Sonographic imaging of extra-testicular focal lesions: comparison of grey-scale, colour Doppler and contrast-enhanced ultrasound

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Abstract

Extra-testicular lesions are usually benign but present with nonspecific grey-scale sonography findings. This study assesses conventional sonographic characteristics in the differentiation of extra-testicular tumoural from inflammatory lesions and whether contrast-enhanced ultrasound has a role. A retrospective database analysis was performed. All patients were examined by experienced sonographers employing standard techniques combining grey-scale, colour Doppler sonography and contrast-enhanced ultrasound. Features recorded were: clinical symptoms, size, location, echogenicity, colour Doppler sonography and contrast-enhanced ultrasound enhancement. Vascularity on colour Doppler sonography and contrast-enhanced ultrasound was graded and compared. The lesions were classified as tumoural or inflammatory. The Chi-square test was used to analyse the sonographic patterns and kappa coefficient to measure the agreement between colour Doppler sonography and contrast-enhanced ultrasound. A total of 30 lesions were reviewed (median diameter 12 mm, range 5–80 mm, median age 52 years, range 18–86 years), including 13/30 tumoural and 17/30 inflammatory lesions. Lesions were hypoechoic ($n=12$), isoechoic ($n=6$), hyperechoic ($n=2$) or mixed ($n=10$). Grey-scale characteristics of tumoural vs. inflammatory lesions differed significantly ($P=0.026$). On colour Doppler sonography, lesions had no vessels ($n=16$), 2–3 vessels ($n=10$) and ≥ 4 vessels ($n=4$). On contrast-enhanced ultrasound, lesions showed no vascularity ($n=17$), perfusion similar to testis ($n=7$) and higher ($n=6$). All abscesses identified ($n=9$) showed no vascularity on both colour Doppler sonography and contrast-enhanced ultrasound. There was good agreement between these techniques in evaluating vascularity ($\kappa=0.719$) and no significant difference between colour Doppler sonography and contrast-enhanced ultrasound of tumoural vs. inflammatory lesions ($P>0.05$). The grey-scale appearances of extra-testicular lesions are essential for characterisation. Colour Doppler sonography and contrast-enhanced ultrasound findings are not useful in that respect. Contrast-enhanced ultrasound is excellent in establishing absence of vascularity.

Keywords

Epididymis, tumour, inflammation, ultrasound, contrast

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Introduction

Sonography is vital in the investigation and management of patients who present with a scrotal mass. The site of the scrotal mass is important, with sonography useful in locating the abnormality to an intra-scrotal extra-testicular or intra-testicular position. This is an important distinction in the adult patient; the majority

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of intra-scrotal extra-testicular abnormalities are benign, with prevalence of malignancy approximately 3–16%.^{1–5} The commonest lesion in the extra-testicular position in the scrotum is the epididymal cyst or spermatocele, but a solid lesion is more problematic; extra-testicular primary solid neoplasms arise from the epididymis, spermatic cord and para-testicular connective tissues.⁶ With grey-scale sonography, these lesions have nonspecific appearances, usually presenting as solid lesions close to the testicular capsule of variable echogenicity.^{1,5} Lipomas are the most common para-testicular neoplasms arising from the spermatic cord, with an adenomatoid lesion being the most common epididymal benign tumour, accounting for 30% of all extra-testicular masses,^{6–9} both with variable and non-specific appearances on grey-scale sonography. Inflammatory causes such as epididymal-orchitis, abscess, tuberculosis or sarcoidosis also occur in the para-testicular space. Rarely, a fibrous pseudo-tumour or inflammatory pseudo-tumour may occur, thought to be a fibro-inflammatory reaction most commonly involving the tunica albuginea or vaginalis.¹⁰ A definite diagnosis is often established by histology. Surgical removal of benign scrotal lesions is not without morbidity and includes tumour recurrence, haematoma and infection, and if the tumour is epididymal based, may result in obstruction of the vas deferens.³

