• Clinical Research •

Ultrasonographic features of ciliary body mesectodermal leiomyoma

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Abstract

● **AIM:** To investigate the ultrasonographic features of ciliary body mesectodermal leiomyomas (CBL).

● **METHODS:** Ultrasonographic data of 18 eyes from 18 patients with histopathologically confirmed CBL were analyzed, covering the period from March 2018 to February 2024. The study included 5 male and 13 female patients, aged 14-64y, with a mean age of 40.11±13.54y. The following ultrasonographic features were evaluated: tumor base diameter, thickness, maximum base diameter-to-thickness ratio, shape, internal echogenicity, margin echogenicity, internal echo homogeneity, secondary changes, color Doppler flow imaging (CDFI) findings, and contrast-enhanced ultrasound (CEUS) characteristics.

● **RESULTS:** Conventional ultrasound findings of the 18 CBL cases were as follows: 1) Tumor size: base diameter of (13.48±4.74)×(11.57±4.00) mm^2, thickness of 7.70±2.60 mm, and maximum base diameter-to-thickness ratio of 1.77±0.36. 2) Shape: 14 cases (77.8%) were hemispherical, and 4 cases (22.2%) were irregular. 3) Internal echogenicity: the solid component of the tumor was hypoechoic in 16 cases (88.9%) and low-to-medium echogenic in 2 cases (11.1%). 4) Margin echogenicity: relatively hyperechoic with a "ring-shaped" margin in 15 cases (83.3%) and isoechoic in 3 cases (16.7%; compared with internal echogenicity). 5) Internal echo homogeneity: homogeneous in 11 cases (61.1%) and heterogeneous in 7 cases (38.9%), with 6 cases (33.3%) among the 7 heterogeneous cases exhibiting cystic anechoic areas. 6) Secondary retinal detachment was observed in 4 cases (22.2%). CDFI revealed heterogeneous vascularity within the tumors, with blood flow signals ranging from minimal to marked. CEUS was performed in 14 patients: complete contrast agent perfusion was observed in 10 cases (71.4%), and partial perfusion was noted in 4 cases (28.6%). Additionally, 8 cases (57.1%) showed a rapid wash-in and slow wash-out pattern, while 6 cases (42.9%) demonstrated a rapid wash-in and rapid wash-out pattern.

● **CONCLUSION:** CBL exhibit relatively typical ultrasonographic features, which can provide valuable evidence for the clinical diagnosis and differential diagnosis of intraocular tumors.

● **KEYWORDS:** ciliary body mesectodermal leiomyoma; ultrasound; color Doppler flow imaging; contrast-enhanced ultrasound

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INTRODUCTION

Ciliary body mesectodermal leiomyoma (CBL) is an extremely rare, intraocular, amelanotic benign tumor[1]. In 1950, Blodi[2] first described CBL. Subsequently, in 1977, Jakobiec *et al*[3] first proposed that CBL is a tumor with both myogenic and neurogenic histological characteristics and reported that it originates from neural crest cells. Due to its atypical clinical features, its definitive diagnosis is challenging. Ciliary body tumors, due to their occult anatomical location, present significant challenges for clinical examination and early diagnosis, often leading to misdiagnosis or delayed detection[4]. Therefore, ultrasonography has emerged as a critical diagnostic tool. Despite its importance, there is a paucity of literature, both domestically and internationally, regarding the ultrasonographic features of ciliary body tumors, particularly mesectodermal leiomyomas. To address this knowledge gap, this study aims to elucidate the ultrasonographic features of CBL. The findings of this investigation are intended to provide valuable insights into the diagnosis and differential diagnosis of ciliary body tumors.

