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Sonographic classification of testicular tumors by tissue harmonic imaging: experience of 58 cases

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Abstract

Purpose To evaluate the relationship between our proposed sonographic classification of testicular tumors by tissue harmonic imaging and histological type.

Methods We retrospectively analyzed 58 testicular tumors and tumor-like lesions [seminomatous germ cell tumor (SGCT): 28; non-seminomatous germ cell tumor (NSGCT): 16; lymphoid and hematopoietic tumor (LHT): 7; Leydig cell tumor: 1; epidermal cyst: 2; and tumor of paratesticular structure (TPS): 4]. We divided a sonographic image into six types for morphological criteria and three types for color Doppler criteria. We examined the relationship between the sonographic classification and histological type.

Results For morphological criteria, there were 21 cases of Type I (36%), 15 Type II (26%), 9 Type III (15%), five Type IV (9%), five Type V (9%), and three Type VI (5%). For color Doppler criteria, there were 47 cases classified as hypervascular (81%), eight as hypovascular (14%), and

three as avascular (5%). Most of the SGCTs were divided into types I and II; the NSGCTs into types III, IV, and V; the LHTs into only type II; and the TPSs into type VI.

Conclusion We established a sonographic classification of testicular tumors with various histological types. This sonographic classification is potentially useful for estimating the histological type of testicular tumors.

Keywords Ultrasonography · Tissue harmonic imaging · Testis · Testicular tumor

Introduction

Although there is only a 1% occurrence of malignant testicular cancer in men, it is considered a major disease in society. Typically, testicular tumors develop in young adults in their 20–30 s, and they have the highest occurrence rate among cancers in young adults [1, 2]. Approximately, 95% of testicular tumors are germ cell tumors that develop from spermatocytes and are characterized by their fast progression [3]. In recent years, the occurrence rate of testicular cancer has increased in many countries [4].

Ultrasonic examination is the primary choice for image evaluation to confirm the presence of testicular tumors, being inexpensive and noninvasive [5]. It has an approximate sensitivity of 100% for detecting testicular tumors and has proven to be very useful for determining the location of a mass as either internal or external to the testes [6]. However, morphological evaluation using ultrasound imaging has proven to be difficult for estimating the histological type [7]. Although an accurate histological diagnosis is difficult, there are several reports of ultrasound findings that reflect the histological type [8, 9].

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Fig. 1 a Schematic representation of morphological criteria: Types I–VI. Gray area testis; dark area lesions; black area cystic components; whitish area echogenic foci with acoustic shadow. **b** Color Doppler criteria: hypervascular, hypovascular, and avascular. Hypervascular: more than the testicular flow; hypovascular: less than the testicular flow; avascular: unseen tumoral flow

(a) Morphological criteria

(b) Color Doppler criteria

Table 1 Histopathological characteristics of 58 patients with testicular tumors

	Age (years)	Size (mm)
SGCT ($n = 28$)	35.8 ± 8.0	53.1 ± 23.3
NSGCT ($n = 16$)	29.6 ± 9.3	40.9 ± 19.0
Embryonal carcinoma ($n = 3$)	29.7 ± 3.5	35.7 ± 14.6
Teratoma ($n = 1$)	27	75
Mixed germ cell tumor ($n = 12$)	29.8 ± 10.7	39.3 ± 18.4
LHT ($n = 7$)	62.3 ± 9.2	55.1 ± 13.1
Lymphoma ($n = 5$)	67 ± 3.9	55.8 ± 15.1
Leukemia ($n = 1$)	56	46
Plasmacytoma ($n = 1$)	45	61
Leydig ($n = 1$)	30	16
EDC ($n = 2$)	44 ± 35.4	36.5 ± 23.3
TPS ($n = 4$)	30.8 ± 8.9	23.0 ± 10.5
Overall ($n = 58$)	37.1 ± 13.7	46.7 ± 21.9

