Subdiaphragmatic bronchogenic cysts: Case series and literature review

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Bronchogenic cysts are congenital malformations caused by aberrant foregut budding. They major occur in the thorax, with subdiaphragmatic cases being uncommon. Here, we present a series of 19 patients diagnosed with subdiaphragmatic bronchogenic cysts histopathologically at a single institution in China from 2012 to 2021. A literature review was also conducted by searching the PubMed database using keywords related to “bronchogenic cysts” and “subdiaphragmatic,” yielding 107 cases. Taken together, the 126 cases had a median age of 41.0 years (interquartile range, 30.0–51.0 years) and 62 of them were male (49.2%). The cysts were most commonly detected in the left adrenal region (36.2%), followed by the pancreatic region (11.5%) and gastric cardia/lesser curvature of the stomach (9.2%). All patients except two underwent surgery for a definite diagnosis, symptom alleviation, and (or) malignancy prevention. Most patients recovered fast and were discharged from the hospital within 1 week after surgery, and the surgical complications were infrequent. The prognosis was generally favorable, as no recurrence was reported during the follow-up as long as 77 months.

Introduction

Bronchogenic cysts are congenital malformations caused by aberrant budding of the primitive foregut or tracheobronchial tree. They usually locate in the thorax, especially in the mediastinum (1–3). However, they can be found in various atypical locations along the developmental pathway of the foregut, ranging from the pharynx to the spinal canal (4, 5). Bronchogenic cysts can occur infrequently below the diaphragm, with the majority located in the retroperitoneal space, particularly the left adrenal region. Subdiaphragmatic bronchogenic cysts (sBCs) can be asymptomatic, and thus are
usually recognized occasionally by imaging analyses. Nevertheless, symptoms, such as fever, abdominal pain, and nausea, appear when the cysts become infected or expand sufficiently to compress nearby organs (6, 7). Due to their rarity and non-specific imaging presentation, sBCs are frequently misdiagnosed, and only histopathological examination can currently provide a definitive diagnosis. Additionally, though generally benign, malignant transformation was observed in several cases (8). Therefore, up to now, surgical resection has been the only therapeutic strategy to alleviate symptoms, establish a definitive diagnosis, and prevent malignant transformation in patients with sBCs.

Despite the fact that cases of sBCs have been previously reported (6, 7), the sample size was generally small, leading to an obscure understanding of the epidemiology, clinical presentation, diagnosis, and management strategy, et al. Here, we aim to provide a better comprehension of sBCs by presenting a series of 19 patients from a single institution as well as a review of related articles.

**Subjects and methods**

All cases of sBCs from 2012 to 2021 at Peking Union Medical College Hospital in China were retrospectively identified from the hospital information system. Only patients with histopathological diagnoses of sBCs were included in the analysis. Parameters, such as demographic characteristics, clinical presentation, imaging findings, surgical information, and histopathological examination, were extracted from electronic medical records. All patients were contacted by phone in May 2022 for information on recurrence and surgical complications.

For the literature review, PubMed was searched in May 2022 using the following keywords: “bronchogenic cyst”, “bronchial cyst”, “subdiaphragmatic”, “retroperitoneal”, and “abdom.” The detailed search strategy can be found in Supplementary Appendix 1. The inclusion criteria of studies were full-text English articles reporting patient(s) diagnosed as sBCs histopathologically with detailed demographic and clinical information. Unpaired t-test or Pearson’s chi-square test was employed when appropriate. All statistical analyses were performed using SPSS 22.0.

