



# CT and MRI characteristics for differentiating mediastinal Müllerian cysts from bronchogenic cysts



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## ARTICLE INFORMATION

### Article history:

Received 11 October 2018

Accepted 20 August 2019

**AIM:** To evaluate how computed tomography (CT) and magnetic resonance imaging (MRI) characteristics can be used to differentiate immunohistochemically confirmed mediastinal Müllerian cysts (MMCs) from bronchogenic cysts (BCs).

**MATERIALS AND METHODS:** Sixteen patients with histopathologically and immunohistochemically confirmed mediastinal cysts (four with MMCs and 12 with BCs) were included in this study. CT and MRI images were reviewed retrospectively and the location, size, CT attenuation, and MRI signal intensity of the two pathologies were compared.

**RESULTS:** On review of CT images, cysts could be located to the anterior mediastinum in four BCs, middle mediastinum in three MMCs and seven BCs, and posterior mediastinum in one MMC and one BC. Contact with a vertebral body was observed in 4/4 MMCs (100%) and 6/12 BCs (50%). The ratios of minimum-to-maximum diameter ( $0.57 \pm 0.09$  versus  $0.74 \pm 0.11$ ,  $p < 0.01$ ), CT attenuation ( $7.8 \pm 6$  versus  $44.3 \pm 12$  HU,  $p < 0.01$ ), and cyst-to-spinal cord signal intensity ratios (SIRs) on T1-weighted images ( $0.56 \pm 0.2$  versus  $1.31 \pm 0.4$ ,  $p < 0.01$ ) were significantly lower for MMCs than BCs. No significant differences in maximum diameter, minimum diameter, and SIRs on T2-weighted images were found between MMCs and BCs.

**CONCLUSION:** In characterising mediastinal cysts in a middle-aged female patient, contact with a vertebral body, flattened configuration, hypodensity on CT, and hypointensity compared to spinal cord on T1-weighted images are features that are specific to MMCs.

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## Introduction

Mediastinal cysts can be divided into two primary categories: congenital and acquired. Mediastinal congenital cysts account for 15–20% of all primary mediastinal masses, and include thymic, pericardial, and foregut cysts (also known as bronchogenic, oesophageal duplication, and

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neuro-enteric cysts). Chest pain, dyspnoea, and cough may occur as the primary symptoms of mediastinal cysts; however, approximately 63% patients with mediastinal cysts are asymptomatic.<sup>1</sup>

Bronchogenic cysts (BCs) are the most common congenital cysts of the mediastinum and arise from abnormal ventral budding or branching of the tracheo-bronchial tree during embryological development. This type of cyst can be found at any age; however, they are more frequently identified in young adults. Histologically, BCs are lined by ciliated, pseudostratified, columnar epithelium, with goblet cells. Their walls usually contain mucous gland tissue, smooth muscle, and cartilage.

Mediastinal Müllerian cysts (MMCs) were first reported by Hattori in 2005.<sup>2,3</sup> They are located in the paravertebral region of the mediastinum, with Müllerian differentiation occurring only in women.<sup>2,3</sup> Histologically, they are lined by a simple cylindrical or cuboidal, non-mucinous, and often ciliated epithelium resembling uterine tubal epithelium. Immunopathological experiments demonstrate that the epithelial cells exhibit positive staining for oestrogen receptors (ER) and progesterone receptors (PgR).<sup>2–4</sup> MMCs are difficult to distinguish from BCs by their histological appearance without tracheobronchial glands or cartilage, because both are lined by ciliated epithelium. In fact in one study, six out of nine MMCs are initially misdiagnosed as BCs.<sup>4</sup>

Complications arising from the presence of BCs include infection of the cyst contents, fistulae growing into surrounding structures, cyst rupture, and haemorrhage of contents into the cystic cavity. In addition, local recurrence of BCs can occur following incomplete excision and malignant transformation. Because 45% of asymptomatic patients with BCs eventually develop symptoms requiring surgery, the evidence for successful conservative management of asymptomatic BCs is very limited.<sup>5</sup> In contrast, although there are a limited number of cases, no serious complications and malignant transformation associated with the presence of MMCs have so far been reported. If appropriate preoperative diagnosis of an MMC is achieved by radiological imaging, conservative therapy may be chosen as the proper treatment; however, to the authors' knowledge, no study has reported detailed imaging findings for MMCs. Therefore, the present study aims to assess the CT and MRI characteristics that can be used to differentiate immunohistochemically confirmed MMCs from BCs.

