1]. CA 19-9 is a glycoprotein that is present in glandular epithelial cells, specifically in ductal cells of the salivary glands, biliary epithelium, pancreatic ductal epithelium, and metaplastic mesothelial cells. Elevated levels are present in patients with benign conditions such as cirrhosis, cholangitis and pancreatitis, but also in pancreatic, biliary and gastrointestinal carcinomas where it serves as a tumor marker [2]. In the last decade, approximately 30 cases of epithelial splenic cysts associated with high serum concentrations of CA 19-9 were reported.

We present a patient with an epithelial splenic cyst accompanied by high levels of CA 19-9 in the serum. We suggest that the relationship between the two may be the rule rather than the exception. We recommend routine pre- and postoperative monitoring of the levels of this marker upon suspicion of splenic cysts. This case study contributes to current knowledge regarding the association between splenic cysts and the CA 19-9 marker.

PATIENT DESCRIPTION

A 32 year old woman was referred to our department by her general practitioner for investigation of a large abdominal cystic lesion. The patient was 4 months postpartum and suffered from long-standing abdominal pain and discomfort that started 2 years prior to the current hospital admission. She complained of early satiety and had lost 10 kg in the previous year. Prenatal follow-up had not revealed any pathological findings and the delivery was normal. However, abdominal pain increased after the delivery. The patient's medical history was unremarkable for any abdominal trauma or close animal contact, B symptoms (intermittent fever, drenching night sweats) or recent infections. On physical examination, a huge abdominal mass occupying her left abdomen was palpated. The mass was smooth and non-tender. The liver was not enlarged and lymphadenopathy was not detected.

Routine laboratory tests were within normal limits, as were serological tests for parasitic infection by *Echinococcus granulosus*. Tumor marker levels were CA 19-9 1300 u/ml (normal levels < 40 u/ml) and carcinoembryonic antigen 20 ng/ml (normal levels < 2.5 ng/ml).

Ultrasound of the abdomen revealed a huge cystic lesion in the left upper abdominal quadrant. Within the cyst an echogenic non-vascular mass measuring 3.8 cm in diameter was observed. This mass was free of any attachments and was moving freely within the cystic fluid with gravitation. A computed tomography scan of the abdomen showed the same findings. There were no clear margins between the lesion and the spleen or the tail of the pancreas, and no vascular involvement was noted. Aspirated fluid from the cyst showed amylase levels similar to those in the serum, and the cytology analysis did not reveal malignant cells. Unfortunately, the cyst fluid was not examined for marker level.

At laparotomy a huge cyst was found emerging from the upper pole of the spleen. The cyst was extensively adherent to the left diaphragm [Figure]. These findings resulted in total splenectomy, which was followed by an uneventful postoperative recovery.

During the 4 weeks after the operation, CA 19-9 dropped to 60 u/ml and CEA to normal. Pathological examination revealed a benign epithelial splenic cyst. The oval mass that was present within the empty cyst was a thick tissue composed of dense fibrin deposits.

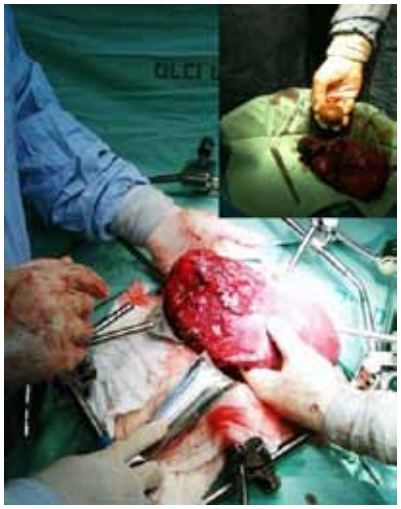
COMMENT

We describe a large splenic cyst in a young woman. The clinical and pathological findings suggested a non-parasitic true cyst of the spleen. Splenic cysts can be either true cysts or pseudocysts depending on the presence or absence of an epithelial lining, respectively. Pseudocysts are usually post-traumatic, commonly representing an organized and liquefied sub-capsular splenic hematoma. They account for 75% of all non-parasitic splenic cysts, although 30% of patients do not recall any trauma [1]. Pseudocysts can also occur after infections such as infectious mononucleosis or malaria, or following infarction of the spleen.