**Case series**

Nineteen patients (4 [21.1%] male; median age, 44.0 years [interquartile range, 35.0–46.5 years]) with histopathological diagnoses of subdiaphragmatic bronchogenic cysts from 2012 until 2021 were identified. Patient demographics are depicted in Table 1. Fourteen patients (73.7%) were asymptomatic and discovered the cyst by accident, either during a regular check-up (n = 12) or a radiographic examination done for unrelated indications (n = 2). Among the symptomatic patients (n = 5), two complained of flank pain, one of abdominal pain, one of coughing, and the other of acid reflux and abdominal distention. In all patients, the cyst was solitary with a median diameter of 5.1 cm (interquartile range [IQR]: 3.6–6.6 cm). The cysts were inclined to locate in the left abdomen (15/19, 78.9%) rather than the midline or right abdomen, the upper abdomen (16/19, 84.2%) instead of the lower abdomen, and the retroperitoneal space (16/19, 84.2%) compared with intra-abdomen. The left adrenal region (7/19, 36.8%) was the most common location, followed by the pancreatic region (3/19, 15.8%) and gastric cardia/lesser curvature of the stomach (3/19, 15.8%). On computed tomography (CT), the density of cysts ranged from low to slightly high. The number of cysts with low to slightly low, soft-tissue, and slightly high density on CT is eight, nine, and two, respectively. Only three patients underwent magnetic resonance imaging (MRI), and all of their cysts were hypointense on T1 weighted image. As for T2 weighted image, two of them were hyperintense while the other was hypointense. Twelve of 19 cysts (63.2%) showed no enhancement on CT or MRI. Ten patients received the B ultrasound examination, displaying an anechoic (n = 3), hypoechoic (n = 3), or mix-echoic (anechoic to hypoechoic) cyst (n = 4). Three of the cysts were multilocular with septa present. The representative appearance of the cysts on CT, MRI, and ultrasound is demonstrated in Figure 1. Due to their rarity, none of the patients were diagnosed with sBCs before the surgery.

Laparoscopic surgery was conducted in most of the patients (16/19, 84.2%), while two underwent laparotomy and one underwent video-assisted thoracoscopic surgery (VATS; Table 2). The content of cysts was found to be either serous (1/13, 7.7%), mucoid (3/13, 23.1%), gelatinous (6/13, 46.2%), brittle (2/13, 15.4%), or mixed (1/13, 7.7%). Specifically, the gross appearance of the cyst from case 18 is depicted in Figure 2, with a cut surface demonstrating the gelatinous content within the cyst. Generally, most patients recovered fast after surgery and were discharged from the hospital within one week post-surgery. Two patients (cases 6 and 13) encountered perioperative complications and thus stayed for an extended period of time in the hospital. Case 6 had lymphatic leakage that improved with local drainage and a low-fat diet. Case 13 experienced gastroparesis and gastrointestinal decompression and acupuncture led to improvement.