SGCT seminomatous germ cell tumor, NSGCT non-seminomatous germ cell tumor, LHT lymphoid and hematopoietic tumors, Leydig Leydig cell tumor, EDC epidermal cyst, and TPS tumors of paratesticular structure

Recent advances in ultrasound equipment has seen the introduction of high-frequency probes and tissue harmonic imaging (THI), which has drastically increased the spatial and contrast resolution of gray-scale images [10]. The sensitivity of the color Doppler method has been improved with digital ultrasound equipment and broadband

transducers, making it easier to perceive blood flow within the testes. We, therefore, investigated the possibility of establishing an ultrasound classification of testicular tumors for future ultrasound diagnosis.

Materials and methods

This retrospective study was approved by our institutional review board (No. 2112). The subjects of this study consisted of 58 patients with testicular tumors or tumor-like lesions that had been histologically evaluated by preoperative ultrasound examinations during the period from January 2001 to August 2010. All lesions were unilateral. High inguinal orchiectomy was carried out in 56 patients. Two patients underwent exploratory examination via the inguinal approach for excision of the lesion outside the tunica albuginea of the testis.

The final pathological diagnoses were seminomatous germ cell tumor (SGCT; $n = 28$); non-seminomatous germ cell tumor (NSGCT; $n = 16$), which included embryonal carcinoma ($n = 3$), teratoma ($n = 1$), and mixed germ cell tumor ($n = 12$); lymphoid and hematopoietic tumors (LHT; $n = 7$), which included lymphoma ($n = 5$), plasmacytoma ($n = 1$), and leukemia ($n = 1$); sex code/gonadal stromal tumors (Leydig cell tumor; $n = 1$); epidermal cyst (EDC; $n = 2$); and tumors of the paratesticular structure (TPS; $n = 4$), which included adenomatoid tumor ($n = 3$) and adenocarcinoma ($n = 1$).

Fig. 2 Results of morphological criteria. **a** Overall distribution of morphological criteria, **b** Type I, **c** Type II, **d** Type III, **e** Type IV, **f** Type V, and **g** Type VI

Fig. 3 Results of color Doppler criteria. **a** Overall distribution of color Doppler criteria, **b** hypervascular, **c** hypovascular, and **d** avascular

The types of ultrasound equipment used were a SONOLINE Elegra (Siemens Medical Systems, Erlangen, Germany) and an Aplio XV: SSA700A (Toshiba Medical Systems, Tochigi, Japan). The probes were high-frequency linear 7.5L40 and PLT-805AT.

Gray-scale images were obtained by THI (phase-inversion THI with a transmission frequency of 4.5 MHz and a receive frequency of 9.0 MHz, or differential THI with a transmission frequency of 9 MHz). Color Doppler images were magnified on a timely basis, and region of interest

size was kept within the scope of the lesion site and normal part. The velocity range was set below 5 cm/s and color gain was individually optimized.

Obtained images were classified according to the morphological and internal texture. The morphological criteria were classified into six types. Type I: a nodular lesion that is elliptical to lobular; Type II: a diffuse lesion that is between patchy to geographic; Type III: a lesion containing an internal cystic component; Type IV: a lesion containing echogenic foci (excluding testicular microlithiasis); Type V: a lesion mixed with cystic components and echogenic foci; Type VI: a lesion outside the tunica albuginea of the testes (Fig. 1a).

Color Doppler classification was performed using normal parenchymal blood flow as the criteria. When the color signal of the lesion area was higher than that of the surrounding normal parenchyma, it was classified as hypervascular and, when lower, hypovascular. If no color signal was found within the lesion, it was classified as avascular (Fig. 1b).

Results

The average age of the patients was 37.2 ± 13.6 years. The average tumor diameter was 46.9 ± 21.8 mm (Table 1).

