

Increased serum levels of carbohydrate antigen 19-9 related to epithelial splenic cyst: a case report

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ABSTRACT

Epithelial cystic lesions of the spleen are a relatively rare entity which should be differentiated from secondary (pseudo-)cysts or echinococcal cysts. These cysts have been associated with increased serum levels of carbohydrate antigen (CA) 19-9. A 29-year old woman presented to our department complaining of fever and diarrhea. Imaging revealed the presence of a multi-lobar cystic lesion of the spleen. Serum CA 19-9 levels were remarkably high (3781.47 U/ml) and serology for Echinococcus was negative. The patient underwent total splenectomy. After 7 weeks of follow-up, CA 19-9 levels have returned to normal. The possibility of an epithelial splenic cyst should be included in the differential diagnosis of a splenic cystic lesion, especially when the anti-echinococcal antibodies are negative. Surgical procedures currently aim for conservation of as much splenic tissue as possible.

Key words: epithelial splenic cyst, CA 19-9.

INTRODUCTION

Non-parasitic, benign cystic lesions of the spleen are relatively rare. (1) They are categorized into false (or pseudo-)cysts and true cysts. The latter category is further divided into mesothelial and epithelial groups depending on the type of its cellular endothelial lining. There are several reports in medical literature concerning the relation between true splenic cysts and high serum levels of carbohydrate antigen (CA) 19-9. (2-15) We report another case of a true splenic cyst accompanied by unusually high levels of CA 19-9 in a patient who was complaining of fever and diarrhea.

CASE PRESENTATION

A 29-year old woman was admitted to our department with diarrhea, intermittent, sharp abdominal pain, malaise, and fever. The patient had a negative medical history.

Physical examination revealed abdominal tenderness, increased bowel sounds, and a palpable spleen 3 cm under the left costal margin. Laboratory tests showed an elevated level of CA 19-9 and cancer antigen 125 (CA 125): 3781.47 U/ml and 66.7 U/ml respectively (normal laboratory

values are ≤ 37 and ≤ 31.3 U/ml). Other tumor markers (Carcinoembryonic antigen-CEA, CA 15-3, and alpha fetoprotein) were within normal levels. Stool samples were negative for occult bleeding, Clostridium difficile toxin A, and parasites. Serologic testing for antibodies against Echinococcus granulosus was negative.

Abdominal ultrasonography revealed a multilobular cyst on the upper pole of the spleen; this finding was further confirmed by computed tomography. Magnetic resonance imaging was used to measure the dimensions of the cyst (60.13×47.15 mm).

The patient had no history of abdominal trauma, and since the serologic test for Echinococcus was negative, it was hypothesized that the elevated CA 19-9 and CA 125 levels were related to the newly found splenic cyst. During the patient's hospitalization, the CA 19-9 and CA 125 levels continued to rise (8640 U/ml and 95.5 U/ml respectively).

The patient was discharged 8 days after admission with the diagnosis of gastroenteritis. The splenic cyst was scheduled to be surgically removed.

Subsequently, the patient was electively admitted

to the surgical department of our hospital. The serum CA 19-9 level was 2800.08 U/ml and the CA 125 was 56.9 U/ml at that presentation. Pre-operatively, the patient was vaccinated against *Streptococcus Pneumoniae* and *Haemophilus influenzae* type B. She underwent a total open splenectomy as scheduled. Surgical specimen weighed 180 gr and included a multilobular cyst containing gelatinous-mucous fluid (Figure 1).



Figure 1. The multilobar splenic cyst (operative specimen)

Fluid culture did not yield any pathogen and cytology was negative for malignancy. Histologic examinations revealed that the endothelial lining consisted mostly of single-layered (and locally multi-layered) squamous epithelium. Immunohistochemical analysis showed that the epithelial lining was positive for CA 19-9, CEA, and cytokeratin 5/6, but negative for calretinin. (Figure 2) A formal diagnosis of an epithelial splenic cyst was made.



Figure 2. Endothelial lining consisting mostly of single-layered (and locally multi-layered) squamous epithelium. Immunohistochemical analysis showed that the epithelial lining was positive for CA 19-9, CEA, and cytokeratin 5/6, but negative for calretinin.

The postoperative course was uneventful and the

patient was discharged 4 days after surgery. Seven weeks later the serum levels of CA 19-9 and CA 125 have returned to normal range (26 U/ml and 18.5 U/ml respectively).