## Materials and methods

### Patients

The present study was approved by the human research committee of the institutional review board of the hospital, and complied with the guidelines of the Health Insurance Portability and Accountability Act of 1996. The requirement for informed consent was waived due to the retrospective nature of this study. The hospital's electronic medical chart system for April 2004 to March 2018 was searched for

consecutive patients with histologically proven mediastinal congenital cysts that had been treated by complete surgical resection. Of the 28 patients identified, seven patients with thymic cysts and four with pericardial cysts were excluded from the study, because histological diagnosis had been performed easily using haematoxylin–eosin slides.

Among the remaining 17 patients with mediastinal congenital cysts, the initial histological diagnoses were BCs in 15 patients, Müllerian cyst in one patient, and serous cyst in the remaining patient. A pathologist with 32 years of post-training experience re-reviewed the haematoxylin–eosin slides for these 17 patients and carefully assessed the presence of tracheobronchial glands and cartilage within the cyst walls. Subsequently, immunohistochemical evaluation was performed. Primary antibodies were directed against the following antigens: thyroid transcription factor (TTF)-1 (clone SPT24, dilution 1:200; Novocastra); ER (clone SP1, pre-diluted; Ventana); and PgR (clone 1E2, pre-diluted; Ventana). Immunopositivity was determined by nuclear expression of the epithelial lining within the cysts. As a result of these microscopic and immunohistochemical evaluations, the mediastinal cysts were classified into two categories, MMC and BC, according to following diagnostic criteria. The diagnosis of an MMC was based on<sup>1</sup> the absence of tracheobronchial glands and cartilage<sup>2</sup>; a positive result for ER and PgR; and<sup>3</sup> a negative result for TTF-1. The diagnosis of a BC was based on<sup>1</sup> the presence of tracheobronchial glands and/or cartilage<sup>2</sup>; a negative result for ER and PgR, and<sup>3</sup> a positive result for TTF-1. BC was diagnosed based on a positive test for TTF-1 in cases where the presence of tracheobronchial glands and cartilage could not be confirmed. One case was excluded from this study, because it was inconsistent with both diagnostic criteria.

In total, four patients with MMCs (four women; age range, 20–55 years; mean age, 44 years) and 12 with BCs (five men and seven women; age range 19–84 years; mean age, 52 years) were included in the present study. No clinical symptoms were observed in patients with MMCs. A cough was observed in one patient with a BC. Patient characteristics are summarised in [Table 1](#).

### CT imaging

A CT examination was performed in all 16 patients. A 16-section CT system (LightSpeed Ultra 16, GE Healthcare, Milwaukee, WI, USA) was used for seven patients, a 64-section CT system (Brilliance CT 64, Philips Medical Systems, Best, The Netherlands) for seven patients, and a 64-section CT system (Discovery CT 750HD, GE Healthcare, Milwaukee, WI, USA) for two patients. Transverse unenhanced CT images were reconstructed using a 5-mm section thickness and no overlap.

### MRI

Fifteen patients (three patients with MMC, 12 patients with BC) were examined using a 1.5-T MRI system (Intera Achieva 1.5 T Pulsar; Philips Medical Systems, Amsterdam,

**Table 1**  
Patient characteristics of MMC and BC.

Characteristics	MMC	BC
Number of patients	4	12
Age (year)		
Median	44	52
Range	20–55	19–84
Gender		
Male	0 (0)	5 (42)
Female	4 (100)	7 (58)
Initial pathological diagnosis		
MMC	1 (25)	0 (0)
BC	2 (50)	12 (100)
Serous cyst	1 (25)	0 (0)
Histopathological findings		
Tracheobronchial gland (+)	0 (0)	9 (75)
Cartilage (+)	0 (0)	2 (17)
Immunostaining findings		
ER (+)	4 (100)	0 (0)
PgR (+)	4 (100)	0 (0)
TTF-1 (+)	0 (0)	12 (100)
Clinical symptom		
Asymptomatic	4 (100)	11 (92)
Symptomatic	0 (0)	1 (8)
Radiological examination		
CT	4 (100)	12 (100)
MRI	3 (75)	12 (100)

Data (excluding age) are numbers of patients, and numbers in parentheses are frequencies expressed as percentages.