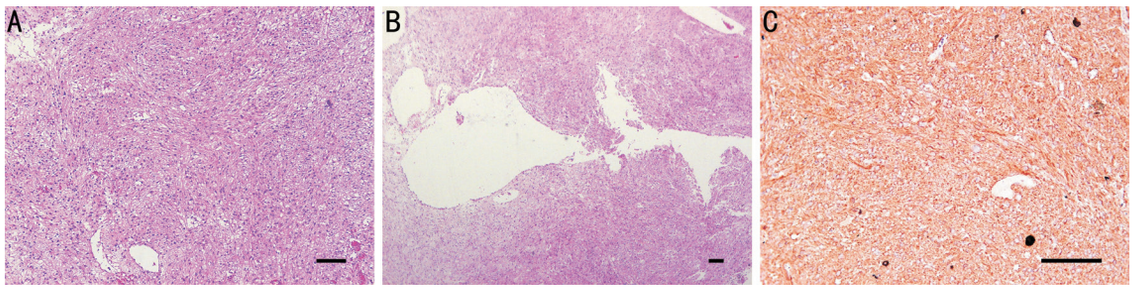

Figure 1 Histopathologic image of CBL A: The tumor is composed of spindle-shaped and oval cells. The cells contain small and gentle nuclei and fibrillar eosinophilic cytoplasm, and there is no atypia or pathological mitosis (HE×100); B: Large cavity structures are observed in the tumor, but no haemorrhage or necrosis is observed (HE×50). C: IHC staining for smooth muscle actin is positive in the tumor (IHC×200). CBL: Ciliary body mesectodermal leiomyomas; HE: Hematoxylin and eosin staining; IHC: Immunohistochemical. Scale bar=100 μm.

PARTICIPANTS AND METHODS

Ethical Approval This study adhered to the Declaration of Helsinki and was approved by the Ethics Review Committee of Beijing Tongren Hospital (No.TRECKY 2015-17), Capital Medical University. All patients signed informed consent forms before undergoing contrast-enhanced ultrasound (CEUS) examinations.

A total of 18 patients with CBL confirmed by histopathology between March 2018 and February 2024 at the Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University were enrolled in this retrospective, descriptive study. This study included 5 males and 13 females, aged 14-64y, with an average age of 40.11±13.54y. Eight cases involved the right eye, and 10 involved the left eye. The histopathological diagnostic criteria for CBL were: under the light microscope, the tumor cells can be spindle, round or oval. The nucleus of tumor cells was small and gentle, small nucleoli could be seen in some tumor cells, and there was no atypia or pathological mitosis. Immunohistochemical staining showed strong positive reaction of smooth muscle actin, the expression of glial fibrillary acidic protein, cytokeratin, soluble protein-100, human melanoma black-45 and Melan-A were all negative (Figure 1).

All patients underwent ultrasound examinations, and all ultrasonographic data were independently analyzed by three senior ultrasound imaging specialists, who were blinded to clinical information and pathological results. The inclusion criteria for this study were patients with CBL confirmed by histopathology. The exclusion criteria for this study included: 1) Patients who were misdiagnosed as having other ciliary body tumors and received radiotherapy or chemotherapy; 2) Patients who had received chemotherapy for neoplasms in other organs. The patients underwent a standard clinical evaluation, including best-corrected visual acuity, intraocular pressure, slit lamp microscopy, indirect ophthalmoscopy, fundus color photography, ultrasonography, CEUS, and systemic examination.

Equipment and Methods The MyLab 90 (Esaote, Genova, Italy) and EPIQ 7 (Philips, The Netherlands) color Doppler diagnostic systems were used. For conventional ultrasound examinations, a probe frequency of 6-18 MHz was selected, while for CEUS, a probe frequency of 3-9 MHz was used. The output power was adjusted to around 20%, with the mechanical index controlled below 0.23.

For conventional ultrasound examinations, both transverse and longitudinal scans were used to evaluate the tumor. The echogenicity of normal orbital adipose tissue was used as a reference for medium echogenicity. If the echogenicity was significantly lower than the echogenicity of normal orbital adipose tissue, it was classified as hypoechoic, while those between hypoechoic and isoechoic were designated as low-to-medium echogenic. We documented the tumor base diameter, thickness, maximum base diameter-to-thickness ratio, shape, internal echogenicity, and echo homogeneity. We then selected the optimal examination plane for CEUS. Blood flow signals were graded using color Doppler flow imaging (CDFI) according to the Adler *et al*[5] grading system.