For the morphological criteria, ultrasound imaging of the 58 patients showed 21 cases of Type I (36%), 15 cases of Type II (26%), nine cases of Type III (15%), five cases

Table 2 Relations between histopathological type and sonographic criteria

	SGCT	NSGCT	LHT	Leydig	EDC	TPS
Morphological criteria						
Type I	18 (64)			1 (100)	1 (50)	1 (25)
Type II	8 (29)		7 (100)			
Type III	2 (7)	7 (44)				
Type IV		5 (31)				
Type V		4 (25)			1 (50)	
Type VI						3 (75)
Color Doppler criteria						
Hypervascular	28 (100)	12 (75)	7 (100)			
Hypovascular		3 (19)		1 (100)		4 (100)
Avascular		1 (6)			2 (100)	

n (%)

SGCT seminomatous germ cell tumor, *NSGCT* non-seminomatous germ cell tumor, *LHT* lymphoid and hematopoietic tumors, *Leydig* Leydig cell tumor, *EDC* epidermal cyst, and *TPS* tumors of paratesticular structure

Fig. 4 **a** Seminoma in a 42-year-old man. THI US scan showing a well-circumscribed markedly hypoechoic lesion (Type I). **b** Color Doppler US (hypervascular). **c** Seminoma in a 30-year-old man. THI US scan showing multiple cystic components (Type III) (white

arrow). **d** Photomicrograph (hematoxylin-eosin stain; original magnification $\times 2$) showing intratumoral hemorrhage (black arrow). THI tissue harmonic imaging, US ultrasound

of Type IV (9%), five cases of Type V (9%), and three cases of Type VI (5%) (Fig. 2a).

The specific distributions for each type were as follows (Fig. 2 b-g). Type I: SGCT ($n = 18$; 85%), Leydig cell tumor ($n = 1$; 5%), EDC ($n = 1$; 5%), and TPS ($n = 1$;

5%); Type II: SGCT ($n = 8$; 53%) and LHT ($n = 7$; 47%); Type III: SGCT ($n = 2$; 22%) and NSGCT ($n = 7$; 78%); Type IV: NSGCT ($n = 5$; 100%); Type V: NSGCT ($n = 4$; 80%) and EDC ($n = 1$; 20%); Type VI: TPS ($n = 3$; 100%).

Fig. 5 **a** NSGCT (mixed form; embryonal carcinoma, teratoma) in a 32-year-old man. THI US scan showing multiple cystic components (Type III) (white arrow). **b** Multilocular cyst in the area of the teratoma component (hematoxylin-eosin stain; original magnification $\times 2$). **c** NSGCT (embryonal carcinoma) in a 30-year-old man. THI US scan showing a small cystic area and grouped echogenic foci

with indistinct acoustic shadow (Type V) (white arrow). **d** Photomicrograph (hematoxylin-eosin stain; original magnification $\times 10$) showing intratumoral necrosis with calcification (black arrow). NSGCT non-seminomatous germ cell tumor, THI tissue harmonic imaging, US ultrasound

The classifications according to the color Doppler criteria were as follows (Fig. 3a): hypervascular ($n = 47$; 81%), hypovascular ($n = 8$; 14%), and avascular ($n = 3$; 5%). The specific distributions for the color Doppler criteria were as follows (Fig. 3b–d). Hypervascular: SGCT ($n = 28$; 60%), NSGCT ($n = 12$; 25%), and LHT ($n = 7$; 15%); hypovascular: NSGCT ($n = 3$; 38%), Leydig cell tumor ($n = 1$; 12%), and TPS ($n = 4$; 50%); avascular: NSGCT ($n = 1$; 33%) and EDC ($n = 2$; 67%).