MMC, mediastinal Müllerian cyst; BC, bronchogenic cyst, ER, oestrogen receptor, PgR, progesterone receptor, TTF, thyroid transcription factor.

The Netherlands). All images were obtained at a section thickness of 4 mm with a 1-mm intersection gap, and a 32×32–38×38-cm field of view. Axial non-fat-suppressed T2-weighted fast spin-echo (2,764–4,000 ms repetition time [TR], 80–100 ms echo time [TE]) and axial non-fat-suppressed T1-weighted spin-echo (687–833 ms TR, 8 ms TE) images were obtained in 15 patients.

### Image assessment

Two radiologists with 19 and 5 years of post-training experience individually reviewed all CT and MRI images, and any disagreements were resolved by consensus.

CT images were evaluated for cyst location, contact between the cyst and a vertebral body, maximum and minimum cyst diameter, intralesional calcification, intralesional air collection, and CT attenuation of cystic components. Mediastinal compartments were classified into three categories according to International Thymic Malignancy Interest Group (ITMIG) classification: anterior (prevascular), middle (visceral), and posterior (paravertebral) mediastinum.<sup>6</sup> If the lesion extended from one compartment to another, the centre of the lesion (defined as its centre point on the axial CT image displaying the largest area of cyst) was used to localise the abnormality to a specific compartment.<sup>6</sup>

MRI images were evaluated to assess the fluid–fluid level on T2-weighted images and signal intensity of cystic components on T1- and T2-weighted images. The reviewer defined the regions of interest (ROIs) within the cysts and spinal cords to measure the signal intensity. The cyst-to-

spinal cord signal intensity ratios (SIRs) were calculated as follows: signal intensity of cyst/signal intensity of spinal cord. The spherical or elliptic ROIs were manually placed in the centre of cysts and spinal cords at the same level as the cysts to encompass cystic cavities and spinal cords as much as possible on MRI images. The different ROI sizes were set according to sizes of the cysts and spinal cords.

### Statistical analysis

All statistical analyses were performed using SPSS version 22.0 (SPSS, IBM, Chicago, IL, USA). The Mann–Whitney *U*-test was used to compare the age, maximum and minimum diameter, the ratios of minimum-to-maximum diameter, CT attenuation, and SIRs on T1 and T2-weighted images between MMCs and BCs. Null hypotheses of no difference were rejected if *p*-values were less than 0.05.

## Results

Qualitative imaging findings are summarised in Table 2. All MMCs and BCs were found to be unilocular. According to ITMIG classification, the cysts were located in the anterior mediastinum in four BCs, middle mediastinum in three MMCs and seven BCs, and posterior mediastinum in one MMC and one BC. Contact with a vertebral body was observed in 4/4 MMCs (100%) and 6/12 BCs (50%). Among the cysts in contact with a vertebral body, 4/4 MMCs were located on the right side (100%), whereas 4/6 BCs were located on right side (67%), with the remainder on the left side in 2/6 (33%). Among the cysts in contact with a vertebral body, three MMCs were located at the level of T6 and one at T7/8, whereas one BC was located at T3, two at T5–7, two at T6, and one at T7/8. Intralesional calcification was observed in 0/4 MMCs (0%) and 1/12 BCs (8%). No intralesional air collection was observed in either type of cyst. Fluid–fluid level formation on T2-weighted images was observed in 0/3 MMCs (0%) and 3/12 BCs (25%).

