A Splenic Epithelial Cyst: Increased Size, Exacerbation of Symptoms, and Elevated Levels of Serum Carcinogenic Antigen 19-9 after 6-year Follow-up

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Abstract

A 58-year-old man, who had presented with a large cyst between the pancreatic tail and splenic hilum 6 years previously, was referred to our hospital with exacerbation of abdominal distention. Computed tomography revealed a well-demarcated, unilocular cyst, with a beak sign for the pancreas, without wall thickening or nodules suggestive of a non-neoplastic cyst. Compared with 6 years previously, the cyst had increased in size from 14.7 cm to 19.5 cm, and the serum carcinogenic antigen 19-9 level had increased from 635 U/mL to 1,918 U/mL. To prevent spontaneous rupture, laparotomy was performed, and the cyst was pathologically diagnosed as a splenic epithelial cyst.

Key words: splenic cyst, epithelial cyst, CA19-9, diagnosis, follow-up, resection

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Introduction

Splenic cysts are uncommon entities and classified as parasitic or nonparasitic cysts (1, 2). The latter are further divided into true cysts, those lined with epithelium or endothelium, and false cysts, those not lined with epithelium (1, 2). Epithelial cysts were reported in 0.07% of 42,327 autopsies (1). They are primarily benign and can be generally differentiated from malignant variants by clinical images (3, 4), including various types of cysts, such as epidermoid cyst, dermoid cyst, and lymphoepithelial cyst (2). However, epithelial cysts are occasionally accompanied by increased levels of serum tumor markers (2, 5), which can impede their diagnosis. They occasionally cause complications, such as rupture (5, 6), infection (7), and bleeding (5, 6), which can be lethal. For these reasons, epithelial cysts, especially large cysts, are often treated by prophylactic surgery. Therefore, the natural history of epithelial cysts has not been previously reported. Epithelial cysts are not specific to the spleen. They can also develop at the pancre-

atic tail, with similar characteristics regarding age, image findings, and elevated serum tumor markers (8-10). We herein describe a patient with a large splenic cyst, which was difficult to differentiate from a cyst of pancreatic origin, who was followed up for 6 years. The cyst was eventually surgically resected due to an increase in size and exacerbation of the patient's symptoms.

Case Report

A 52-year-old man was referred to our hospital for an investigation of a cystic lesion located between the pancreatic tail and splenic hilum. The cyst was accompanied by pain in the left-upper abdomen. Computed tomography (CT) revealed a well-demarcated, unilocular cyst (14.4×11.6×14.7 cm), with a beak sign for the pancreas, but without wall thickening or mural nodules (Fig. 1). Magnetic resonance imaging (MRI) demonstrated high-intensity signals on both T1- and T2-weighted images, thus suggesting a concentration of the fluid with the protein rich contents, and no obvious communication with the pancreatic duct on magnetic

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Figure 1. Enhanced computed tomography (CT) [horizontal (A) and coronal (B) views] at the initial presentation showing an unilocular cyst, 14.7 cm in maximum diameter, in the upper left quadrant with a beak sign in the pancreas (small arrow).

Figure 2. A T2-weighted magnetic resonance image (MRI) at the initial presentation showing a very high-intensity signal within the cyst (A). Magnetic resonance cholangiopancreatography (MRCP) showing no obvious communication between the pancreatic duct and the cyst (arrow pointing to the visible end of the main pancreatic duct) (B).

resonance cholangiopancreatography (MRCP) (Fig. 2). The patient had a history of diabetes mellitus and hypertension, but his family history was unremarkable. His condition was uneventful until this onset and negative for findings suggestive of a parasitic infection. Although the cyst was large and associated with an elevated level of serum carbohydrate antigen 19-9 (CA-19-9) (635 U/mL, normal: <37 U/mL), a non-neoplastic cyst (11) was strongly suspected, and the patient selected observation rather than surgery at that time.