We attempted to contact all patients for information on recurrence and long-term complications in May, 2022, with 12 responses. Unfortunately, not every patient had regular imaging examinations after surgery, but they all claimed no signs of recurrence until their most recent imaging assessment, and the longest one was 77 months after surgery. As for long-term complications, two patients (cases 8 and 12) had incision hernias and both received surgery for repairment. Additionally, left renal artery stenosis and left renal atrophy were discovered.
| Case | Year | Age (years) | Sex | Clinical symptoms | Cyst number | Cyst localization | Size (cm) | CT features | Other imaging studies | Preoperative diagnosis |
|------|------|-------------|-----|-------------------|-------------|-------------------|-----------|-------------|----------------------|----------------------|
| 1    | 2012 | 52          | Female | None              | 1           | Left adrenal region | 2.7       | Slightly high density, no enhancement | NA                  | Adrenal adenoma       |
| 2    | 2012 | 39          | Male | None              | 1           | Left adrenal region | 7.7       | Soft-tissue density, slight enhancement | SRS: negative        | Adrenal adenoma       |
| 3    | 2013 | 30          | Female | None              | 1           | Left adrenal region | 3.7       | Slightly low density, slight enhancement | BUS: well-defined, hypoechoic to anechoic | Adrenal adenoma       |
| 4    | 2014 | 44          | Female | None              | 1           | Left diaphragm      | 5.0       | Low to iso density, no enhancement | NA                  | Benign lesion         |
| 5    | 2014 | 45          | Female | Flank pain        | 1           | Left diaphragm      | 6.4       | Soft-tissue density, no enhancement | SRS: negative        | Adrenal ganglioneuroma |
| 6    | 2015 | 45          | Female | Flank pain        | 1           | Left adrenal region | 3.5       | Soft-tissue density. | BUS: well-defined, hypoechoic MRI: hypointense on T1WI, hypointense on T2WI, and enhancement around the boundary. SRS: negative | Adrenal adenoma       |
| 7    | 2015 | 37          | Male | None              | 1           | Pancreatic region   | 6.8       | Soft-tissue density, no enhancement | BUS: anechoic, with septa. | Gastrointestinal stromal tumor |
| 8    | 2016 | 62          | Male | None              | 1           | Lesser curvature of stomach | 4.7       | Slightly low density, no enhancement | BUS: hypoechoic to anechoic | Gastrointestinal stromal tumor |
| 9    | 2016 | 48          | Female | None              | 1           | Left adrenal region | 4.1       | Soft-tissue density, no enhancement | MIBG scan: negative | Adrenal adenoma       |
| 10   | 2017 | 44          | Female | None              | 1           | Presacral space     | 5.1       | Soft-tissue density, heterogeneous enhancement | BUS: anechoic, with septa | Colorectal carcinoma |
| 11   | 2017 | 39          | Male | None              | 1           | Left adrenal region | 3.5       | Low density, no enhancement | NA                  | Adrenal ganglioneuroma |
| 12   | 2018 | 62          | Female | Abdominal pain | 1           | Lesser curvature of stomach | 6.0       | Soft-tissue density, no enhancement | NA                  | Gastrointestinal stromal tumor |
| 13   | 2018 | 31          | Female | Cough             | 1           | Pancreatic tail     | 9.4       | Low density, enhancement at cyst wall | BUS: mixed echo | Mucinous cystic neoplasms |
| 14   | 2019 | 30          | Female | None              | 1           | Presacral space     | 7.4       | Low density, slight enhancement | BUS: anechoic, with septa MRI: hypointense on T1WI, and hyperintense on T2WI | Epidermoid cyst |
| 15   | 2020 | 44          | Female | None              | 1           | Posterior inferior to the left kidney | 8.9       | Low density, no enhancement | NA                  | Gastrointestinal stromal tumor |
| 16   | 2020 | 36          | Female | None              | 1           | Left adrenal region | 2.5       | Low density, slight enhancement. | BUS: hypoechoic MRI: hypointense on T1WI, and hyperintense on T2WI | Adrenal adenoma       |
| 17   | 2020 | 34          | Female | None              | 1           | Right adrenal region | 5.5       | Low density, no enhancement | BUS: well-defined, hypoechoic SRS: negative | Adrenal ganglioneuroma |
| 18   | 2020 | 65          | Female | None              | 1           | Pancreatic tail     | 6.0       | Slightly high density, no enhancement | BUS: well-defined, hypoechoic to anechoic | Lymphocyst |
| 19   | 2021 | 29          | Female | Acid reflux and abdominal distension | 1 | Lesser curvature of stomach | 3.4       | Soft-tissue density, no enhancement | NA                  | Gastrointestinal stromal tumor |

BUS, B ultrasound; CT, computed tomography; MIBG, meta-iodobenzylguanidine; MRI, magnetic resonance imaging; NA, not available; SRS, somatostatin receptor scintigraphy.
FIGURE 1
Appearance of subdiaphragmatic bronchogenic cysts on computed tomography (CT), magnetic resonance imaging (MRI), and B ultrasound.
(A) Non-enhanced CT showed a low-density cystic lesion between the pancreatic tail, stomach, spleen, and diaphragm from case 13.
(B) Enhanced CT showed slight enhancement of the cystic wall from case 13.
(C) Non-enhanced CT showed a soft-tissue density lesion adjacent to the lesser curvature of the stomach from case 19.
(D) Enhanced CT showed no enhancement of the lesion from case 19.
(E) T1 weighted image on MRI showed a hypointense lesion at the left adrenal region from case 16.
(F) T2 weighted image on MRI showed a hyperintense lesion at the left adrenal region from case 16.
(G) B ultrasound showed a well-defined, hypoechoic lesion at the right adrenal region from case 17. Arrows indicate the cysts.

8 months after surgery in case 5 whose cyst was located in the left adrenal region. Later, this patient received a left nephrectomy.

Literature review

194 records were retrieved initially after searching the PubMed using the strategy displayed in Supplementary Appendix 1. Among them, 49 were non-English, and the full text was not available for 21 English citations. Of the remaining 124 articles, 95 were identified to describe cases of sBCs and were included for further analysis (6, 7, 9–101).

The detailed information of all included studies is displayed in Supplementary Table 1.