Quantitative measurements are summarised in Table 3. The ratios of minimum-to-maximum diameter ( $0.57\pm 0.09$  versus  $0.74\pm 0.11$ ,  $p<0.01$ ), CT attenuation ( $7.8\pm 6$  versus  $44.3\pm 12$  HU,  $p<0.01$ ), and SIRs on T1-weighted images ( $0.56\pm 0.2$  versus  $1.31\pm 0.4$ ,  $p<0.01$ ) were significantly lower

**Table 2**  
Qualitative imaging findings of MMC and BC.

	MMC (n=4)	BC (n=12)
Location in the mediastinum		
Anterior	0 (0)	4 (33)
Middle	3 (75)	7 (58)
Posterior	1 (25)	1 (8)
Contact with vertebral body	4 (100)	6 (50)
Calcification	0 (0)	1 (8)
Air	0 (0)	0 (0)
Fluid–fluid level	0 (0)	3 (25)

Data (excluding age) are numbers of patients, and numbers in parentheses are frequencies expressed as percentages.

MMC, mediastinal Müllerian cyst; BC, bronchogenic cyst.

**Table 3**  
Quantitative measurements of MMC and BC.

	MMC (n=4)	BC (n=12)	p-Value
Age (year)	43.8 ± 16.1	52.2 ± 18.1	0.521
Maximum diameter (mm)	25.5 ± 6.1	34.0 ± 12.5	0.212
Minimum diameter (mm)	14.8 ± 5.1	25.0 ± 9.3	0.078
The ratios of MMD	0.57 ± 0.09	0.74 ± 0.11	0.008 <sup>a</sup>
CT attenuation (HU)	7.8 ± 6.0	44.3 ± 12.0	0.005 <sup>a</sup>
SIRs on T1-weighted image	0.56 ± 0.20	1.31 ± 0.40	0.009 <sup>a</sup>
SIRs on T2-weighted image	2.80 ± 0.42	2.81 ± 0.55	0.112

Data are shown as the mean ± 1 standard deviation.

MMC, mediastinal Müllerian cyst; BC, bronchogenic cyst; MMD, minimum-to-maximum diameter; SIR, cyst to-spinal cord signal intensity ratio.

<sup>a</sup> The value of BCs was significant higher than those of MMCs ( $p < 0.01$ ).

for BCs than MMCs (Figs 1–3); however, no significant differences in age ( $43.8 \pm 16.1$  versus  $52.2 \pm 18.1$  years;  $p = 0.521$ ), maximum diameter ( $25.5 \pm 6.1$  versus  $34 \pm 12.5$  mm;  $p = 0.212$ ), minimum diameter ( $14.8 \pm 5.1$  versus  $25 \pm 9.3$  mm;  $p = 0.078$ ), and SIRs on T2-weighted images ( $2.80 \pm 0.42$  versus  $2.81 \pm 0.55$ ;  $p = 0.112$ ) were found between MMCs and BCs.

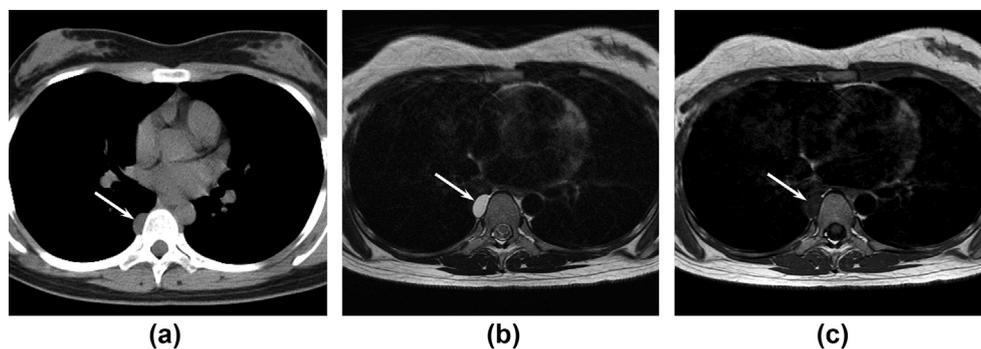
## Discussion

Müllerian cysts arise from remnants of the Müllerian duct. They commonly occur in the male pelvis (prostate) or female pelvis (uterus and vagina), but Müllerian cysts in the mediastinum, retroperitoneum, or skin have rarely been reported. MMCs account for 5.5–15.8% of mediastinal cysts.<sup>2,4,7</sup> Similarly, MMCs accounted for 4/28 (14.3%) of mediastinal congenital cysts in the present study. Moreover, among mediastinal cysts in contact with a vertebral body in females, MMCs accounted for more than half (4/7, 57%).