CEUS examinations were performed on 14 patients. We used SonoVue sulfur hexafluoride microbubbles (manufactured by Bracco) as the contrast agent and prepared the agent according to the manufacturer's instructions. A 1.0 mL bolus of contrast agent was administered intravenously *via* the cubital vein, followed by a 5 mL saline flush. The timer was started simultaneously with the contrast agent administration. We continuously observed and recorded the entire process of contrast agent perfusion and wash-out within the tumor. The data were saved and exported in Dicom format. We analyzed the circulatory characteristics of the contrast agent within the tumor using the contrast agent perfusion and wash-out in the normal eye wall as a reference.

RESULTS

Characteristics of Patients The primary symptom was vision decline, with a symptom onset duration ranging from 1mo to 3y. Visual acuity ranged from hand motion to 0.4. Six tumors

Table 1 Clinical data of eighteen patients with CBL

Case No.	Age (y)	Sex	Eye	Visual acuity	IOP (mm Hg)	Quadrant	Clinical manifestation	Management	Ocular symptoms
1	24	F	L	20/50	19	Superotemporal	Nonpigmented	Resection	Vision decline for 6mo
2	20	M	R	20/100	15	Inferior	Pigmented	Resection	Blurred vision for 2mo
3	28	F	L	20/200	24	Temporal	Pigmented	Resection	Vision decline for 3mo
4	42	F	R	NLP	14	Temporal	Pigmented	Resection	Blurred vision for 1y
5	60	F	R	20/500	14	Temporal	Nonpigmented	Resection	Blurred vision for 6mo
6	43	F	L	HM	13	Superotemporal	Pigmented	Resection	Vision decline for 11mo
7	64	M	R	20/63	16	Superonasal	Nonpigmented	Resection	Blurred vision for 1y
8	44	F	R	20/50	13	Temporal	Nonpigmented	Resection	Vision decline for 9mo
9	60	F	L	FC	28	Inferonasal	Nonpigmented	Resection	Vision decline for 1y
10	38	F	R	20/200	13	Temporal	Pigmented	Resection	Vision decline for 2mo
11	14	M	L	NLP	21	Inferior	Pigmented	Resection	Vision decline for 1y
12	40	F	L	20/63	10	Inferonasal	Pigmented	Resection	Vision occlusion for 2mo
13	43	F	L	20/100	12	Superior	Pigmented	Resection	Blurred vision for 6mo
14	53	F	L	20/200	19	Inferior	Pigmented	Resection	Vision decline for 6mo
15	39	M	L	20/200	22.2	Superonasal	Pigmented	Resection	Blurred vision for 2y
16	40	M	R	FC	13	Superior	Nonpigmented	Resection	Vision decline for 1y
17	34	F	R	20/667	17.1	Inferior	Pigmented	Resection	Vision decline for 3y
18	36	F	L	20/200	22	Superior	Pigmented	Resection	Vision decline for 1y

CBL: Ciliary body mesectodermal leiomyomas; IOP: Intraocular pressure; NLP: No light perception; HM: Hand movement; FC: Finger counting; F: Female; M: Male; L: Left; R: Right.

appeared non-pigmented (grayish-white or pink), and 12 were pigmented (brown or brownish). Transillumination tests on the pigmented tumors revealed that 9 were non-transilluminable, and 3 were partially transilluminable (Table 1, Figure 2).