The distributions of the individual histological type patterns were as follows (Table 2). For SGCT: Type I ($n = 18$; 64%), Type II ($n = 8$; 29%), and Type III ($n = 2$; 7%); hypervascular ($n = 28$; 100%) (Fig. 4). For NSGCT: Type III ($n = 7$; 44%), Type IV ($n = 5$; 31%), and Type V ($n = 4$; 25%); hypervascular ($n = 12$; 75%), hypovascular ($n = 3$; 19%), and avascular ($n = 1$; 6%) (Fig. 5). For LHT: Type III ($n = 7$; 100%); hypervascular ($n = 7$; 100%) (Fig. 6). The morphological criterion for Leydig cell tumor was Type I and the color Doppler criterion was hypovascular (Fig. 7). The morphological criteria for EDC were Type I ($n = 1$; 50%) and Type V ($n = 1$; 50%), and the color Doppler criterion for both was avascular (Fig. 8).

The morphological criteria for TPS were Type I ($n = 1$; 25%) and Type VI ($n = 3$; 75%), and the color Doppler criterion was hypovascular (100%) (Fig. 9).

Discussion

Testicular tumors have the characteristic of typically developing in infants and young adults and show an extremely fast progression. These tumors are malignant with a poor prognosis in advanced cases. Proper early clinical diagnosis is necessary to improve treatment outcomes [11]. Testicular tumors are treated by performing a high inguinal orchiectomy without biopsy, and deciding a treatment plan upon making a definitive histological diagnosis [12]. However, the minority of patients with benign testicular tumors must be excluded from these excessive invasive treatments.

In our investigation as to whether it would be possible to estimate the histological type based on the ultrasound pattern classification, we found that each histological type has its own characteristics (Table 3).

Fig. 6 **a** Non-Hodgkin lymphoma (diffuse, large, B cell) in a 71-year-old man. THI US scan showing a diffuse hypoechoic lesion (Type II). **b** Color Doppler US (hypervascular). **c** Photomicrograph

(hematoxylin-eosin stain; original magnification $\times 4$) showing diffuse infiltration of atypical lymphocytes. THI tissue harmonic imaging, US ultrasound

In general, SGCTs are solid and hypervascular lesions. For morphological criteria, the majority of SGCTs were Type I and Type II ($n = 26$; 93%). The color Doppler criterion was hypervascular in all cases. However, although it was a minority, Type III ($n = 2$; 7%) was included. The histological findings of these two cases reflected a blood congestion and necrosis etiology. Analysis by Schwerk et al. also found tissues containing small cystic areas in 10% of SGCTs, which is consistent with this study [13].

NSGCTs showed various morphological criteria, namely, Type III, Type IV, and Type V. This is thought to be due to the histological mixing of single embryonal carcinoma, yolk sac tumors, choriocarcinoma, and teratoma or multiple histological types including SGCT. However, a majority showed nonuniform internal characteristics containing a cyst or hyperechoic foci. Conventional NSGCT sonographic findings have shown heterogeneous internal characteristics [14]. Howlett et al. demonstrated characteristic sonographic findings of cysts and calcification [15]. In that case, the cause of Type III was a multilocular cyst in the area of the teratoma component. For Type IV, the causes have been found to be calcification, ossification, and chondrogenesis, matching the report of Hamm et al. [16].

All LHTs were Type II and hypervascular. Ultrasound findings for LHTs showed testicular swelling and a restricted or diffuse hypoechoic area [17]. As these findings are also observed for SGCTs, distinguishing between LHTs and SGCTs from ultrasound images alone is difficult. It is known, however, that the age distribution for LHTs is high [18]. As observed in this study, SGCT patients have an average age of 36.0 ± 8.0 years, which shows a clear discrepancy compared with the LHT patients, who have an average age of 62.3 ± 9.2 years. Thus, for sonographic classification, it is necessary to take age into account when making a judgment.

Although the Leydig cell tumors were classified as Type I, similarly to SGCTs, the blood flow was poor in comparison, making discrimination possible by color Doppler [19]. EDCs have no blood flow for Type I or Type V, and it was shown to be avascular by color Doppler [20]. In the case of TPS, it was thought possible to distinguish it from testicular cancer by carefully observing whether the lesions are internal or external to the tunica albuginea [21].