DISCUSSION

The majority (~90%) of non-parasitic splenic cysts do not have inner epithelial lining (pseudocysts), and are considered secondary to, often unremarkable, trauma.(1) On the other hand, the models proposed for the pathogenesis of true splenic cysts include embryonic inclusion of epithelial cells from adjacent tissues, or post-traumatic invagination of mesothelial cells.(3) It had also been proposed that epithelial cysts are derived from mesothelial cysts sustaining squamous metaplasia. Additionally, there is some evidence that epithelial cysts may slowly lose their lining wall, becoming over time similar to, and impossible to differentiate from, pseudocysts. Epidermoid cysts with CA 19-9 overexpression have been described in accessory splenic tissue as well.(5,9) Familial cases, though rare, have also been described.(4,10)

One remarkable feature of our case was that although the epithelial cells were positive for CEA, its levels remained normal during the patients' follow-up period. Increased CEA levels often accompany the CA 19-9 levels in epithelial splenic cysts.(6,11,12,13) However, there have been reports of CEA expression and increased CEA levels inside the cystic fluid, without corresponding elevation in serum CEA levels.(4,9,10) Although immunohistochemistry for CA 125 was not performed, it can be assumed that its high levels were also a product of the cyst wall, due to the relative frequency with which it is found in epithelial splenic cysts, (7,8,10,15) as well as the fact that its levels subsided shortly after splenectomy. The combination of positive immunohistochemistry result for CA 19-9, CEA, and cytokeratins, and negative result for calretinin (an indicator of mesothelial origin) led to a safe diagnosis of epithelial cyst, similar to the results of Palmieri et al.(6)

The possible complications of an epithelial splenic cyst include rupture, hemorrhage, and infection. Atypical symptoms such as left subcostal pain or discomfort are rare when the cyst does not exceed 7-8 cm in diameter. Any symptomatic or

complicated cyst, however, should be surgically removed. Although a total splenectomy was performed to the patient of our case, modern surgical literature suggests procedures that are

either minimally invasive (2,14) or lead to conservation of splenic tissue, including partial splenectomy, cystectomy, or fenestration.

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ΠΑΡΟΥΣΙΑΣΗ ΠΕΡΙΣΤΑΤΙΚΟΥ

Αυξημένα επίπεδα καρκινικού αντιγόνου Ca 19-9 σχετιζόμενα με επιθηλιακή κύστη σπληνός

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Περίληψη

Η επιθηλιακή κύστη σπληνός είναι μια σπάνια καλοήθης οντότητα, η οποία πρέπει να διαφοροδιαγνωσθεί από τις υδατίδες (εχινokokkικές) κύστες, τις κακοήθους αιτιολογίας κύστες, και τις ψευδοκύστες. Αυτές οι κύστες έχουν σχετισθεί με αυξημένα επίπεδα του καρκινικού αντιγόνου CA 19-9 στον ορό. Περιγράφουμε μία τέτοια κύστη σπληνός ως παραεύρημα σε μία γυναίκα 29 ετών, η οποία προσήλθε στο Τμήμα Επειγόντων λόγω εμπύρετου διαρροϊκού συνδρόμου. Ο υπερηχογραφικός έλεγχος κοιλίας ανέδειξε πολύχρωμο κυστικό μόρφωμα στον άνω πόλο του σπλήνα. Ο αιματολογικός έλεγχος ανέδειξε εξαιρετικά υψηλή τιμή CA 19.9 (3781.47 U/ml) ενώ ορολογικός έλεγχος για αντιεχινokokkικά αντισώματα ήταν αρνητικός. Η ασθενής υπεβλήθη σε ολική σπληνεκτομή. Σε διάστημα 7 εβδομάδων μετά την επέμβαση η τιμή του CA 19.9 είχε επανέλθει σε φυσιολογικά επίπεδα (26 U/ml). Η επιθηλιακή κύστη θα πρέπει να υπεισέρχεται στη διαφορική διάγνωση ενός κυστικού μορφώματος του σπλήνα, ιδίως όταν ο έλεγχος αντιεχινokokkικών αντισωμάτων είναι αρνητικός. Νεότερες χειρουργικές τεχνικές ελάχιστης επεμβατικότητας και διατήρησης του σπληνικού ιστού έχουν προταθεί ως αποτελεσματικότερες λύσεις, ειδικά σε νεώτερης ηλικίας άτομα.

Λέξεις ευρετηρίου: Επιθηλιακή κύστη σπληνός, CA 19-9