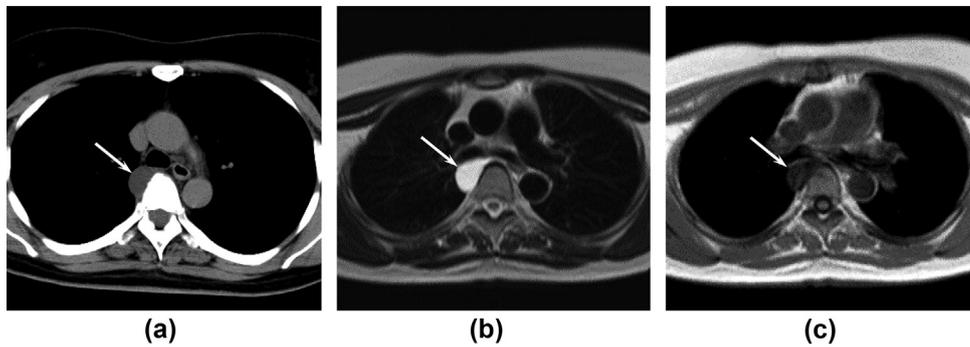
To date, 39 cases of patients with MMCs have been reported in the literature.<sup>2–4,7–28</sup> According to a review of 43 cases of patients with MMCs including the present four cases, patients' ages ranged from 18 to 59 years (median, 49 years) and all the patients with MMCs were female. Patients were asymptomatic in 26/43 cases (60%), whereas cough was observed in 8/43 (19%) and chest pain in 6/43 cases (14%). Laterality of the lesion was to the right in 21/41 (51%) and left in 20/41 patients (49%), excluding two cases of lesions in bilateral and prevertebral locations. The median

MMC size was 30 mm (range, 12–81 mm). Among 27 of 39 reported cases with referable CT or MRI images, direct contact between MMCs and a vertebral body was observed in 27/27 (100%) patients.<sup>2–4,7–12,14,15,17,18,20–28</sup> Among 33 of 39 reported cases with referable vertebral heights, 17/33 cases (51%) occurred at the level of single vertebral body, whereas 16/33 (49%) occurred at the level of more than two vertebral bodies. MMCs commonly occurred at the level of T4 vertebra in 16/33 cases (48%). Although 30/33 cases (91%) occurred at the level of vertebrae between T3 and T6, the remaining 3/33 cases (9%) did not occur at the level of vertebrae between T3 and T6.<sup>4,7,26</sup> These three unusual cases occurred at the level of T1–2,<sup>7</sup> T8,<sup>4</sup> and T10<sup>26</sup> vertebrae. In the present study, direct contact between MMCs and a vertebral body was observed in 4/4 (100%), and MMCs occurred at the level of single vertebral body (T6) in 3/4 (75%) and at the level of more than two vertebral bodies (T7–8) in 1/4 (25%). In summary, MMCs were always in contact with a vertebral body and usually occurred at the level of vertebrae between T3 and T6.

Among 17 patients with symptomatic MMCs of 39 reported cases, chest symptoms were relieved following surgery in four patients,<sup>9,11,18,24</sup> therefore, symptomatic MMCs may be indication for surgery; however, because surgical complications, including Horner's syndrome and hypohidrosis, occurred in 2/39 cases (5%),<sup>20,22</sup> it is necessary to consider the need for surgery carefully. On the other hand, four patients with asymptomatic MMCs of 39 reported cases were followed closely without therapy before surgery (range of follow-up period, 12–84 months; mean, 36 months), then, two MMCs slightly increased in size and the remaining two MMCs were unchanged.<sup>8,14,22</sup> In addition, among 39 reported cases of MMCs, no serious complications and malignant transformation associated with the presence of MMCs have so far been reported. In the present study, no MMCs with symptoms and/or post-operative complications were observed, and two MMCs slightly increased in size and the remaining one MMC was unchanged among three MMCs, which were followed closely without therapy before surgery (range of follow-up period, 7–60 months; mean, 25 months). Based on these results, although the standard therapy for MMCs remains