Occasionally, magnetic resonance (MR) imaging is used as a problem-solving tool to further characterise the scrotal lesions, specifically targeting fat content of the abnormality, distinguishing between intra- and extra-testicular masses in the periphery of the testis as well as demonstrating lesion vascularity.^{6,11,12} Microbubble contrast agents are established in the assessment of focal liver lesions,¹³ with many investigators assessing the efficacy of microbubble contrast in other organs.¹⁴ There has been an increasing interest in the role of contrast-enhanced ultrasound (CEUS) in diagnosis and management of scrotal lesions.¹⁵ The use of CEUS can potentially improve the characterisation of testicular lesions in terms of better delineation of the lesions,^{16–18} establishing their location and pattern of enhancement. Poor or absent enhancement is evident in the majority of non-neoplastic lesions.^{19,20–24}

There have been no reports regarding the appearances of benign and/or inflammatory extra-testicular lesions with CEUS. The aim of this study is to evaluate the conventional sonographic characteristics of extra-testicular intra-scrotal lesions and ascertain whether CEUS has any additional value.

Materials and methods

Ethics Review Board approval was sought for this retrospective study but waived. All patients provided

informed verbal consent for the sonographic evaluation including the use of microbubble contrast, which is the standard departmental practice. The patients were selected retrospectively from a departmental database maintained over a period of 5 years (2010–2014) by one of the authors (PSS). All patients were referred by the primary care physician or from Urology, undergoing a routine grey-scale sonographic examination according to departmental protocol, with the addition of colour Doppler sonography (CDS) assessment when required. A CEUS examination for further characterisation of the scrotal lesions was performed by consensus by the practitioners conducting the examination.

All patients were scanned by two experienced operators in testicular sonography and CEUS (PSS 16 years and MES 10 years). A standard testicular sonographic technique was used in all cases with standard high frequency transducers. All grey-scale and CDS examinations were performed with either a 14L5 or 9L4 linear transducer on a Siemens Acuson S2000 system (Siemens Medical Solutions, Mountain view, CA). For CEUS imaging, the 9L4 linear transducer was used with conventional low Mechanical Index (MI) imaging (Cadence Contrast Pulse Sequencing, CPSTM, Siemens, Mountain View, CA), after a bolus injection of 4.8 ml of SonoVueTM (Bracco SpA, Milan, Italy) as microbubble contrast media. On grey-scale sonography, characteristics of each lesion including echogenicity in comparison to the adjacent testis, shape, margin, location (upper, mid or lower epididymis or spermatic cord) and the lateralisation (right or left) were described by consensus by two reviewers (PSS, MES).

The vascularity of each lesion on CDS and CEUS imaging was recorded by consensus by the reviewers and divided on CDS imaging as follows: (I) no vascularity; (II) 2–3 vessels; and (III) ≥ 4 vessels. The vascularity on CEUS was graded as follows: (I) no vascularity; (II) similar vascularity to adjacent testis; (III) more vascularity than adjacent testis. Diagnosis was confirmed at excisional biopsy, MR imaging or stable appearances with follow-up sonography demonstrating continuing characteristic sonographic features or resolution. For statistical analysis, due to the small number of some types of lesions, two groups were formed, the tumoural and the non-tumoural or inflammatory lesions. The former group included lipoma, adenomatoid and leiomyoma, whereas the latter group included abscesses, pseudo-tumours, infarction and sarcoidosis. The Chi-square test with a significance level set to 0.05 was used to indicate any statistically significant difference in the frequencies of echogenicity and vascularity on CDS and CEUS patterns between these two groups. The agreement between CDS and CEUS in the characterisation of lesion vascularity was evaluated by calculating the kappa coefficient.