The 95 citations reported 107 cases (58 [54.2%] male) in total (Table 3). The median age of the cases was 41.0 years, with an IQR of 27.0–51.0 years. Specifically, the cysts could be identified as early as the prenatal stage (19, 64, 87), and were histopathologically diagnosed as sBCs later either through an autopsy after a spontaneous abortion or surgery after birth. The cases were reported from 24 countries around the world, and China is the one that described the most (25/107, 23.4%). Different from our series (5/19, 26.3%), more than half of the cases from the literature were symptomatic (59/103, 57.3%). Abdominal pain/flank pain was the most common symptom (59/103, 57.3%). Abdominal pain/flank pain was the most common symptom (59/103, 34.0%), and other symptoms included nausea, vomiting, and abdominal discomfort, et al.

sBC was solitary in 96.3% (103/107) cases. One case had two cysts in the left adrenal region (62), and one case had three cysts arising from the stomach (73). In one case, the cysts were found to be bilateral, affecting both the left and right adrenal regions (66). Moreover, multiple cysts could be identified on both sides of the diaphragm, as one patient had one cyst in the left adrenal region with three in the left lung (75). The median size of the 111 sBCs reported in the literature was 5.0 cm (IQR: 3.5–7.3 cm), and could be as large as 18.9 cm (30). It should be noticed that the sBCs might enlarge over time, as manifested in several studies (19, 25, 37, 38, 50). Similar to our series, the cysts reported in the literature were more likely to be detected in the left abdomen (85/111, 76.6%), upper abdomen (105/111, 94.6%), and retroperitoneal space (85/111, 76.6%). The three most frequent areas for sBCs were the left adrenal region (40/111, 36.0%), pancreatic region (12/111, 10.8%), and gastric cardia/lesser curvature of the stomach (9/111, 8.1%).

Generally speaking, patients with sBCs usually showed normal blood tests, though abnormalities could be seen seldomly. For instance, several patients had significantly elevated serum levels of carbohydrate antigen 19-9 (CA19-9), even reaching 4330.7 U/mL. In these cases, bronchial epithelial cells were positive for CA19-9 in the immunohistochemical study on surgical specimens and the serum levels returned to normal after surgery (27, 81, 98). Interestingly, one study illustrated that the sBC was able to uptake radioiodine in the single photon emission computed tomography (SPECT) examination (68). Whether this is universal awaits further evidence.

All patients except two underwent surgery in the literature. Laparoscopy was the most common surgical procedure for patients with sBCs (42/72, 58.3%), followed by laparotomy (23/72 31.9%). One of the two patients that did not receive surgery was diagnosed with sBC based on the pathohistological examination of the specimen gained from CT-guided biopsy.
The patient was followed up for 3 years with a CT examination every 6 months, showing a stable lesion. The other patient was diagnosed through core biopsy guided by both fine needle aspirate (FNA) and endoscopic ultrasound (EUS), but the follow-up information was absent in the article (82). Though predominantly benign, malignant transformation has