Ultrasonographic Features In the 18 patients with CBL, the conventional ultrasound findings were as follows: 1) Tumor size: a base diameter of (13.48±4.74)×(11.57±4.00) mm^2, a thickness of 7.70±2.60 mm, and a maximum base diameter-to-thickness ratio of 1.77±0.36; 2) Shape: 14 tumors (77.8%) were hemispherical, and 4 (22.2%) were irregular; 3) Echogenicity: a) Internal echogenicity: the solid component of the tumor was hypoechoic in 16 cases (88.9%) and low-to-medium echogenic in 2 (11.1%); b) Margin echogenicity: relatively hyperechoic with a "ring-shaped" margin in 15 cases (83.3%) and isoechoic in 3 cases (16.7%; compared with internal echogenicity); c) Internal echo homogeneity: homogeneous in 11 cases (61.1%) and heterogeneous in 7 cases (38.9%), with 6 (33.3%) out of those 7 cases exhibiting cystic anechoic area; 4) Secondary retinal detachment: 4 cases (22.2%) were observed; 5) CDFI features: blood flow signals were detected in all tumors, with marked blood flow signals in 5 cases (27.8%) presenting multiple punctate and linear flow signals, moderate blood flow signals in 5 cases (27.8%) showing linear flow signals, and minimal blood flow signals in 8 cases (44.4%) exhibiting only punctate flow signals (Figures 3 and 4; Table 2).

Contrast-Enhanced Ultrasound Characteristics CEUS were performed on 14 patients. We recorded the level of contrast enhancement as well as the wash-in and wash-out patterns in the solid component of the tumor. Complete perfusion was observed in 10 cases (71.4%), and partial perfusion was seen in 4 cases (28.6%). In cases with partial perfusion, the areas of perfusion defects corresponded to cystic anechoic areas on ultrasound (Figure 5). Eight cases (57.1%) demonstrated a rapid wash-in and slow wash-out pattern, while six cases (42.9%) exhibited a rapid wash-in and rapid wash-out pattern (Figure 6).

DISCUSSION

Intraocular leiomyomas most commonly occur in the ciliary body, accounting for approximately 73.8% of uveal leiomyomas, while occurrences in the iris and choroid are rare[6-7]. CBL are more prevalent in young females, with no difference between eyes. The growth of CBL is generally slow, though rapid growth has been observed in a few cases[8-10]. The most common symptom is blurred vision, which may be caused by complications such as lens subluxation, cataracts, or secondary retinal detachment. The second most common presentation is incidental diagnosis or discovery of a localized mass. Clinical symptoms typically become more severe as the tumor size increases[4]. CBL are typically non-pigmented and exhibit a roughly spherical shape. They may appear pinkish and are generally translucent[11]. When covered by ciliary pigment epithelium, they can appear brown or brownish-black. In this case series, 66.7% of the tumors were brownish-black, resembling melanomas. Transillumination tests can be particularly useful for the clinical diagnosis of ciliary body and anterior choroidal tumors. In cases where the tumor is

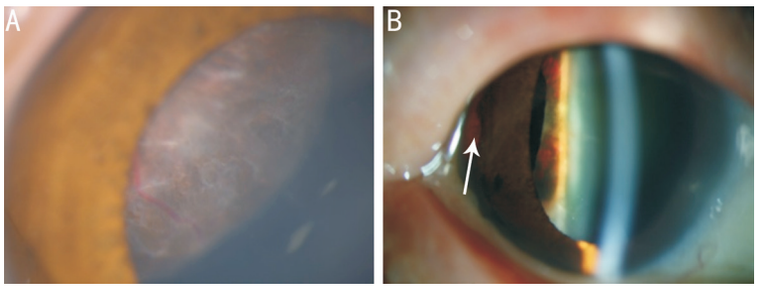

Figure 2 Images of the anterior segment of CBL A: The tumor surface is encapsulated by a pigmented membrane, presenting a brownish appearance. The tumor is non-transilluminable. B: Transillumination test shows partial transillumination of the tumor (arrow). CBL: Ciliary body mesectodermal leiomyomas.

