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Radiology Case Reports 17 (2022) 19–22

Available online at www.sciencedirect.com

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Case Report

Carbohydrate antigen 19-9-producing splenic cyst: a case report

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ARTICLE INFO

Article history:
Received 9 July 2021
Revised 24 September 2021
Accepted 28 September 2021

Keywords:
splenic cyst
carbohydrate antigen 19-9 (CA19-9)

ABSTRACT

We describe the case of a 40s woman with a carbohydrate antigen (CA)19-9-producing splenic cyst. The lesion was detected incidentally at the splenic hilum, and resected after 5 years of follow-up. Size of the lesion was enlarged from 1.6 cm to 5.3 cm, and serum CA19-9 was elevated from the normal range to 1766 U/ml. Microscopically, CA19-9-producing splenic cyst was diagnosed. It was mimicked pancreatic malignancy due to its location at the splenic hilum. Benign lesions with elevated serum CA19-9 also to be differential diagnosis.

Introduction

Splenic cysts are rare [1], with varying incidence of 0.07 - 0.3% as reported, including true and false cysts [2–4]. In our experience, there are few cases of true splenic cyst or suspected true splenic cyst. Additionally, this case is the first case in our experience, which has been diagnosed as carbohydrate antigen (CA)19-9-producing splenic cyst. More frequent imaging and advancements in imaging have contributed to an increase in the detection of incidental splenic cysts [5]. Although CA19-9 is a well-known marker for pancreatic adenocarcinoma, high levels of CA19-9 may be seen in benign lesions of gastrointestine, hepatobiliary system and the spleen. The first description of a splenic cyst producing CA19-9 was reported in 1991 by Walz et al. [6]. Since then, several cases of true splenic cyst producing CA19-9 have been reported. Imoto et al. reported a case of CA19-9-producing splenic cyst and reviewed 50 cases of CA19-9-producing splenic cysts excluding accessory spleens [7].

We describe the case of a woman with a CA19-9-producing splenic cyst. In this case, other diseases were being followed-up using magnetic resonance imaging (MRI), but the lesion of interest in this report increased in size and serum CA19-9 was greatly elevated at 5 years and 3 months after first identification of the lesion.

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https://doi.org/10.1016/j.radcr.2021.09.063

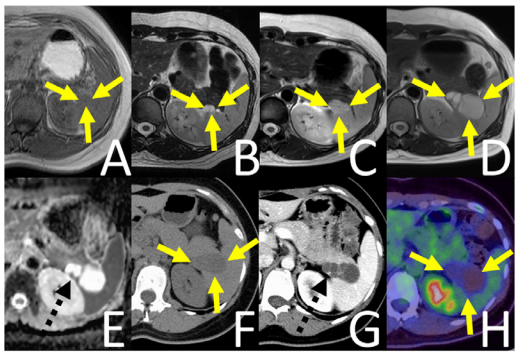

Figure 1 – A, B) T1-weighted (A) and T2-weighted (B) images at first MRI. C) T2-weighted image at 4 years after first identification of the lesion. D, E) T2-weighted image (D) and apparent diffusion coefficient map (E) at 5 years after first identification of the lesion. G) Contrast-enhanced CT at 5 years and 3 months after first identification of the lesion. H) FDG-PET/CT at 5 years and 2 months after first identification of the lesion. Arrows indicate the lesion. Dashed arrows indicate mural nodule-like structures.

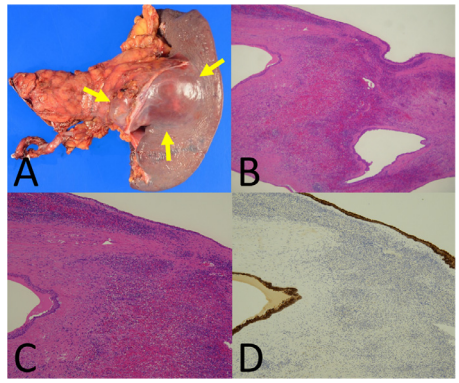

Figure 2 – A) The resected specimen. Arrows indicate the lesion. B, C) Microscopic examination with hematoxylin and eosin staining at ×20 (B) and ×40 (C). D) Cytokeratin AE1/AE3 staining, ×40.