However, 6 years later, the patient was again referred due to exacerbation of abdominal distension, leading to fears that the cyst had ruptured. He requested endoscopic cystic drainage from the stomach (12). During the intervening period, the patient had been in good health and denied any traumatic episodes. The serum CA19-9 level was elevated to 1,918 U/mL, and the cyst had increased in size to 19.5 cm (18.3×14.8×19.5 cm) (Fig. 3). The CT and MRI findings

were mostly unchanged, except for the size of the cyst. An endoscopic ultrasound (EUS) image showed an echolucent fluid-containing lesion attached to the pancreas, without septa or calcification (Fig. 4). These imaging findings and the elevated level of serum CA19-9 strongly suggested an epithelial cyst, either epidermoid (5) or lymphoepithelial (11), of the pancreas or spleen. Intra-abdominal leakage of cystic fluid may cause severe complications (11, 13, 14), and surgery rather than endoscopic cystic drainage was strongly recommended (12).

On laparotomy, the cystic mass was adhered to the spleen and easily detachable from the pancreas and other surrounding viscera. Thus, splenectomy was performed. The cyst was filled with 2,500 mL of serous brown fluid. Rapid cytology of the fluid revealed no atypical cells. The cyst was pathologically proven to be of splenic origin. It was covered with a single layer of squamous epithelium and was diag-

Figure 3. Enhanced CT of the horizontal (A) and coronal (B) views at the second presentation, showing a growing cyst, 19.5 cm in diameter.

Figure 4. Endoscopic ultrasonography (EUS) showing the cyst attached to the pancreas.

Figure 5. The gross appearance of the en bloc resected cyst and spleen (A) and histology of the cyst wall (B). The cyst was incised and decompressed by excluding 2,500 mL of fluid content (A). A stratified, flattened squamous epithelium was visible on the cystic wall (Hematoxylin and Eosin staining, 100×) (B) and immunohistochemically positive for CA19-9 (100×) (C)

nosed as an epithelial cyst of the spleen (Fig. 5). The post-operative course was uneventful, and the serum CA19-9 level decreased to within the normal range in 2 months. During the 2-year postoperative follow-up, there was no evidence of recurrence or other associated complications.

Discussion

With the recent expansion of medical screening systems, the detection of splenic lesions has increased by 0.5-

Table. Reported Cases of Splenic True Cysts Larger than 15 cm (n=22).

Reference No.	Sex	Age	Size (cm)	Diagnosis	Symptom	CA19-9 (U/mL)	Complication	Treatment
30	F	29	18	mesothelial	abdominal pain	NA	none	splenectomy
31	F	21	16	epithelial	abdominal pain	830	none	splenectomy
32	F	12	20	epidermoid	abdominal pain	NA	none	splenectomy
23	F	16	16	epithelial	abdominal pain	NA	none	hemisplenectomy
24	F	26	16	epidermoid	abdominal pain	217	none	laparoscopic splenectomy
33	M	22	18	epithelial	heavy feeling in stomach	502	none	splenectomy
34	F	32	20	non-parasitic	abdominal pain	NA	none	splenectomy
35	F	19	18	epithelial	abdominal pain	273	none	laparoscopic splenectomy
36	F	18	19	epidermoid	abdominal fullness	122	none	laparoscopic splenectomy
37	F	41	20	epidermoid	abdominal pain	NA	none	splenectomy
21	F	32	18	epidermoid	abdominal pain	NA	ruptured	laparoscopic splenectomy
38	F	15	15	epithelial	abdominal fullness	NA	none	splenectomy
39	M	19	15	epithelial	abdominal distension	NA	none	partial splenectomy
28	F	23	17	non-parasitic	abdominal pain	NA	infected (Staphylococcus aureus)	aspiration, splenectomy
40	-	14	20	epidermoid	abdominal distension	NA	none	laparoscopic splenectomy
40	-	11	18	epidermoid	abdominal pain	NA	none	laparoscopic splenectomy
41	F	25	18	epidermoid	epigastric pain	NA	none	laparoscopic splenectomy
42	F	18	20	epidermoid	abdominal pain	88	none	laparoscopic splenectomy
43	F	22	25	epithelial	abdominal pain	66	none	laparoscopic splenectomy
44	M	9	21	epidermoid	abdominal pain	NA	none	laparoscopic splenectomy
45	F	30	20	epidermoid	liver dysfunction	491	none	splenectomy
Current Case	M	58	19.5	epithelial	abdominal pain	1918	none	splenectomy

2% (15). Primary splenic epithelial cysts are uncommon, with only 800 cases reported in the English literature (2). The natural history of these cysts remains unclear because most reported cases have been surgically resected, rather than followed up, to prevent spontaneous rupture, infection, and bleeding (5-7). In the present case, the splenic epithelial cyst, the origin of which was difficult to identify preoperatively, was associated with exacerbation of symptoms, elevated serum CA19-9 levels, and an increased size after 6 years of follow-up.