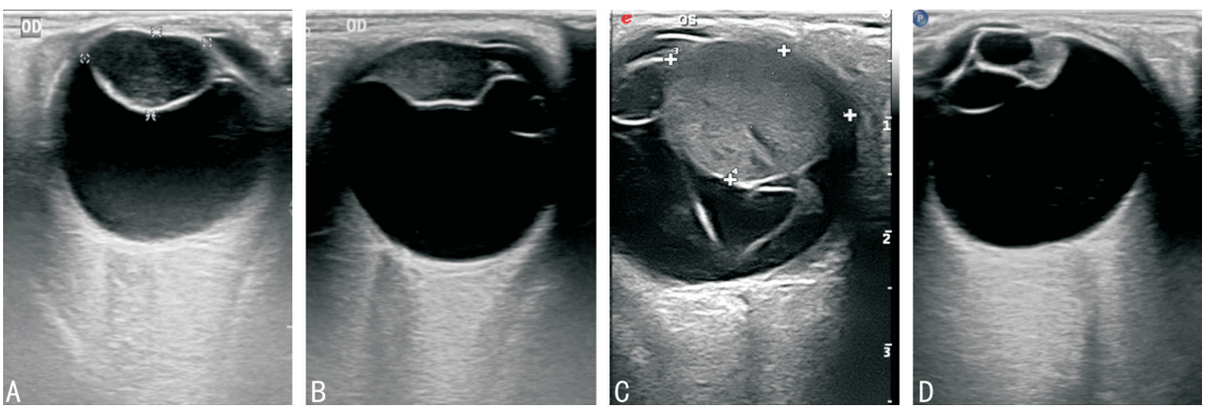

Figure 3 Two-dimensional ultrasound images of CBL A: The tumor is hemispherical, with the margin being hyperechogenic compared with internal echogenicity, displaying a "ring-shaped" margin; B: The tumor is irregularly shaped, with the margin being hyperechogenic compared with internal echogenicity, displaying a "ring-shaped" margin; C: The tumor is hemispherical, showing heterogeneous internal echogenicity. The solid component of the tumor demonstrates low to medium echogenicity (slightly hypoechoic compared with the echogenicity of orbital adipose tissue), interspersed with linear anechoic areas; D: The tumor is irregularly shaped, with heterogeneous internal echogenicity. Within the tumor, a cystic anechoic area is present. The solid component of the tumor is hypoechoic. CBL: Ciliary body mesectodermal leiomyomas; OD: Right eye; OS: Left eye.

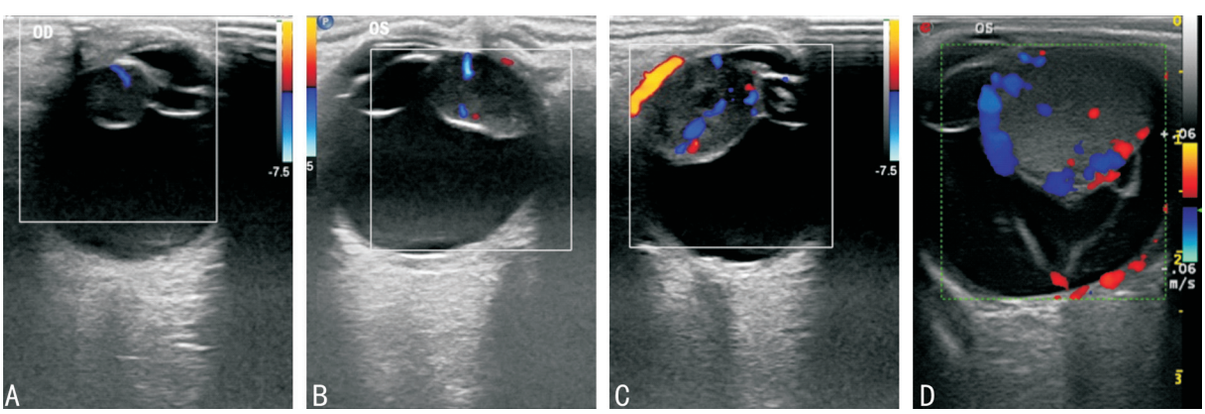

Figure 4 CDFI of CBL A: Minimal blood flow signals within the tumor, characterized by a single linear flow signal; B: Moderate blood flow signals within the tumor, demonstrated by both punctate and linear flow signals; C: Marked blood flow signals within the tumor, evidenced by multiple punctate and linear flow signals; D: Marked blood flow signals within the tumor. Additionally, a V-shaped band-like echogenic structure is seen in the vitreous cavity, connected to the echogenic region of the optic disc. Flow signals are observed along this band-like structure, indicative of secondary retinal detachment. CDFI: Color Doppler flow imaging; CBL: Ciliary body mesectodermal leiomyomas; OD: Right eye; OS: Left eye.