Primary true cysts are subdivided into parasitic – usually the result of *Echinococcus granulosus* infection – and

CEA = carcinoembryonic antigen

The surgical field (main picture), taken from caudal to cranial. The empty cyst of the spleen is shown in its upper pole. The small picture shows the oval mass following extraction from the cyst cavity



non-parasitic, which account for only 10% of all benign splenic cysts. Primary non-parasitic true cysts are further subdivided into congenital and neoplastic. The histological features of the epithelial lining within congenital non-parasitic true cysts render an additional subclassification:

- angiomatous cysts (derived from endothelium), which represent lymphangiomas and hemangiomas
- epidermoid cysts, which comprise 90% of all congenital cysts and have stratified non-keratinizing squamous epithelium
- mesothelial cysts, which have low cuboidal to low columnar epithelium
- dermoid cysts, which have squamous lining with dermal structures [3].

The histopathological sequences leading to the evolvement of primary cysts are not well understood.

Regardless of the pathological origin and pathogenesis, the clinical presentation of non-parasitic splenic cysts has common features including early satiety, nausea, vomiting and weight loss. Left-sided abdominal or epigastric pain radiating to the left shoulder is also common. On physical examination a painless abdominal mass or splenomegaly may be encountered. Laboratory results may reveal thrombocytopenia or anemia [1]. However, the clinical importance of splenic cysts is due to their potential to rupture, to be infected or to bleed, and due to the potential of a serious differential diagnosis of a cystic neoplasm in the left upper abdomen. A cystic tumor of the pancreas should always be considered and ruled out.

Symptoms of pain and weight loss, together with the size of the lesion, prompted the abdominal exploration in our patient. A partial splenectomy was not considered since the diagnosis was not clear and the residual normal spleen was not sufficient (< 25% of the splenic parenchyma). Accepted indications for surgery depend mainly on the clinical manifestations and the size of the cyst. A non-operative approach is the treatment of choice if the diameter of the cyst is less than 5 cm. If the cyst is symptomatic or larger than 5 cm (this cutoff point is determined by the risk for rupture), surgical intervention is advised [1].

Common imaging modalities such as ultrasound or CT scanning are not always useful for determining whether a cystic lesion originates from the tail of the pancreas, the gastric wall, or the spleen. Therefore, additional non-operative modalities have been implemented in the preoperative workup of patients with left upper abdominal cystic lesions. Among them is the acquisition of serum markers. An association between serum levels of CA 19-9 and splenic cysts was first reported in 1994. Terada et al. documented a huge splenic cyst in a 21 year old female patient with a CA 19-9 level exceeding 800 U/ml [4].

Epithelial splenic cysts are commonly diagnosed in the second and third decade of life. Approximately two-thirds of the patients are females [1]. More than 30 cases of benign true splenic cysts associated with elevated CA 19-9 serum levels have been published. Most patients, as expected, are young women.

For the majority, the origin of this tumor marker is the inner epithelial lining of the cyst, as demonstrated by histochemical analysis. Our patient had an elevated CEA level as well, which dropped to normal after surgery. The association of elevated CEA levels and true splenic cyst was reported in the past, though to a lesser extent [5]. The postulated theory for this finding, as for the elevated levels of CA 19-9, is the variability of the cellular differentiation lines of the cells in the cyst wall.

Additional cases of elevated levels of CA 19-9 in patients with splenic cysts have raised the question whether such a finding is the rule or the exception. A splenic cyst with normal level of CA 19-9 in this clinical and histological scenario has also been reported [4]. The current report illustrates an example of what appears to be the rule for the clinical scenario of epithelial splenic cysts: high levels of CA 19-9, which drop to normal a few weeks after removal of the lesion. The occurrence of true epithelial cysts containing large areas of fibrous tissue or mesothelial cells that have only partially undergone metaplasia, as suggested by Pinder et al. [4], seems to be the exception and not the rule. We suggest that every cystic lesion of the spleen with normal serum levels of CA 19-9, for which a mesothelial cyst is suspected, be subjected to further differential diagnosis.

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