Table 1. The findings on grey-scale, colour Doppler and contrast-enhanced ultrasound, histology and follow up/additional imaging are listed for each lesion, for consecutive patients

Grey-scale appearance				Colour Doppler ultrasound		Contrast-enhanced ultrasound	Follow up
Diagnosis	Age	Lesion location	Size (mm)	Description	Lesion vascularity	Lesion vascularity (compared to adjacent testis)	
1 Adenomatoid	35	Right lower epididymis	11	Circumscribed isoechoic with central areas of low reflectivity	2–3 vessels	Similar vascularity	No change
2 Epididymal abscess	82	Right lower epididymis	22	Irregular margins mixed predominantly hypoechoic	0 vessels	No vascularity	Reduction in size
3 Adenomatoid	51	Left lower epididymis	8	Circumscribed hypoechoic	2–3 vessels	Similar vascularity	No change
4 Adenomatoid	31	Left lower epididymis	9	Circumscribed isoechoic	0 vessels	No vascularity	No change
5 Lipoma	43	Right mid epididymis	6	Circumscribed hyperechoic	≥4 vessels	Increased vascularity	No change
6 Inflammatory Pseudo-tumour	44	Left upper epididymis	9	Circumscribed hypoechoic	0 vessels	No vascularity	No follow up
7 Lipoma	31	Right full length epididymis	80	Circumscribed isoechoic	0 vessels	No vascularity	Magnetic resonance imaging
8 Inflammatory Pseudo-tumour	79	Left lower epididymis	9	Circumscribed hypoechoic	≥4 vessels	Similar vascularity	No follow up
9 Epididymal abscess	37	Right upper epididymis	15	Circumscribed hypoechoic	0 vessels	No vascularity	Histology
10 Sarcoidosis	48	Right upper epididymis	12	Circumscribed mixed predominantly hypoechoic	2–3 vessels	Increased vascularity	Reduction in size
11 Adenomatoid	57	Right mid epididymis	14	Circumscribed hypoechoic	≥4 vessels	Increased vascularity	No change
12 Adenomatoid	44	Left lower epididymis	36	Circumscribed hypoechoic	2–3 vessels	Similar vascularity	Histology

(continued)

Table 1. Continued

Diagnosis	Grey-scale appearance			Colour Doppler ultrasound		Contrast-enhanced ultrasound	Follow up
	Age	Lesion location	Size (mm)	Description	Lesion vascularity	Lesion vascularity (compared to adjacent testis)	
13 Tuberculous abscess	50	Right lower epididymis	11	Circumscribed hypoechoic	2–3 vessels	Similar vascularity	Increase in size post-surgery
14 Lipoma	86	Left lower epididymis	14	Circumscribed hypoechoic	2–3 vessels	No vascularity	No change
15 Epididymal abscess	84	Right upper epididymis	10	Circumscribed mixed echogenicity	0 vessels	No vascularity	Resolution
16 Epididymal abscess	85	Left lower epididymis	5	Irregular margins mixed echogenicity	0 vessels	No vascularity	Histology (testis infarction)
17 Epididymal abscess	73	Left lower epididymis	32	Circumscribed mixed echogenicity	0 vessels	No vascularity	Histology (fungal, testis infarction)
18 Epididymal abscess	80	Right lower epididymis	20	Circumscribed mixed echogenicity	0 vessels	No vascularity	No follow-up
19 Epididymal abscess	50	Right lower epididymis	12	Circumscribed mixed echogenicity	0 vessels	No vascularity	Histology (partial testis infarction)
20 Adenomatoid	52	Right upper epididymis	18	Circumscribed mixed echogenicity	2–3 vessels	Increased vascularity	Histology (with central hemorrhage)
21 Multifocal tuberculous abscess	41	Left lower epididymis	10	Circumscribed hypoechoic	≥4 vessels	Increased vascularity	Histology (testis and para-testicular tissue)
22 Epididymal abscess	69	Right lower epididymis	13	Circumscribed mixed echogenicity	0 vessels	No vascularity	Resolution
23 Epididymal abscess	72	Left lower epididymis	52	Ill-defined isoechoic	2–3 vessels	Similar vascularity	Histology (testis infarction)
24 Epididymal abscess	20	Right lower epididymis	30	Circumscribed mixed echogenicity	0 vessels	No vascularity	Reduction in size
25 Lipoma	47	Left lower epididymis	33	Circumscribed hyperechoic	2–3 vessels	Increased vascularity	Histology