large or has a pigmented surface, transillumination may show partial translucency or complete light blockage[4,12-13]. As a rare type of intraocular tumor, its accurate diagnosis based solely on clinical features is challenging. In this case series, 33.3% of CBL were non-pigmented, requiring differentiation from non-pigmented epithelial adenomas, schwannomas, and medulloepithelioma of the ciliary body, the latter being more common in children[14-15]. When covered with pigmented

Table 2 Ultrasonographic features of CBL

Case No.	B-scan						CDFI blood flow grade	CEUS	
	Size (mm)	Shape	Internal reflectivity	Internal structure	Ring shape	anechoic area		Enhancement pattern	Enhancement feature
1	14.6×13.8×9.1	Dome	Low	Regular	Yes	No	Moderate	NA	NA
2	7.9×6.9×5.2	Dome	Low	Regular	Yes	No	Minimal	Completely	Fast-in and slow-out
3	18.4×17.8×13.5	Dome	Low to medium	Irregular	No	Yes	Marked	Completely	Fast-in and slow-out
4	18.6×14.9×10.9	Dome	low	Irregular	Yes	Yes	Marked	Partly	Fast-in and slow-out
5	6.9×6.8×5.3	Dome	Low	Regular	Yes	No	Minimal	Completely	Fast-in and fast-out
6	13.6×12.4×8.1	Dome	Low	Regular	Yes	No	Moderate	Completely	Fast-in and slow-out
7	7.5×4.9×3.9	Dome	Low	Regular	Yes	No	Minimal	NA	NA
8	16.6×16.0×6.7	Irregular	Low	Regular	Yes	No	Marked	Completely	Fast-in and fast-out
9	11×10.2×4.4	Irregular	low	Irregular	No	Yes	Minimal	Partly	Fast-in and slow-out
10	12.6×12.6×8.7	Dome	Low	Regular	Yes	No	Minimal	Completely	Fast-in and fast-out
11	21.8×15.5×11.2	Irregular	Low to medium	Irregular	No	No	Marked	NA	NA
12	18.7×15.7×9.7	Dome	Low	Irregular	Yes	Yes	Minimal	Partly	Fast-in and fast-out
13	10.1×6.9×5.7	Irregular	Low	Irregular	Yes	Yes	Minimal	Partly	Fast-in and fast-out
14	16.7×14.9×7.6	Dome	Low	Regular	Yes	No	Moderate	Completely	Fast-in and slow-out
15	12.2×10.9×7.2	Dome	Low	Regular	Yes	No	Moderate	Completely	Fast-in and fast-out
16	18.9×13.3×9.5	Dome	Low	Irregular	Yes	Yes	Marked	NA	NA
17	7.9×6.8×5.9	Dome	Low	Regular	Yes	No	Minimal	Completely	Fast-in and slow-out
18	8.7×8.0×6.0	Dome	Low	Regular	Yes	No	Moderate	Completely	Fast-in and slow-out

CBL: Ciliary body mesectodermal leiomyomas; CDFI: Color Doppler flow imaging; CEUS: Contrast-enhanced ultrasound; NA: Not applicable.

