Contrast-Enhanced and Microvascular Ultrasound Imaging Features of Testicular Lymphoma: Report of Five Cases and Review Literature

Li Yang
the First Affiliated Hospital of Nanjing Medical University
Yuan Tao
the First Affiliated Hospital of Nanjing Medical University
Bao Meiling
the First Affiliated Hospital of Nanjing Medical University
Zhang Weixin
the First Affiliated Hospital of Nanjing Medical University
Hang Jing (hangjing@jsph.org.cn)
the First Affiliated Hospital of Nanjing Medical University

Research Article

Keywords: lymphoma, contrast-enhanced ultrasound, microvascular ultrasound, testicle

Posted Date: May 4th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-449434/v1

Version of Record: A version of this preprint was published at BMC Urology on January 24th, 2022. See the published version at https://doi.org/10.1186/s12894-022-00957-1.

Abstract

Background: To retrospectively investigate the grey-scale, Doppler, contrast-enhanced and microvascular ultrasound of five patients with primary testicular lymphoma of our institute through review literature analysis.

Methods: From January to November 2020, five patients with primary testicular lymphoma confirmed by histology were preoperatively investigated with a standardized sonographic protocol including contrast-enhanced and microvascular ultrasound.

Results: Conventional ultrasound showed localized hypoechogenicity represented with solitary lesions(2 of 5), multiple lesions (2 of 5), or entire testicular involvement (1 of 5). And increased blood flow appeared by color Doppler ultrasound with straight vascular sign(4 of 5). In contrast-enhanced ultrasound images confirmed this pattern(4 of 5) and presented incresaed enhancement with enlarged range. On microvascular ultrasound imagings, all lesions were presented with straight and parallel course of intralesional vessels(5 of 5).

Conclusions: Here, we identified the increased vascularity with enlarged range on contrast-enhanced ultrasound along with a linear nonbranching pattern by vascular sign on microvascular ultrasonographic of testicular lymphoma.

Introduction

Primary testicular lymphoma(PTL) is a cancer which occurs in an immune-privileged site[1]. PTL is a rare extra-nodal non-Hodgkin's lymphoma (NHL), accounts for about 1-9% of malignant testicular tumors and 1% of NHL[2, 3]. The vast majority pathological subtype of testicular lymphoma is the diffuse large B-cell lymphoma (DLBCL), rare subtypes are mantle-cell lymphoma, NK/T-cell lymphoma and other T-cell lymphomas [2, 4, 5]. Testicular lymphoma is common in the elderly, the median age at diagnosis of testicular lymphoma is 67 years old [6, 7]. Testicular lymphoma is a highly invasive malignant tumor, the progression-free and the overall survival rate are low [2]. The treatment of primary testicular lymphoma includes orchiectomy followed by chemotherapy. Orchidectomy provides a therapeutic advantage, as it may also confer a therapeutic advantage by gaining better local control and removing a possible sanctuary site for relapse[8].

If there was a history of testicular swelling or clinical evidence of testicular mass or enlargement, ultrasonography (US) was the first choice for diagnosis. Due to the low incidence of PTL, there were few systematic studies [9,10,11] on US features of testicular lymphoma. Grayscale and color Doppler findings were reported[10], and the appearance of well-defined homogeneous hypoechoic lesions in the testis in US with marked hypervascularization were the features of PTL. The sensitivity of intensifying the visibility of vasculature was improved by contrast-enhanced ultrasound (CEUS), and the practice had recently expanded to evaluate testicular lesions[11]. Furthermore, CEUS was also introduced into a routine preoperative workup of testicular surgery patients[12,13]. In CEUS images, a rapid filling time (< 7s) and straight vessel pattern were the sonographic hallmarks of PTL[14]. A recent study[15] based on multiparametric sonography found that PTL was characterized by increased blood vessels on color Doppler and CEUS along with the increased lesion stiffness on strain elastography.

Microvascular ultrasound, a latest development of color Doppler technology, is a non-invasive microvascular imaging technique using low flow Doppler signal processing[16]. Slow and fine vascular flows had possibly

precise detected using microvascular US[17,18]. So far, no papers was published on microvascular US image in PTL. Therefore, we reported the CEUS and microvascular US features of five cases of PTL, along with summarizing the US, CEUS and microvascular features of the tumor.