**Figure 1** A 20-year-old woman with Müllerian cyst in the posterior mediastinum. (a) Unenhanced CT image shows a flattened hypodense lesion (arrow) in contact with vertebral body (T7). (b) T2-weighted image (3,000 ms TR/80 ms TE) shows a hyperintense unilocular cystic lesion relative to spinal cord (arrow) with flattened configuration. (c) T1-weighted image (687 ms TR/8 ms TE) shows a hypointense cystic lesion relative to spinal cord (arrow).



**Figure 2** A 48-year-old woman with Müllerian cyst in the middle mediastinum. (a) Unenhanced CT image shows a flattened hypodense lesion (arrow) in contact with vertebral body (T6). (b) T2-weighted image (3,272 ms TR/90 ms TE) shows a hyperintense unilocular cystic lesion relative to spinal cord (arrow) with flattened configuration. (c) T1-weighted image (833 ms TR/8 ms TE) shows a hypointense cystic lesion relative to spinal cord (arrow).

controversial, it seems reasonable that patients with asymptomatic MMCs should be treated conservatively.

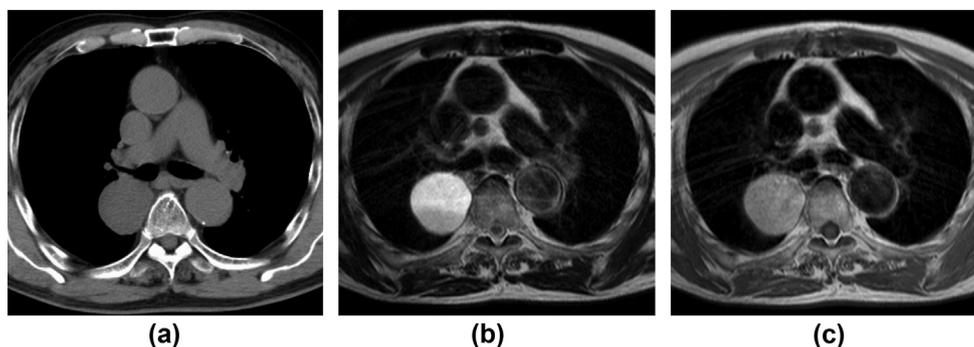
Batt *et al.* have explained the pathogenesis and anatomical location of a T6 paravertebral endosalpingiotic cyst using Ludwig's embryology theory of pathogenesis for Mayer–Rokitansky–Küster–Hauser syndrome.<sup>9</sup> In meticulous embryology studies, Ludwig demonstrated that in stage 16 embryos (37 postovulatory days), a thickening of the coelomic epithelium develops on the cranial end of the plica mesonephrica, at the level of the third to fifth vertebral blastema, and then forms the anlage of the funnel area (in the fallopian tubes).<sup>29</sup> This theory accounts nicely for the characteristic location of MMCs between T3 and T6.

BCs originate from the tracheobronchial bud that arises at the embryonic foregut. Histopathologically, tracheobronchial glands and cartilage are typically observed in BCs; however, in the current study 3/12 BCs (25%) showed neither tracheobronchial glands nor cartilage; therefore, it was difficult to obtain an accurate diagnosis of BC using only morphological criteria. BC walls are lined with ciliated epithelial cells, which are derived from tracheobronchial tree, and these epithelial cells display positive nuclear staining for TTF-1.<sup>5</sup> In contrast, according to reports using referable immunochemical results, MMCs are always

negative for TTF-1 and almost all MMCs are positive for ER and PgR, due to Müllerian differentiation.<sup>7,8,11,13,19–24</sup> Accordingly, the final diagnoses in this study were based on the immunostaining results.