| Case | Surgical procedure   | Duration of surgery (minutes) | Content of cyst               | Post-surgery hospital stay (days) | Follow-up                                                                 |
|------|----------------------|-------------------------------|------------------------------|----------------------------------|---------------------------------------------------------------------------|
| 1    | Laparoscopy          | 55                            | NA                           | 3                                | NA                                                                        |
| 2    | Laparoscopy          | 180                           | NA                           | 6                                | NA                                                                        |
| 3    | Laparoscopy          | 60                            | Gelatinous substance         | 4                                | NA                                                                        |
| 4    | Video-assisted thoracoscopic surgery | 110         | NA                           | 3                                | Last imaging examination in 2014/09 showed no signs of recurrence. Remained asymptomatic until 2022/05 |
| 5    | Laparoscopy          | 105                           | Mucoid substance             | 6                                | Last imaging examination in 2021/04 showed no signs of recurrence. Perioperative lymphatic leakage. Long-term follow up not available |
| 6    | Laparoscopy          | 55                            | NA                           | 19                               | Perioperative gastroparesis. Long-term follow up not available             |
| 7    | Laparotomy           | 105                           | Gelatinous substance         | 7                                | Last imaging examination in 2018/03 showed no signs of recurrence. Remained asymptomatic until 2022/05 |
| 8    | Laparoscopy          | 95                            | Brittle tissue              | 5                                | Last imaging examination in 2018/06 showed no signs of recurrence. Underwent incision hernial repair in 2018/06. |
| 9    | Laparoscopy          | 90                            | Mucoid substance             | 5                                | NA                                                                        |
| 10   | Laparoscopy          | 60                            | Gelatinous substance mixed with brittle tissue | 7                                | Last imaging examination in 2022/03 showed no signs of recurrence. Remained asymptomatic until 2022/05 |
| 11   | Laparoscopy          | 65                            | NA                           | 4                                | Last imaging examination in 2017/07 showed no signs of recurrence. Remained asymptomatic until 2022/05 |
| 12   | Laparoscopy          | 130                           | Brittle tissue              | 6                                | Last imaging examination in 2021/08 showed no signs of recurrence. Underwent incision hernial repair in 2021/08 |
| 13   | Laparotomy           | 260                           | Mucoid substance             | 20                               | Perioperative gastroparesis. Long-term follow up not available             |
| 14   | Laparoscopy          | 110                           | NA                           | 7                                | Last imaging examination in 2020/12 showed no signs of recurrence. Remained asymptomatic until 2022/05 |
| 15   | Laparoscopy          | 60                            | Serous substance             | 2                                | Last imaging examination in 2020/07 showed no signs of recurrence. Remained asymptomatic until 2022/05 |
| 16   | Laparoscopy          | 110                           | Gelatinous substance         | 8                                | Last imaging examination in 2022/04 showed no signs of recurrence. Remained asymptomatic until 2022/05 |
| 17   | Laparoscopy          | 120                           | Gelatinous substance         | 5                                | NA                                                                        |
| 18   | Laparoscopy          | 95                            | Gelatinous substance         | 4                                | Last imaging examination in 2021/05 showed no signs of recurrence. Remained asymptomatic until 2022/05 |
| 19   | Laparoscopy          | 85                            | Gelatinous substance         | 7                                | Last imaging examination in 2021/08 showed no signs of recurrence. Remained asymptomatic until 2022/05 |

NA, not available.
### TABLE 3 Literature review and our series of subdiaphragmatic bronchogenic cysts.