(continued)

Table 1. Continued

Diagnosis	Grey-scale appearance			Colour Doppler ultrasound		Contrast-enhanced ultrasound
	Age	Lesion location	Size (mm)	Description	Lesion vascularity	Lesion vascularity (compared to adjacent testis)
26 Adenomatoid	33	Right lower epididymis	12	Circumscribed isoechoic	0 vessels	No vascularity
27 Chronic Inflammation of spermatic cord	84	Left spermatic cord	26	Circumscribed mixed echogenicity	0 vessels	No vascularity
28 Extra-testicular haematoma	18	Right lower epididymis	30	Circumscribed hypoechoic	0 vessels	No vascularity
29 Sperm granuloma	32	Right mid epididymis	7	Circumscribed isoechoic	0 vessels	No vascularity
30 Spermatic cord leiomyoma	56	Left spermatic cord	10	Circumscribed mixed echogenicity	2–3 vessels	Similar vascularity
						Follow up
						No follow-up
						Histology
						Resolution
						Unchanged
						Histology

The SPSS package (IBM SPSS Statistics v 22) was used to conduct all analyses.

Results

The ultrasonographic findings are summarised in Table 1. A total of 30 patients were reviewed, age range 18–86 years with median age of 52 years. There was equal distribution of lesions between right and left scrotum (right $n=17$, left $n=13$). A painless scrotal mass ($n=18$) was the most frequent clinical reason for the sonographic examination; other lesions were incidental findings ($n=12$). The distribution of the lesions was as follows: lower epididymis ($n=19$), mid epididymis ($n=3$), upper epididymis ($n=5$), spermatic cord ($n=2$) and one lesion along the entire epididymis. The lesions were hypoechoic ($n=12$), isoechoic ($n=6$), hyperechoic ($n=2$) and mixed echoic ($n=10$). After dividing the lesions into the tumoural and non-tumoural inflammatory groups, tumoural lesions ($n=13$) were predominantly hypoechoic and isoechoic, while non-tumoural lesions ($n=17$) tended to be hypoechoic or of mixed echogenicity. The differences in the echogenicity pattern on grey-scale sonography were statistically significant ($P=0.026$). The echogenicity patterns of the lesions are summarised in Table 2. All lesions, apart from the epididymal abscess, had well defined margins. The range of maximum diameter of the lesions was 5–80 mm.

The lesions demonstrated a variable degree of vascularity on CDS; there were 16/30 (53.4%) avascular lesions, 10/30 (33.3%) lesions with 2–3 vessels and only 4/30 (13.3%) lesions perfused by ≥ 4 vessels. Similarly, on CEUS 17/30 (56.7%) lesions were completely avascular, 7/30 (23.3%) lesions perfused similarly to the adjacent testis and 6/30 (20.0%) lesions with higher perfusion compared to the testis. Absence of vascularity was better and more readily delineated on CEUS in 17/30 (56.7%) cases. The degree of vascularity as detected on both CDS and CEUS was not statistically significantly different between the two groups ($P=0.076$ and $P=0.20$, respectively). The overall agreement of CDS and CEUS in the characterisation of lesion vascularity was found to be good, with a kappa value calculated as 0.719. Only in five cases, the degree of vascularity detected on CDS did not match the CEUS findings.

The characteristics of tumoural lesions identified were mostly hypoechoic or isoechoic and demonstrated 2–3 vessels on CDS. On CEUS of tumoural lesions, there was variability of the perfusion pattern. Adenomatoid lesions were predominantly hypoechoic and moderately vascularised (Figure 1). Lipomas were hyperechoic, with half of them showing no vascularity on CEUS and half increased vascularity (Figure 2). Inflammatory non tumoural lesions were predominantly hypoechoic or of

Table 2. Grey-scale findings of tumoural and inflammatory lesions

Lesion type	Echogenicity pattern			
	Hypoechoic	Isoechoic	Hyperechoic	Mixed
Tumoural	4	5	2	2
Inflammatory	8	1	0	8