MMCs usually contain serous and clear fluid, whereas BCs normally consist of proteinaceous fluid. The latter tend to be tense cysts due to elevated intracystic pressure. In the present study, the ratios of minimum-to-maximum diameter were significantly lower for MMCs than BCs. In addition, MMCs tended to show a flattened configuration in comparison with BCs, reflecting the different intracystic pressures. This shape difference may also be useful for differentiating the two types of cyst. Actually, among 23 reported cases with referable transaxial CT or MRI images, the ratios of minimum-to-maximum diameter of MMCs ranged from 0.40 to 0.90 (mean, 0.62).<sup>3,7,9–12,14–16,18,20–25,27,28,30</sup> This result is quite similar to the present results.

In the four patients with MMCs studied in this report, the presence of serous liquid within cysts was confirmed by reference to surgical records, but the visual appearances at surgery cannot be used to determine the actual contents of the cysts. In 12 other reported cases that had referable cyst contents, MMCs were found to contain serous liquid, with the colours reported as clear or yellowish.<sup>2–4,9,10,13,14,16,19,23,25–27</sup>



**Figure 3** A 48-year-old man with bronchogenic cyst in the middle mediastinum. (a) Unenhanced CT image shows a spherical isodense lesion (arrow) in contact with vertebral body (T6). (b) T2-weighted image (2,764 ms TR/90 ms TE) shows a hyperintense unilocular cystic lesion relative to spinal cord (arrow) with fluid–fluid level formation. (c) T1-weighted image (822 ms TR/8 ms TE) shows a hyperintense cystic lesion relative to spinal cord (arrow).

Prior literature reports suggest that MMCs always appear hyperintense relative to spinal cord on T2-weighted images (100%, 12/12)<sup>3,8–12,14,15,20,25,27,28</sup> and hypointense relative to spinal cord on T1-weighted images (100%, 5/5).<sup>8,11,14,15,20</sup> In contrast, BC components include proteinaceous fluid, mucus, calcium, and blood debris. Therefore, CT attenuation and SIRs on T1-weighted images were significantly higher in BCs than in MMCs. In agreement with the present results, high CT attenuation of BCs (mean, 44.5 HU) has been reported elsewhere.<sup>31</sup> In other studies, 25–43% of BCs were classified as water attenuation (<20 HU), whereas 43–62% were classified as solid attenuation (>20 HU).<sup>30,32</sup>

Surgical excision of BCs has historically been performed for three main reasons: first, to confirm the diagnosis; second, to prevent the development of symptoms and complications, thus pre-empting possible surgery for complex inflammatory lesions; and third, to avoid the potential for malignant transformation.<sup>5</sup> There is good evidence to support excision of symptomatic BCs, and many surgeons also recommend surgery for asymptomatic BCs. This meta-analysis stated that 45% of asymptomatic BCs eventually develop complications, whereas some were successfully followed for over 20 years.<sup>5</sup> Because MMC was first reported in 2005, some MMCs may have been misdiagnosed as BCs and might be included in such meta-analysis data. Therefore, true risk and appropriate surgical indication should be explored among immunohistochemically confirmed BCs. This would further support the argument that the distinction from MMC is important.

This study had some limitations. First, the study population was small, because the research was conducted using data from patients at a single institution and also because MMCs are rare and congenital; therefore, the number of cases is very low; however, in spite of the small number of patients with MMCs, significant image-based differences were found between MMCs and BCs, which will facilitate accurate diagnosis in the future. Second, chemical analysis of the cyst contents was not performed due to the retrospective nature of this study. In the future, chemical analysis of the cyst contents may provide a reason for the different imaging characteristics between MMC and BC.

To conclude, in characterising mediastinal cysts in a middle-aged female patient, contact with a vertebral body, flattened configuration, hypodensity on CT, and hypointensity compared to spinal cord on T1-weighted images are features that are specific to MMCs. In contrast, spherical configuration, hyperdensity on CT, and hyperintensity compared to spinal cord on T1-weighted images are characteristics specific to BCs.

## Funding

No funding was received for this study.

## Conflict of interest

The authors declare no conflict of interest.

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