Case report

A woman in her 40s was being followed-up for hepatic cavernous hemangioma. A cystic lesion 1.6 cm in greatest diameter was incidentally detected at the splenic hilum on first MRI. This initial imaging showed a cystic lesion displaying isointense signals on T1-weighted imaging (Fig. 1A) and hyperintense signals on T2-weighted imaging (Fig. 1B). The appearance of the lesion was smooth marginal and multilocular on MRI and ultrasonography. The course of imaging findings and serum concentrations of CA19-9 are shown below (Table 1, Fig. 1).

After about 4 years, the lesion had increased in size to 2.7 cm (Fig. 1C). Five years after the first MRI, the lesion had increased to 5.3 cm (Fig. 1D). Additionally, mural nodule-like structures showing diffusion restriction (0.9×10^{-3} mm^2/s on apparent diffusion coefficient mapping) appeared (Fig. 1E). At that time, serum CA19-9 concentration was 15.5 U/ml (normal, <37 U/ml).

At 5 years and 3 months after first MRI, contrast-enhanced CT showed that lesion size remained basically unchanged. No calcification was evident in the cystic wall. The mural nodule-like structures observed on previous MRI were enhanced (Fig. 1F, 1G). However, serum CA19-9 at that time had increased dramatically to 1766 U/ml. In addition, 2-[^{18}F]-fluoro-2-deoxy-D-glucose-positron emission tomography/computed tomography (FDG-PET/CT) showed no FDG accumulation (Fig. 1H).

A malignant neoplasm such as mucinous cystadenocarcinoma of the pancreas was suspected because the lesion size and serum CA19-9 concentration had increased and mural nodule-like structures had appeared. No contributory findings were obtained from medical history, life history, or family history. Abdominal symptoms were consistently absent. Other than CA19-9 levels, no abnormalities were seen in blood and biochemistry tests.

Laparoscopic distal pancreatectomy and splenectomy were performed. A mural nodule-like structure was also seen on intraoperative ultrasound. Gross inspection of the resected specimen showed a multilocular cystic lesion between the spleen and pancreas tail (Fig. 2A). No infiltration into the spleen or pancreas was observed.

Microscopically, stratified squamous epithelium covered the inner wall (Fig. 2B, 2C). Epithelium showed positive staining for cytokeratin AE1/AE3 (Fig. 2D). Splenic tissues with trabeculae were observed around the lesion. No histological continuity between the lesion and pancreas was observed. No malignant tissue was identified. Findings corresponding to the mural nodule-like structures observed on MRI, contrast-enhanced CT, and intraoperative ultrasound were not identified microscopically. CA19-9 concentration in the cyst fluid exceeded the limit of detection (> 999,999.9 U/ml).

Serum CA19-9 decreased to 16.7 U/ml by 1 month after surgery and to 6.1 U/ml as of 1 year postoperatively. Based on these findings, the final diagnosis was CA19-9-producing

Table 1 – Course of imaging, lesion size and serum CA19-9 concentrations

	First visit	4 years later	5 years later	5 years and 3 months later
Images	MRI	MRI	MRI	contrast enhanced CT
Size (cm)	1.6×0.9	2.7×1.3	5.3×3.5	5.3×3.5
Serum CA19-9 (U/ml)			15.5	1766

splenic cyst. On follow-up 1 year after the operation, no sign of recurrence was seen on either contrast-enhanced CT or serum CA19-9. Written consent was obtained from the patient for publication of the case information.

Discussion

Splenic cysts are rare [1]. The reported incidences are, for example: Roberson detected 2 splenic cysts in 646 splenectomy cases (0.3%) [2].; Robbins et al. reported a review of 42,327 autopsy records revealed 32 benign splenic cysts (0.07%) [3].; Yuri et al. detected a splenic cyst in 1 of 892 cases (0.1%) in mass survey on abdominal ultrasonography [4]. McClure et al. classified splenic cysts into true cysts lined by a membrane with specific secretory capacity and false cysts with no specific lining [1]. False (secondary) splenic cysts are more common overall representing nearly 80% of all splenic cysts [5]. True cysts were subdivided into epithelial, endothelial, and parasitic, while false cysts were subdivided into hemorrhagic, serous, inflammatory, and degenerative liquefaction (caused by infarction).