Chi-square test: $P=0.026$

Figure 1. Ultrasound findings in a patient with adenomatoid tumour of the epididymis (Patient 1). Grey-scale ultrasound (a) identified a circumscribed isoechoic lesion with central areas of low reflectivity (arrow) situated in the lower part of the right epididymis. Colour Doppler ultrasound (b) could identify 2–3 vessels (arrows) within the lesion. CEUS image (c) demonstrates similar vascularity (arrows) of the lesion to the adjacent testis (T).

mixed echogenicity and variably perfused both on CDS and CEUS. The epididymal sarcoid lesion showed a characteristic mixed echogenicity and increased vascularity, consistent with its inflammatory nature

(Figure 3). A sperm granuloma was isoechoic and hypo-vascularised (Figure 4). All abscesses identified ($n=9$) were avascular on CDS and demonstrated with clarity with CEUS (Figure 5).

Figure 2. Ultrasound findings in a patient with a paratesticular lipoma (Patient 14). Grey-scale ultrasound (a) identified a circumscribed hyperechoic lesion (arrow) located in the lower part of the left epididymis. Colour Doppler ultrasound (b) revealed 2–3 blood vessels (arrows). Contrast-enhanced ultrasound (c) revealed no vascularity of the lesion (L), which is relatively hypoechoic compared to the adjacent testis (T).

Histology was available in 11 patients, establishing the diagnoses of adenomatoid lesion ($n=2$), abscess formation ($n=3$), chronic tuberculosis (TB) ($n=1$), chronic inflammation ($n=2$), fungal infection ($n=1$), leiomyoma ($n=1$) and lipoma ($n=1$). One lipoma was assessed on MR imaging. Two patients with suspected lipoma declined surgery and one patient was a surgical risk. Fourteen patients had a follow-up examination, with 13 patients showing stable appearance or resolution of the lesions and one case (scrotal TB abscess) showing an increase in size. Two cases of suspected pseudo-inflammatory fibrous tumours did not have follow-up imaging.

Discussion

The sonographic features of para-testicular lesions in the current series were variable with the majority demonstrating a predominantly well circumscribed, hypoechoic extra-testicular lesion with absence of vascularity both on CDS and CEUS. The echogenicity pattern on grey-scale ultrasound was essential in the appropriate characterisation of extra-testicular lesions as tumoural or inflammatory. The lesion vascularity was also variable, both on CDS and CEUS and could not be reliably used for a differential diagnosis. Furthermore, the addition of CEUS did not improve

Figure 3. Ultrasound findings in a patient with epididymal sarcoid (Patient 10). Grey-scale ultrasound (a) revealed the presence of a circumscribed mass of mixed echogenicity but predominantly hypoechoic (arrow), situated in the upper part of the right epididymis. Colour Doppler ultrasound (b) revealed 2–3 blood vessels (arrows). On contrast-enhanced ultrasound (c), the mass showed increased vascularity (arrows) compared to the normal testicular parenchyma.

the CDS interpretation of lesion vascularity or pattern of vascularity, with matching results in the majority of cases. However, as previously described^{21,23–25} CEUS accurately delineates necrotic tissue in all cases and thus unequivocally establishes the diagnosis of an abscess. Grey-scale imaging of an abscess may not be confirmatory as the majority of abscesses were of mixed echogenicity or hypoechoic. Overall, the combination of grey scale sonography, CDS and CEUS provided confirmation of the extra-testicular location, which despite variable reflectivity and vascularity of each lesion was in favour of a benign pathology.