|                      | Total ($n=126$) | Literature ($n=107$) | Our series ($n=19$) | $p$ value |
|----------------------|-----------------|----------------------|---------------------|-----------|
| **Age, years**       |                 |                      |                     |           |
| Median               | 41.0            | 41.0                 | 44.0                | 0.261     |
| IQR                  | 30.0–51.0       | 27.0–51.0            | 35.0–46.5           | –         |
| Range                | 0.0–81.0        | 0.0–81.0             | 29.0–65.0           | –         |
| **Sex**              |                 |                      |                     |           |
| Male                 | $n=126$         | $n=107$              | $n=19$              | 0.008     |
| Female               | $n=62$ (49.2%)  | 58 (54.2%)           | 4 (21.1%)           | –         |
| **Country**          |                 |                      |                     |           |
| Asia                 | $n=87$ (69.0%)  | 68 (63.6%)           | 19 (100%)           | –         |
| China                | $n=44$ (34.9%)  | 25 (23.4%)           | 19 (100%)           | –         |
| Europe               | $n=21$ (16.7%)  | 21 (19.6%)           | 0 (0%)              | –         |
| North America        | $n=12$ (9.5%)   | 12 (11.2%)           | 0 (0%)              | –         |
| Oceania              | $n=3$ (2.4%)    | 3 (2.8%)             | 0 (0%)              | –         |
| South America        | $n=2$ (1.6%)    | 2 (1.9%)             | 0 (0%)              | –         |
| Africa               | $n=1$ (0.8%)    | 1 (0.9%)             | 0 (0%)              | –         |
| **Symptoms**         |                 |                      |                     |           |
| Asymptomatic         | $n=122$         | $n=107$              | $n=19$              | 0.013     |
| Symptomatic          | $n=38$ (31.1%)  | 35 (34.0%)           | 3 (15.8%)           | –         |
| Abdominal pain/flank pain | $n=122$ | $n=107$              | $n=19$              | 0.761     |
| **Cyst number**      |                 |                      |                     |           |
| 1 cyst               | $n=122$         | $n=107$              | $n=19$              | 0.761     |
| 2 cysts              | 2 (1.6%)        | 2 (1.9%)             | 0 (0%)              | –         |
| 3 cysts              | 1 (0.8%)        | 1 (0.9%)             | 0 (0%)              | –         |
| 4 cysts              | 1 (0.8%)        | 1 (0.9%)             | 0 (0%)              | –         |
| **Cyst size, cm**    |                 |                      |                     | 0.462     |
| Median               | 5.0             | 5.0                  | 5.1                 | –         |
| IQR                  | 3.5–7.1         | 3.5–7.3              | 3.6–6.6             | –         |
| Range                | 1.5–18.9        | 1.5–18.9             | 2.5–9.4             | –         |
| **Cyst localization**|                 |                      |                     |           |
| Left abdomen         | $n=130$         | $n=111$              | $n=19$              | 0.126     |
| Midline              | 5.0             | 5.0                  | 5.1                 | –         |
| Right abdomen        | 100 (76.9%)     | 85 (76.6%)           | 15 (78.9%)          | 0.892     |
| Upper abdomen        | 12 (9.2%)       | 10 (9.0%)            | 2 (10.5%)           | 0.892     |
| Lower abdomen        | 18 (13.8%)      | 16 (14.4%)           | 2 (10.5%)           | 0.892     |
| Retroperitoneal      | 121 (93.1%)     | 105 (94.6%)          | 16 (84.2%)          | 0.126     |
| Intra-abdominal      | 9 (6.9%)        | 6 (5.4%)             | 3 (15.8%)           | 0.564     |
| Left adrenal region  | 101 (77.7%)     | 85 (76.6%)           | 16 (84.2%)          | 0.564     |
| Pancreatic region    | 29 (22.3%)      | 26 (23.4%)           | 3 (15.8%)           | 0.564     |
| Gastric cardia/lesser curvature of stomach | 47 (36.2%) | 40 (36.0%) | 7 (36.8%) | – |
| **Enhancement on CT/MRI** | $n=69$ | $n=50$             | $n=19$             | 0.375     |
| No                   | 49 (71.0%)      | 37 (74.0%)           | 12 (63.2%)          | –         |
| Yes                  | 20 (29.0%)      | 13 (26.0%)           | 7 (36.8%)           | –         |
| **Surgical procedure** | $n=91$ | $n=72$             | $n=19$             | –         |
| Laparoscopy          | 58 (63.7%)      | 42 (58.3%)           | 16 (84.2%)          | –         |
| Laparotomy           | 25 (27.5%)      | 23 (31.9%)           | 2 (10.5%)           | –         |
| Robotic surgery      | 2 (2.2%)        | 2 (2.8%)             | 0 (0%)              | –         |
| Thoracotomy          | 2 (2.2%)        | 2 (2.8%)             | 0 (0%)              | –         |
| VATS                 | 2 (2.2%)        | 1 (1.4%)             | 1 (5.3%)            | –         |
| **Follow-up time for recurrence, months** | $n=45$ | $n=33$             | $n=12$             | –         |
| Median               | 12              | 12                   | 19                  | –         |
| IQR                  | 6–24            | 6–24                 | 7–30                | –         |
| Range                | 1–77            | 2–49                 | 1–77                | –         |

Unpaired $t$-test or Pearson’s chi-square test was employed when appropriate. CT, computed tomography; IQR, interquartile range; MRI, magnetic resonance imaging; VATS, video-assisted thoracoscopic surgery.
been demonstrated in two cases, one with well-differentiated papillary adenocarcinoma (17) and the other with intermediate-grade neuroendocrine tumor (89). The latter patient remained asymptomatic and had no recurrence for 14 months after surgery. In addition to this, the follow-up information was also provided for another 32 cases and the longest reached 49 months. There was no sign of recurrence in any of the cases, indicating a good prognosis of sBCs.

Discussion

Bronchogenic cysts are primitive-foregut-derived congenital cystic abnormalities that usually occur in the thorax, particularly in the mediastinum (1–3). Infrequently, they can be found in subdiaphragmatic region, and only around 100 cases were reported in English up to now based on our database searching. Our case series reported here added another 19 cases.