Materials And Methods

Patient selection

The researchers retrospectively analyzed the images of patients with testicular tumors who underwent conventional ultrasound, CEUS and microvascular ultrasound in the department of ultrasound and urology of the first affiliated hospital of Nanjing Medical University between January to November 2020. The study was approved by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University(Nanjing, China) and performed according to the Helsinki Declaration. Informed consent was waived since this was a retrospective study. All the participants gave their informed consent for the publication of their images in an online open-access publication. The enrolled patients registered their personal information before examination. Clinical information and laboratory data such as clinical history, tumor side, swelling and pain were also recorded in detail. According to the immunohistochemical results, the confirmed diagnosis of PTL cases and the corresponding images were enrolled in this study.

US, CEUS and microvascular US examination of testis

Two US doctors with more than 10 years' experience (L.Y. and Y.T.) in testicular ultrasound examined all the testicular masses included in this study. Gray-scale US, color Doppler flow imaging (CDFI) and CEUS imaging were performed using a real-time US device (Philips Healthcare, Eindhoven, the Netherlands) equipped with a 6-15 MHz linear array transducer. Microvascular US image was collected using a real-time US device (Aixplorer, SuperSonic Imagine, Aix-en-Provence, France) equipped with a 4-15 MHz linear array transducer. The CEUS examinations were also performed by the same transducer at a low mechanical index (0.08), focus positioned behind the region of interest after the injection of 2.4mL of the sulfur hexafluoride contrast agent SonoVue (Bracco SpA, Milan, Italy), followed by 10mL of 0.9% saline. When the microvascular US was activated, the transducer was placed on the surface of scrotum without compression or movement.

Sonographic Interpretation

The doctors examined the conventional US images first and focused on homogeneity, size, echogenicity (compared with surrounding normal testicular tissue), boundary, margin, extent of infiltration, calcification and presence of the formerly described “straight vessel [9]” or “linear echogenic strands [19]” pattern of testicular mass. The tumor’s flow grade [20], velocity, resistance index (RI) and exist of “straight vessel pattern” were also recorded during the color Doppler evaluation.

CEUS was performed on the lesions including normal testicular tissue and at least more than 50% of the tumor area. During the CEUS examination, the probe was placed on the skin surface of scrotum without movement, and the dynamic images were observed more than 2 minutes after SonoVue injection. The CEUS evaluation was performed by two doctors with more than 10 years working experience in CEUS (L.Y. and H.J.). Size change was compared to the same section in grey-scale US at the peak time in CEUS. Time-intensity curve (TIC) analysis was performed for evidence of the degree of overall enhancement (microperfusion) within the target lesions. And peak

intensity(PI), time to peak(TTP), and rise time of tumor and surrounding normal testicular tissue were recorded. According to TIC results, we classified increased, decreased, or similar enhancement patterns of the mass (compared with the intensity of surrounding testicular tissue or contralateral testis). Boundary (clear or unclear), size change and homogeneity were also assessed in enhancement images. We also focused on presence of the formerly described " linear nonbranching[15]" in macrovascular pattern of CEUS images.

The microvascular US was assessed for evidence of the degree of overall enhancement (microperfusion) within the target lesions, which was characterized as increased, decreased, or similar to normal parenchyma, and the macrovascular pattern was described as linear nonbranching or random similar to CEUS.

Histopathology and immunophenotype

The enrolled four cases were diagnosed by immunohistochemical pathological results after operation or testicular core needle biopsy. All specimens were fixed with 3.7% neutral formaldehyde solution, routinely dehydrated, embedded in paraffin, 3um thick sections, HE and immunohistochemical staining. Immunohistochemical staining: En Vision two-step method was used, and negative and positive controls were also set up. All primary antibodies (EBER, CD20, PAX5) were purchased from Fuzhou Maixin Biotechnology Co., Ltd., and TBS was used as negative control instead of primary antibody.