Grey-scale sonography has been found to be 98–100% sensitive in differentiating between intra-testicular and extra-testicular lesions, without any more recent

evidence to reverse this finding.^{5,26–28} Occasionally, a lesion originating from the capsule or one that is extra-testicular and firm (indenting the capsule and protruding into the testis) can be difficult to localise on the grey-scale sonography. Given the benign nature of these lesions, follow up imaging documenting benign growth or stability is the preferred approach. Patient anxiety or clinical uncertainty may ultimately lead to surgical excision. MR imaging is occasionally used as a problem solving tool in order to characterise the lesion, in particular ascertaining the fat content of a lipoma.^{29,30} A previous study³¹ using ultrasonography in the differential diagnosis of focal epididymal lesions concluded that the presence of a hypoechoic or hyper-echoic halo favoured the diagnosis of a benign

Figure 4. Ultrasound findings in a patient with sperm granuloma (Patient 29). Grey-scale ultrasound (a) identified a circumscribed isoechoic lesion (arrow) situated in the mid part of the right epididymis. Colour Doppler ultrasound (b) revealed no blood vessels within the lesion. Contrast-enhanced ultrasound (c) identified no vascularity within the mass.

epididymal lesion rather than an inflamed epididymis. In contrast to the findings of the present study, vascularity as assessed on CDS was found to be greater in cases of inflammatory lesions compared to tumoural ones, but these were not abscesses but focal areas of inflammatory tissue. However, the lesion size and the clinical symptoms of tenderness and symptom duration were essential in the image interpretation.³¹

The addition of CEUS is important due to its ability to better demonstrate lesion characteristics of vascularity, particularly with the true intravascular nature of the contrast, and as such will clearly demonstrate the non-vascularized areas. CEUS therefore aids delineation and sizing of the lesion, as well as helping to establish whether it is intra- or extra-testicular.^{16,24,25} When the lesion is vascularised, the degree of vascularity detected on CDS matched the CEUS results in the majority of the cases. But unlike intra-testicular lesions, where hypervascularity and malignancy have a strong relationship,^{17,18} in extra-testicular solid masses, it is difficult to establish a direct link between any pattern of vascularisation and the nature of lesions encountered.¹

There are several limitations to this case series: a small number of patients were identified but this reflects the relative rarity of the solid extra-testicular masses. There was no patient with malignant disease identified in this study, a very rare occurrence. As a consequence, differential diagnosis between benign and malignant diseases, in contrast to intra-testicular lesions, where CEUS has been proven accurate,¹⁸ cannot be analysed. It is noted that less than 100 cases of liposarcoma and 50 of leiomyosarcoma have been reported.⁶ Only three patients had histologic diagnosis but in one case additional MR imaging was performed and in the remainder of the cases, follow up imaging confirmed the absence of progression or regression of the lesions in favour of benign pathology.

Conclusion

In conclusion, the para-testicular mass lesions are of benign aetiology in the majority of cases. Conventional grey-scale features play an important role in the characterisation of these patients. The addition of CEUS can better characterise these lesions, particularly their location, but its value in demonstrating vascularity is not

Figure 5. Ultrasound findings in a patient with epididymal abscess (Patient 2). A lesion of mixed echogenicity but pre-dominantly hypoechoic (arrow) was identified in the lower part of the right epididymis (a). Colour Doppler ultrasound (b) revealed the absence of blood vessels within the lesion. CEUS (c) confirmed the absence of vascularity within the mass. Increased peripheral vascularity was noted on both CDS and CEUS (arrows).

significantly superior to CDS, with which it shows good agreement. It is particularly of value when there is a lesion without vascularity present e.g. an abscess. The nonspecific appearances and variable vascularity of the para-testicular lesions, however, precludes CEUS as a definite diagnostic tool in demonstrating subsets of benign disease, but it is useful in differentiating tumour lesions from inflammatory change.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: VC lectures for Bracco, Samsung and Toshiba. PSS lectures for Bracco, Siemens, Hitachi and GE. MES and AD lecture for Bracco.

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Ethical approval

Local approval to report this review was obtained in conjunction with a larger CEUS study (KCH14-102).

Guarantor

PSS.

Contributorship

PSS, VR, HR, EK, DYH, MES, AD, VC, AMI researched the literature and conceived the study. PSS, HR, EK, VR designed the study overview. PSS, VR, HR performed the data analysis. HR wrote the first draft of the manuscript. PSS, VR wrote the final version of the manuscript. All authors reviewed and approved the final version of the manuscript.

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