As displayed in three articles, sBCs can be detected even during pregnancy (19, 64, 87), but most patients discovered the cyst(s) in their thirties and forties. As for sex distribution, our study and the literature produced different results. Females predominated in our study, while males had a slightly higher proportion in the literature review. One possible reason is that the sample size of our series is insufficient, while reporting bias of the articles is an alternative explanation. As our series and the literature illustrated, most of the cysts were solitary. Only on rare occasions were they reported to be multiple, either unilateral or bilateral, either on the same side or the both sides of diaphragm. The size of sBCs varied greatly, ranging from 1.5 to 18.9 cm based on available data from our cases and citations, but the diameter of the cysts was mostly between 3.0 and 7.0 cm (Supplementary Table 1). When it comes to the localization, our research demonstrated that the cysts were more likely to be found in the left abdomen, upper abdomen, and retroperitoneal space. Moreover, in addition to the previously reported left adrenal region and pancreatic region (7), our analysis revealed that gastric cardia/lesser curvature of the stomach was another predilection site for sBCs.

A large proportion of patients with sBCs were asymptomatic (73.7% in our series, and 42.7% in the literature review). Symptoms caused by sBCs were usually non-specific, mainly due to complications such as local compression and infection. For example, one patient with sBC in the left adrenal region had a 5-year history of hypertension (63). After the cyst was resected completely, his blood pressure returned to normal. This patient's hypertension might be caused by a compression on the adrenal gland, kidney, or renal artery. In one of our cases (case 13), the cystic fluid was found to be turbid and smelly during the surgery. The culture of cystic fluid was positive for Streptococcus anginosus, providing direct evidence of intra-cyst infection. Patients with sBCs lacked specific symptoms, which was the same for laboratory findings. The tumor markers test did not aid in the diagnosis of sBCs, as nearly all patients tested negative for them. Seldomly, the epithelial cells lining the cyst were able to produce tumor markers like CA19-9, leading to a significantly elevated
serum level (27, 81, 98). Additionally, it was also difficult to differentiate sBCs from other more common subdiaphragmatic cystic lesions based on imaging examinations. The density of sBCs on CT ranged from low to high, with either enhancement or no enhancement. It could be multilocular with septa or unilocular. In summary, sBCs could not be diagnosed preoperatively as they lack a distinct clinical presentation as well as laboratory and imaging findings. Furthermore, their rarity complicates the diagnosis.

Up to now, a histopathological examination is required for the diagnosis of sBCs. Biopsy guided by CT or EUS could provide the specimen before surgery. Several cases from the literature were diagnosed based on biopsy, and two of them did not receive surgery because the patients were asymptomatic (56, 82). In particular, the lesion of one patient remained stable during the 3-year follow-up (56). According to Berger-Richardson et al., core needle biopsy of retroperitoneal lesion had low rates of both early complications and needle tract seeding (102). Given that nearly 80% of sBCs were found in retroperitoneal space and they were generally benign, it might be feasible to perform a biopsy for a diagnosis and thus avoid surgery for some of the patients with retroperitoneal bronchogenic cysts. However, it should be noticed that the biopsy might be non-diagnostic due to the sampling issue (46). Furthermore, quite a few patients had symptoms that could only be alleviated by surgery. Additionally, though rare, malignant changes were detected in two cases and only affected a portion of the cyst in both cases (17, 89). Other clinical parameters, such as symptoms, cyst size, tumor marker levels, and imaging findings, did not help predict malignancy. Therefore, it was very likely that malignancy was missed due to the sampling issue of biopsy. According to our cases and the literature, patients usually recovered quickly after surgery, with a low rate of post-surgery complications. Because of the aforementioned factors, though biopsy might help with the diagnosis of sBCs, it could not yet replace surgery at present.

After the complete cyst(s) resection, patients with sBCs generally had a good prognosis. Forty-five (n = 12 in our series, and n = 33 in the literature) patients had no recurrence during the follow-up, and the longest one reached 77 months in our series. Particularly, one patient with malignant change reported in the literature was also free of recurrence for 14 months after surgery (89).

In conclusion, our series added another 19 cases to the list of rarely reported sBCs. Together with the 107 published cases, we demonstrated that the sBCs are predisposed to locate in the left adrenal region, pancreatic region, and gastric cardia/lesser curvature of the stomach. Patients with sBCs lack specific clinical symptoms, laboratory examinations, and imaging features. Surgery is still the best management strategy for patients for a definite diagnosis, symptom alleviation, and complication prevention. The prognosis is generally favorable after complete resection of the lesion.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. The ethics committee waived the requirement of written informed consent for participation.

Author contributions

WL conceived the study. JX and XZ contributed to the case collection, discussion, literature review, and first manuscript draft. WL, HZ, TH, BL, and XH provided critical revisions. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2022.993091/full#supplementary-material
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