When establishing an ultrasound classification of testicular tumors, it is best to proceed by combining shape assessment and Doppler assessment. For lesions that are Type I in terms of morphological criteria and

Fig. 7 **a** Leydig cell tumor in a 30-year-old man. THI US scan showing a well-circumscribed hypoechoic lesion (Type I). **b** Color Doppler US (hypovascular). **c** Photomicrograph (hematoxylin-eosin stain; original magnification $\times 2$) showing a well-circumscribed mass

lesion. **d** Photomicrograph (hematoxylin-eosin stain; original magnification $\times 20$) showing uniform sheets of eosinophilic tumor cells. *THI* tissue harmonic imaging, *US* ultrasound

Fig. 8 **a** Epidermal cyst in a 19-year-old man. THI US scan showing a well-circumscribed hypoechoic lesion (Type I) with an onion-ring appearance. **b** Color Doppler US (avascular). *THI* tissue harmonic imaging, *US* ultrasound

hypervascular on Color Doppler, SGCT should be considered foremost. Lesions that are Type II and hypervascular should be regarded as SGCT if the age is below 50 years and as LHT if the age is more than 60 years. For lesions that are Type III, Type IV, or Type V, NSGCT should be considered with no regard for color Doppler criteria. However, EDC should be suspected for specific findings such as an “onion ring appearance” [22]. TPS

should be suspected with Type VI extraglandular lesions in terms of morphological criteria and when hypovascular on color Doppler.

The depth of field for testicular tumors is sufficient at 4–6 cm, given that a linear probe for the body surface is used. There has been an indication of a trend toward standardization, and it is recommended that a high-frequency probe with a center frequency of 5–10 MHz be

Fig. 9 **a** Adenomatoid tumor in a 32-year-old man. THI US scan showing a well-circumscribed isoechoic lesion (Type VI). **b** Color Doppler US (hypovascular). **c** Photomicrograph (hematoxylin-eosin stain; original magnification $\times 4$). THI tissue harmonic imaging, US ultrasound

Table 3 Sonographic classification of testicular tumors

	Type I	Type II	Type III	Type IV	Type V	Type VI
Hypervascular	SGCT	SGCT LHT	NSGCT SGCT	NSGCT	NSGCT	
Hypovascular	Leydig TPS		NSGCT	NSGCT	NSGCT	TPS
Avascular	EDC		NSGCT		EDC	

SGCT seminomatous germ cell tumor, NSGCT non-seminomatous germ cell tumor, LHT lymphoid and hematopoietic tumors, Leydig Leydig cell tumor, EDC epidermal cyst, and TPS tumors of paratesticular structure

used [23]. The B-mode imaging here was performed by THI. THI is useful for increasing contrast, reducing artifacts, and emphasizing contours, and is reported to improve the contrast between normal parenchyma and lesions [24]. We would like to actively utilize THI as it increases image contrast in combination with compound scans. With the color Doppler method, the blood flow within the testicular parenchyma is slow, and the velocity range needs to be made at approximately 3–5 cm/s.

In recent years, there have been reports of testicular ultrasound based on new imaging methods, such as contrast ultrasonography and elastography [25, 26]. These are still limited to the assessment of tissue ischemia and blood

vascular systems, such as in acute scrotum and varicose veins. It is eagerly hoped that these new imaging techniques will have clinical applications for testicular cancer in the near future.

Some limitations of this study include the small number of cases examined and the possibility of the results being affected by the equipment used.

In conclusion, we established a sonographic classification of testicular tumors with various histological types. Each histological type was found to have specific ultrasound findings. Thus, sonographic classification may be considered useful for estimating the histological type of testicular tumors.

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Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest associated with this article.

Ethical considerations All procedures followed were in accordance with the Helsinki Declaration of 1964 and later versions. The institutional review board of our university hospital approved this retrospective study and informed consent was waived.

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