Concerning the preoperative diagnosis of the current case, an epithelial cyst (10), including epidermoid (8) or lymphoepithelial (9, 11) cysts, was strongly suspected due to the extremely high level of serum CA19-9 (2, 5, 8, 9).

Because inner epithelial cells of the cyst produce CA19-9, which is retained within the cyst, increased intracystic pressure is thought to move the exuding of CA19-9 into the bloodstream through the surrounding splenic tissues. The

level was disproportionate to the negative imaging findings and suggestive of malignancy. However, the origin of the cyst (pancreatic or splenic) could not be determined. On CT images, the beak sign (16) is often used to differentiate the origin of a cyst not attached to adjacent organs, as was performed in the current case (Fig. 1, 3). A significant trend may be observed in the cyst's size. According to a literature survey, non-neoplastic epithelial cysts of the pancreas tend to be smaller (mostly <12 cm) (8-10) than those of the spleen (average 14.3 cm (17)) (≥ 15 cm, Table). Caution is needed when judging the organ of origin of non-neoplastic cysts attached to both the pancreas and the spleen in clinical images, especially when they are relatively small. The origin can include the gastric wall and mesentery.

If we presume that the current cyst had an ellipsoid body, then the volume of the cyst at the time of the initial presentation was 1,285 mL. After 6 years, it was 2,764 mL, which was nearly the amount of fluid surgically aspirated from the

cyst. Within the 6 years, the volume of the cyst increased more than twice that of the original volume (doubling time: 1,832 days), and this was accompanied by a parallel increase in the level of serum CA19-9 (635 to 1,918 U/mL). Branch duct type, intraductal papillary mucinous neoplasms of more than 3 cm in size typically develop into cysts quite slowly (18). Although data are available for only one case (the current case), the speed of growth of splenic epithelial cysts may be faster than that of cystic neoplasms. Thus, to avoid potential critical events, surgical treatment is recommended for splenic epithelial cysts.

The indications for surgical treatment of splenic epithelial cysts have generally been a symptomatic cyst or an asymptomatic cyst of ≥ 5 cm (17, 19). Observation is recommended for small, asymptomatic cyst (17), as spontaneous regression can be expected (20). However, this agreement is based on the facility of surgical treatment, rather than solid data. According to recent reviews, the incidence of overall complications in cases of splenic epithelial cysts was 5.2-8.5% (21, 22), and ruptured cysts ranged in size from 5.5 cm to 15 cm or more (20, 23, 24). In an analysis of 23 splenic epithelial cysts, the average size was 14.3 cm (range: 1-25 cm), and none of the cysts were associated with complications, including rupture and infection (17). In a survey of PubMed data on splenic epithelial cysts of ≥ 15 cm in size, only 2 of 22 (9.1%) patients had complications, despite complaints in all 22 cases (22, 25) (Table). Thus, the incidence of splenic epithelial cysts appears to be rare. Simply coughing during an asthma attack can cause cystic rupture (26). Small cysts (5 cm) may spontaneously rupture (27), leading to life-threatening events. In cases of congenital cysts, rupture may occur in infants who often tumble or fall on their stomach (17). Cystic rupture is also common in pregnant women with limited abdominal space (28). The recent surgical trend has shifted from laparotomy to less-invasive, laparoscopic splenectomy. Although cystic decapsulation occasionally causes recurrences, partial laparoscopic splenectomy is excellent in preserving the splenic function (25, 29). Laparoscopic splenectomy also facilitates prophylactic surgery, rather than observation, at the time of the initial diagnosis of a splenic epithelial cyst.

In conclusion, we described a case of a giant splenic epithelial cyst, which grew rapidly and was associated with exacerbated symptoms after 6 years of follow-up. Caution is required when diagnosing the organ of origin of epithelial cysts. Less invasive treatment, possibly laparoscopic partial splenectomy, should be applied in cases with a definitive preoperative diagnosis.

The authors state that they have no Conflict of Interest (COI).

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