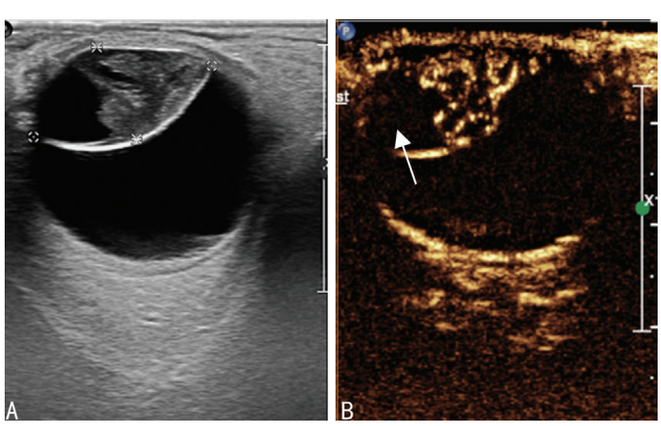

Figure 5 CEUS images of CBL A: Two-dimensional ultrasound image shows a hemispherical tumor with heterogeneous internal echogenicity, irregular cystic anechoic area, and hyperechogenic margin, displaying a "ring-shaped" margin; B: Contrast-enhanced ultrasound reveals the perfusion defect within the tumor corresponds to cystic anechoic area on two-dimensional ultrasound (arrows). CEUS: Contrast-enhanced ultrasound; CBL: Ciliary body mesectodermal leiomyomas.

epithelium, differentiation from ciliary body melanomas is required. Misdiagnoses as melanomas have been frequently reported, leading to unnecessary enucleation in some cases. To prevent misdiagnosis and inappropriate treatment, precise diagnosis before initiating therapy is crucial[1,8,12,16]. Ocular ultrasonography is an important method for the diagnosis, differential diagnosis, and follow-up of intraocular tumors. As a non-invasive and readily available examination technique, it can provide critical information for the clinical diagnosis of CBL. Previously, detailed reports on the ultrasonographic features of CBL are relatively scarce. This study showed that these tumors predominantly present with a spherical shape, followed by irregular shapes. The average ratio of maximum base diameter-to-thickness was 1.77±0.36. They did not show the mushroom-like or elevated growth patterns typically seen in melanomas. Compared with the echogenicity of orbital adipose tissue, the internal echoes of the tumors were mostly hypoechoic, which is consistent with findings in some previously reported cases[17]. In this study, 33.3% of the tumors showed cystic echogenicity, a feature rarely reported before. Lai *et al*[18] reported a case of CBL with focal hemorrhage and myxoid degeneration. Kim *et al*[10] found a cystic anechoic area in the central region of the tumor on ultrasound, corresponding to the necrotic area revealed in histopathological examination. In this study, we observed cavitary structures present within the tumor during histopathological examination, but no hemorrhage or necrosis was found. In the comparison of echogenicity within the tumor and at its margin, 77.8% of tumors exhibited significantly higher echogenicity at the margin compared to the internal echogenicity, presenting a "ring-shaped" margin feature. We propose that this ultrasound feature results from the tumor being in the ciliary body or suprachoroidal space, with the tumor surface covered by partial ciliary muscle, ciliary