Results

Clinical features and histological findings

We reviewed and analyzed the clinical and ultrasonographic data of 18 patients with testicular mass in this study. According to the results of pathological immunohistochemistry, the images of 6 patients with testicular lymphoma were selected. One case was excluded because of incomplete imaging data. Finally, US and CEUS images of 5 patients were included in this study. The baseline clinical characteristics of the included cases were shown in Table 1. The median age of the enrolled patients was 64 (range31-91). All the patients had no cryptorchidism, hypospadias, inguinal lymph node enlargement and lumbago. Three cases were painless testicular mass and two cases were complicated with testicular swelling and pain. The average clinical history was 1.60±0.89 months, and the average diameter was 46.3±10.9mm. Four patients were DLBCL and one patient was extra-nodal NK/T cell lymphoma.

US, CEUS and microvascular US features

In gray-scale US images, all the enrolled lesions showed irregular solid hypoechoic testicular lesions without calcification or cystic degeneration. Four lesions were located in testis and one lesion involved extra-testicular, including ipsilateral epididymal head and spermatic cord. Straight vessel pattern showed in 4 of 5(Fig 1, 3, 4) and linear echogenic strands appeared in 1 of 5(Fig 2). Diffuse infiltration of the entire testis in 2 of 5 and homogeneous hypoechoic in 4 of 5. In CDFI images, five lesions presented marked hypervascularization with flow grade III. Straight blood vessel sign in 4 of 5(Fig 1, 3, 4).

According to the analysis of TIC curve, five testicular lymphoma lesions showed increased enhancement pattern in CEUS images (Fig 1, 2, 3, 4). Among the measured parameters, PI(9.06±5.68dB) of testicular lymphomas were higher than those of normal testes(3.43±1.95dB), but TTP(31.81±8.50s) was shorter than normal testes(38.01±11.25s). All the enrolled lesions showed a rapid increased enhancement with enlarged range and

unclear boundary after CEUS. In most cases(4 of 5), a linear nonbranching pattern was seen(Fig 1, 3, 4). On microvascular US images, all the lesions presented an increased flow with linear nonbranching pattern(Fig 1, 2, 3, 4).The detailed US data of the 5 testicular lymphoma lesions were shown in Table1.

Pathological and histological results

Grossly, the resected testicular lesions showed white or brown solid masses on the section, with size ranging from 3 to 6 cm. Histopathologically, the tumor had a diffuse growth pattern, mainly involving interstitial tissue, surrounded by atrophic seminiferous tubules in the five lesions. The tumor cells of testicular lymphoma showed an obvious vascular centrality and vascular invasive growth pattern. In one case, invasion of epididymis and spermatic cord was found. All the five testicular lymphoma cases were diagnosed by immunohistochemical examination. One case was extra-nodal NK/T cell lymphoma (EBER+), and the other three cases were DLBCL (CD20 +, PAX5 +).

Discussion

Testicular lymphoma is a rare malignant hematological tumor, and its treatment is very different from other types of testicular tumors[21]. Conventional US images were difficult to distinguish it from other types of testicular tumors. In this report, we retrospectively analyzed the CEUS and microvascular US features of five cases of testicular lymphoma. And revealed that the testicular lymphoma lesions presented with an increased enhancement by enlarged range in CEUS along with a linear nonbranching vascular pattern on microvascular US. Compared with normal testicular tissue, testicular lymphoma showed a fast-forward hyperenhancement mode by TIC curve analysis. After combination of the focal hypoechoic, hypervascularization with straight vessel pattern in US images, testicular lymphoma could be indicated.

So far, there had six reports about US images of testicular lymphoma[9, 10, 14, 15, 22], along with our report. Two reports were about the grey-scale US and CDFI images[9, 10], and three reports were focused on CEUS images[14, 15, 22]. In these papers, the image characteristic of straight vessel sign was proposed. Table 2 summarized the detailed clinical and ultrasonic features in this report.