Urrutia et al. reported on correlations between radiological and pathological findings for cystic masses of the spleen. The characteristics of true cysts were a single, unilocular lesion with thin, smooth walls and no peripheral calcification [8]. In the present case, the lesion was a single, multilocular lesion with thin, smooth walls and no calcification. These findings thus showed overlap of splenic cyst types, and diagnostic imaging was not easy. Although true splenic cysts (including CA19-9-producing cysts) showing multilocularity and wall calcification have been reported [9–11], these are not specific for CA19-9-producing splenic cysts.

Preoperatively, we could not determine whether the organ of origin was the spleen or pancreas. Beak sign, phantom (invisible) organ sign, embedded organ sign and prominent feeding artery sign can be used to identify the organ of origin [12]. In this case, increases in size of the cystic lesion compressed the spleen more than the pancreas, yielding results similar to a mild phantom (invisible) organ sign. Preoperative determination that the lesion was derived from the spleen might have been possible using this sign. Mural nodule-like structures were observed on MRI, contrast-enhanced CT, and intraoperative ultrasound, but no corresponding structures were found histopathologically. We considered that the splenic tissue around the lesion mimicked a mural nodule. We did not perform superparamagnetic iron oxide (SPIO)-enhanced MRI preoperatively. SPIO-enhanced MRI would have contributed to the differentiation between malignant mural nodules and splenic tissue [13]. Irregular cyst walls, mural nodules, and elevated levels of tumor markers reflect malignant tumors [14]. In this patient, the increases in lesion size and level of serum CA19-9 and the appearance of mural nodule-like structure unavoidably suggested malignancy.

Most cases of CA19-9-producing splenic cysts are finally diagnosed based on the following four findings: elevated serum CA19-9; high concentration of CA19-9 in cystic fluid; epithelium showing positive immunochemical staining for of CA19-9; and decreased serum levels of CA19-9 after surgery. Lacum et al. described a case of CA19-9-producing splenic cyst in which a cellular lining was not evident. They considered that the decapsulation technique with suction of cystic fluid may have destroyed the cellular lining [15]. Other cases of primary splenic cysts without epithelial lining have also been reported [16, 17]. Some cases have been reported without immunostaining for CA19-9 [10, 18, 19]. Buda et al. [18] and Paksoy et al. [19] described cases of CA19-9-producing epidermoid splenic cyst in which the squamous epithelium showed positive staining for cytokeratin. Even in our case, the cyst epithelium stained positive for cytokeratin AE1/AE3, and a final diagnosis of CA19-9-producing splenic cyst was considered appropriate. No reasons for the high serum levels of CA19-9 other than the splenic cyst were found.

Most true splenic cysts are epithelial in origin and are thought to contain embryonic inclusions of epithelial cells from adjacent structures [20]. True splenic cysts can be associated with high production of tumor antigens, including carcinoembryonic antigen, CA19-9, CA125, and CA50, detectable in both in the serum and cystic contents [21]. Because the inner epithelial cells of the cyst produce CA19-9, which is then retained within the cyst, increased intracystic pressure may drive exudation of CA19-9 into the bloodstream through the surrounding splenic tissues [22]. Matsui et al. reported a splenic epithelial cyst resected after 6 years of follow-up [22]. In that case, compared with the baseline 6 years previously, the cyst had increased in size from 14.7 cm to 19.5 cm, and serum CA19-9 level had increased from 635 U/ml to 1,918 U/ml. In the present case, follow-up was continued for about 5 years from a state in which the lesion was relatively small and serum CA19-9 levels were normal. The natural history of the splenic cysts remains unclear because most reported cases have been surgically resected, rather than followed up [22].

We have described a rare case of CA19-9-producing splenic cyst that required differentiation from pancreatic malignancy.

Declaration of Competing Interest

none

Acknowledgements

none

Patient Consent Statement

Written consent was obtained from the patient for publication of the case information.

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