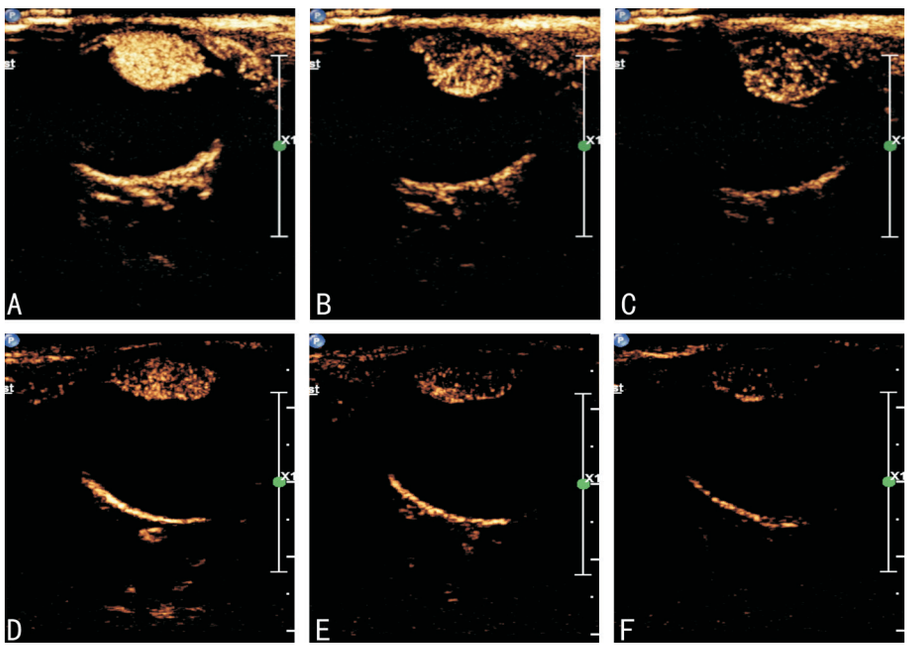

Figure 6 CEUS of CBL A: 18s post-contrast injection: complete contrast agent perfusion in both tumor and eye wall; B: 60s: varying degrees of contrast agent wash-out in both tumor and eye wall; C: 90s: substantial contrast enhancement in the tumor, while the eye wall shows more extensive contrast agent wash-out, demonstrating a rapid wash-in and slow wash-out pattern in the tumor; D: 19s post-contrast injection: complete contrast agent perfusion in both tumor and eye wall; E: 60s: varying degrees of contrast agent wash-out in both the tumor and eye wall; F: 90s: near-complete contrast agent wash-out in the tumor, with the eye wall retaining slight enhancement, exhibiting a rapid wash-in and rapid wash-out pattern in the tumor. CEUS: Contrast-enhanced ultrasound; CBL: Ciliary body mesectodermal leiomyomas.

epithelium, or a surrounding capsule. Due to the difference in acoustic impedance, the margin appears hyperechogenic compared to the tumor, resulting in the observed "ring-shaped" feature[6,19-21]. This feature aids in differentiating between tumors of ciliary epithelial origin and malignant melanomas.

CEUS is more sensitive in detecting blood flow than CDFI[22]. By observing the perfusion characteristics in the tumor through intravenously injected microbubble contrast agent, it provides important information for the diagnosis and differential diagnosis of tumors[23-24]. In recent years, CEUS has emerged as a safe and successful method for diagnosing ocular diseases[25-27]. Among the 14 patients who underwent CEUS in this study, 4 cases (28.6%) showed partial contrast agent perfusion in the tumor, with perfusion defects corresponding to anechoic cysts, indicating no vascular structures within these cystic areas. In our previous studies on the characteristics of ultrasound contrast-enhanced imaging of intraocular tumors, we found that choroidal melanomas mostly exhibited a rapid-in and rapid-out pattern. However, in this study, 6 cases (42.9%) of ciliary leiomyomas also displayed a similar rapid-in and rapid-out pattern, mimicking the appearance of melanomas. Nevertheless, 8 cases (57.1%) of ciliary leiomyomas demonstrated different characteristics on ultrasound contrast-enhanced imaging, showing a rapid-in and slow-out pattern, which was similar to that of choroidal hemangiomas[27]. For the imaging diagnosis of CBL, the rapid wash-in and slow wash-out pattern on the CEUS provides crucial clues for preliminarily ruling out malignant ciliary body melanomas. This information is crucial for guiding eye-preserving treatments for intraocular tumors.

Limitations of the study: Due to the rarity of CBL, this study utilized a single-center, retrospective design with a relatively small sample size of CEUS examinations. Multi-center, comparative, in-depth studies are needed to establish more precise diagnostic criteria for CBL and similar conditions through quantitative analysis of CEUS. Furthermore, we should conduct a more in-depth analysis of the relationship between the diverse manifestations of CEUS and histopathology.

In conclusion, CBL exhibit distinct ultrasonographic features. On ultrasound, these tumors typically appear as hemispherical in shape. They often present with homogeneous, hypoechoic internal echogenicity, and some tumors may show cystic anechoic areas. The "ring-shaped" margin and the rapid wash-in and slow wash-out pattern on CEUS are helpful in differentiating these tumors from other ciliary body tumors.

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Authors' Contributions: Li DJ and Yang WL conceptualized and designed the study, coordinated and supervised data collection. Yang WL and Wei WB critically reviewed the manuscript. Li DJ, Zhao Q, Li YF, Cui R, Shen L, Liu Q and Zhang X collected data. Li DJ, Wang ZY and Chen W analyzed the data. Li DJ drafted the initial manuscript. Li DJ,

Yang WL and Wei WB revised the manuscript. All authors read and approved the final manuscript.

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