The pathological cytological changes of testicular lymphoma were different from those of other testicular malignant tumors. It was characterized by tumor cells surrounding and compressing seminiferous tubules and normal testicular vessels, involving interstitial tissue[2, 6]. This pathological change might be the reasons for the appearance of straight vessel sign in US or CDFI images. However, this feature was not unique to testicular lymphoma. In other invasive tumors (such as plasmacytoma OR leukemic infiltration) and non-neoplastic diseases (such as chronic inflammatory diseases), the similar sonographic findings might also be appeared. In this report, the straight vessel pattern was also seen on grey-scale and CDFI images. This result was consistent with those of previous reports and demonstrated that US had high repeatability and reliability in the evaluation of testicular lymphoma. In our report, a linear echogenic strands pattern, as reported in the previous research, was presented in the conventional US images of one case. And this was similar to the previously reported thyroid DLBCL images[19]. These fibrous bands separated the tumor body into a map shape, which indirectly reflected the pathological process of tumor tissue infiltrating growth and fibrous connective tissue proliferation encircling repeated antagonism.

The use of CEUS improved the characteristics of testicular lesions and could evaluate the microvascular information of testicular lesions in detail[13]. There were few reports focusing on CEUS findings of testicular lymphoma in the past [14, 15, 22]. In our report, it was found that the CEUS of testicular lymphoma showed a rapid increased enhancement pattern, and the range of the tumor lesion after CEUS enlarged than that of prey-scale US images. These image features were consistent with the invasive growth pattern of testicular lymphoma. Lock et al[14] analyzed the CEUS findings of seven testicular lymphoma lesions and found straight vessel pattern and rapid filling time were the CEUS characteristics of testicular lymphoma. In our study, combined with TIC quantitative analysis, it was found that the TTP (s) was shorter than that of normal testis, while the Wash in slope (dB/s) was longer than that of normal testis. All these findings were similar to the previously reported [14] rapid filling time in CEUS. In addition, we also found that the testicular lymphoma presented the characteristics of increased enhancement with enlarged range. The reason for this characteristic might be related to the high expression of VEGF in malignant tumors, along with dysplasia of neovascularization forms arteriovenous anastomosis, which made the contrast medium passing quickly in the tumor and formed increased enhancement. On the other hand, the invasive growth pattern of testicular lymphoma caused the unclear boundary and enlarged lesion range in CEUS images. This phenomenon was similar to the numerous small echogenic spots with a speckled appearance in CEUS of lymph node in Non-hodgkin lymphoma reported by Rubaltelli [23]. However, whether these findings were the characteristic CEUS changes of testicular lymphoma remained to be confirmed by a multicenter large sample prospective study.

Our report was the first attempt to investigate the advanced US technique of microvascular image in PTL patient. As a noninvasive technique, microvascular imaging can detect slow and fine vascular flow, even the hepatic subcapsular[24]. As a malignant tumor of blood system, PTL has some particular pathological cytological changes. An appearance of straight vessel sign was found to help diagnose PTL. In our report, a linear nonbranching vascular pattern on microvascular US was presented in PTL, which was similar to straight vessel sign.

Conclusion

Testicular lymphoma is a kind of testicular malignant tumor with poor prognosis, while lacking an early non-invasive diagnosis. In this report, the CEUS images of testicular lymphoma showed an increased enhancement with enlarged range and unclear boundary along with a linear nonbranching pattern by vascular sign on microvascular US image. Combined with straight vascular signs on grey-scale US and painless testicular mass of physical examination, it can provide some help for early non-invasive diagnosis of testicular lymphoma.

Abbreviations

PTL: primary testicular lymphoma

NHL: non-Hodgkin's lymphoma

DLBCL: diffuse large B-cell lymphoma

US: ultrasonography

CEUS: contrast-enhanced ultrasound

CDFI: color Doppler flow imaging

TIC: time-intensity curve

PI: peak intensity

TTP: time to peak

Declarations

Ethics approval and consent to participate

This research is retrospective and involves the collection of existing data and records. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration. Informed consent was waived since this was a retrospective study.The ethical committee of the first affiliated hospital of Nanjing Medical University approved all procedures of the study and provided a waiver for the written informed consent.

Consent for publication

Informed consent for publication is obtained from all participants.

Availability of data and materials

The datasets will be available from the corresponding author upon reasonable request.

Competing interests

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

Funding

This work was supported by Jiangsu Province Key Research & Development Plan (No. BE2018703).

Author Contributions

J.H, Y.L and T.Y. conceived the case report and wrote the manuscript. J.H and Y.L collected the data. Y.L, W.X.Z and M.L.B prepared figure 1 and 2. All authors contributed to the article and approved the submitted version.

Acknowledgments

Dr. Jing Hang would like to thank Pro. Zengjun Wang, Pro. Ninghong Song and Pro. Chao Qin for their help and previous work. They have encouraged me to develop this research.

Authors' information

1Department of Urology, the First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China.

2Department of Ultrasound, the First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China.

3Department of Pathology, the First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China.

References

1. Swerdlow SH, Campo E, Harris NL, et al. WHO classification of tumours of haematopoietic and lymphoid tissues. 4th ed. Lyon, France: IARC Press; 2008.
2. Cheah CY, Wirth A, Seymour JF. Primary testicular lymphoma. Blood. 2014;123(4):486-493.
3. Bhatia K, Vaid AK, Gupta S, Doval DC, Talwar V. Primary testicular non-Hodgkin's lymphoma--a review article. Sao Paulo Med J. 2007 Sep 6;125(5):286-8.
4. Vitolo U, Seymour JF, Martelli M, et al. Extranodal diffuse large B-cell lymphoma (DLBCL) and primary mediastinal B-cell lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2016;27:v91-v102.
5. Wang C, Wang H, Wang Q, Shi B. Primary testicular lymphoma: experience with 13 cases and literature review. Int J Hematol. 2013 Feb;97(2):240-5.
6. Nasir Shahab DCD. Testicular lymphoma. Seminars in oncology. 1999;26(3):11.
7. Gundrum JD, Mathiason MA, Moore DB, Go RS. Primary testicular diffuse large B-cell lymphoma: a population-based study on the incidence, natural history, and survival comparison with primary nodal counterpart before and after the introduction of rituximab. J Clin Oncol. 2009 Nov 1;27(31):5227-32.
8. Twa DDW, Mottok A, Savage KJ, Steidl C. The pathobiology of primary testicular diffuse large B-cell lymphoma: Implications for novel therapies. Blood Rev. 2018 May;32(3):249-255.
9. Suresh Bhat JS, Ramaprasad, Suma Job. Striated pattern on scrotal ultrasonography: A marker for Non-hodgkins lymphoma of testis. Indian J Urol. 2014;30(1):2.
10. Bertolotto M, Derchi LE, Secil M, et al. Grayscale and Color Doppler Features of Testicular Lymphoma. Journal of Ultrasound in Medicine. 2015;34(6):1139-1145.
11. Valentino M, Bertolotto M, Derchi L, et al. Role of contrast enhanced ultrasound in acute scrotal diseases. Eur Radiol. 2011 Sep;21(9):1831-40.
12. Dieckmann KP, Frey U, Lock G. Contemporary diagnostic work-up of testicular germ cell tumours. Nat Rev Urol. 2013 Dec;10(12):703-12.
13. Lock G, Schmidt C, Helmich F, Stolle E, Dieckmann KP. Early experience with contrast-enhanced ultrasound in the diagnosis of testicular masses: a feasibility study. Urology. 2011 May;77(5):1049-53.
14. Lock G, Schmidt C, Schröder C, Löning T, Dieckmann KP. Straight Vessel Pattern and Rapid Filling Time: Characteristic Findings on Contrast-Enhanced Sonography of Testicular Lymphoma. J Ultrasound Med. 2016 Jul;35(7):1593-9.
15. Kachramanoglou C, Rafailidis V, Philippidou M, et al. Multiparametric Sonography of Hematologic Malignancies of the Testis: Grayscale, Color Doppler, and Contrast-Enhanced Ultrasound and Strain Elastographic Appearances With Histologic Correlation. J Ultrasound Med. 2017 Feb;36(2):409-420.
16. Machado P, Segal S, Lyshchik A, Forsberg F. A Novel Microvascular Flow Technique: Initial Results in Thyroids. Ultrasound Q. 2016 Mar;32(1):67-74.
17. Lee DH, Lee JY, Han JK. Superb microvascular imaging technology for ultrasound examinations: Initial experiences for hepatic tumors. Eur J Radiol. 2016 Nov;85(11):2090-2095.

18. Lim AKP, Satchithananda K, Dick EA, Abraham S, Cosgrove DO. Microflow imaging: New Doppler technology to detect low-grade inflammation in patients with arthritis. Eur Radiol. 2018 Mar;28(3):1046-1053.
19. Orita Y, Sato Y, Kimura N, et al. Characteristic ultrasound features of mucosa-associated lymphoid tissue lymphoma of the salivary and thyroid gland. Acta Otolaryngol. 2014 Jan;134(1):93-9. 20. Adler DD CP, Rubin JM, Quinn-Reid D. Doppler ultrasound color flow imaging in the study of breast cancer: preliminary findings. Ultrasound Med Biol. 1990;16(6):7.
20. Barrisford GW KE, Preston MA, Rodriguez D, Harisighani MG, Feldman AS. Role of imaging in testicular cancer: current and future practice. Future Oncol. 2015;11(18):12.
21. Peil-Grun A, Trenker C, Görg K, Neesse A, Haasenritter J, Görg C. Diagnostic accuracy and interobserver agreement of contrast-enhanced ultrasound in the evaluation of residual lesions after treatment for malignant lymphoma and testicular cancer: a retrospective pilot study in 52 patients. Leuk Lymphoma. 2018 Nov;59(11):2622-2627.
22. Rubaltelli L KY, Tregnaghi A, Stramare R, et al. Evaluation of lymph node perfusion using continuous mode harmonic ultrasonography with a second-generation contrast agent. J Ultrasound Med. 2004;23(6):8.
23. Lee S, Kim MJ, Lee MJ, et al. Hepatic subcapsular or capsular flow in biliary atresia: is it useful imaging feature after the Kasai operation? Eur Radiol. 2020 Jun;30(6):3161-3167.

Tables

Table 1 Clinical and ultrasound features of testicular cases in this series

	Patient	1	2	3	4	5
Clinical features	Age	64	91	46	31	65
	Tumor side	L	R	R	R	R
	Pathological result	DLBCL	DLBCL	DLBCL	NK/T cell lymphoma	DLBCL
Grey-scale US	Size(mm)	35	37	48.5	62	49
	Extra-testicular findings	No	Yes	No	Yes	Yes
	Straight vessel	Yes	Yes	No	Yes	Yes
CDFI	Straight vessel	Yes	Yes	No	Yes	Yes
	Flow grade	III	III	III	III	III
CEUS	Size change	enlarged	enlarged	enlarged	enlarged	enlarged
	Boundary	unclear	unclear	unclear	unclear	unclear
	PI(dB)	4.36	9.68	3.32	10.43	17.53
	TTP(s)	27.19	44.48	35.13	22.18	30.07
	Rise time(s)	5.34	8.70	9.13	4.35	0.51
	Linear nonbranching	Yes	Yes	No	Yes	Yes
Microvascular US	Flow degree	Increased	Increased	Increased	Increased	Increased
	Pattern	Linear	Linear	Linear	Linear	Linear

L, left; R, right; NK/T cell lymphoma, extra-nodal natural killer/T-cell lymphoma.

Table 2 Summary of ultrasound and CEUS features of testicular lymphoma cases

Author	Number of cases	Tumor side	Ultrasound features	CEUS features	Microvascular US features
Suresh Bhat	1	bilateral	Straight vessel pattern	-	-
Michele Bertolotto	36	3 bilateral/19R/14L	Straight vessel pattern	-	-
Guntram Lock	6	-	marked hypervascularization	Straight vessel pattern，rapid filling time	-
Kachramanoglou C	8	1 bilateral/4R/3L	Straight vessel pattern	linear nonbranching	-
This report	5	4R/1L	Straight vessel pattern	linear nonbranching, increased enhancement with enlarged range	linear nonbranching

L, left; R, right.

Figures

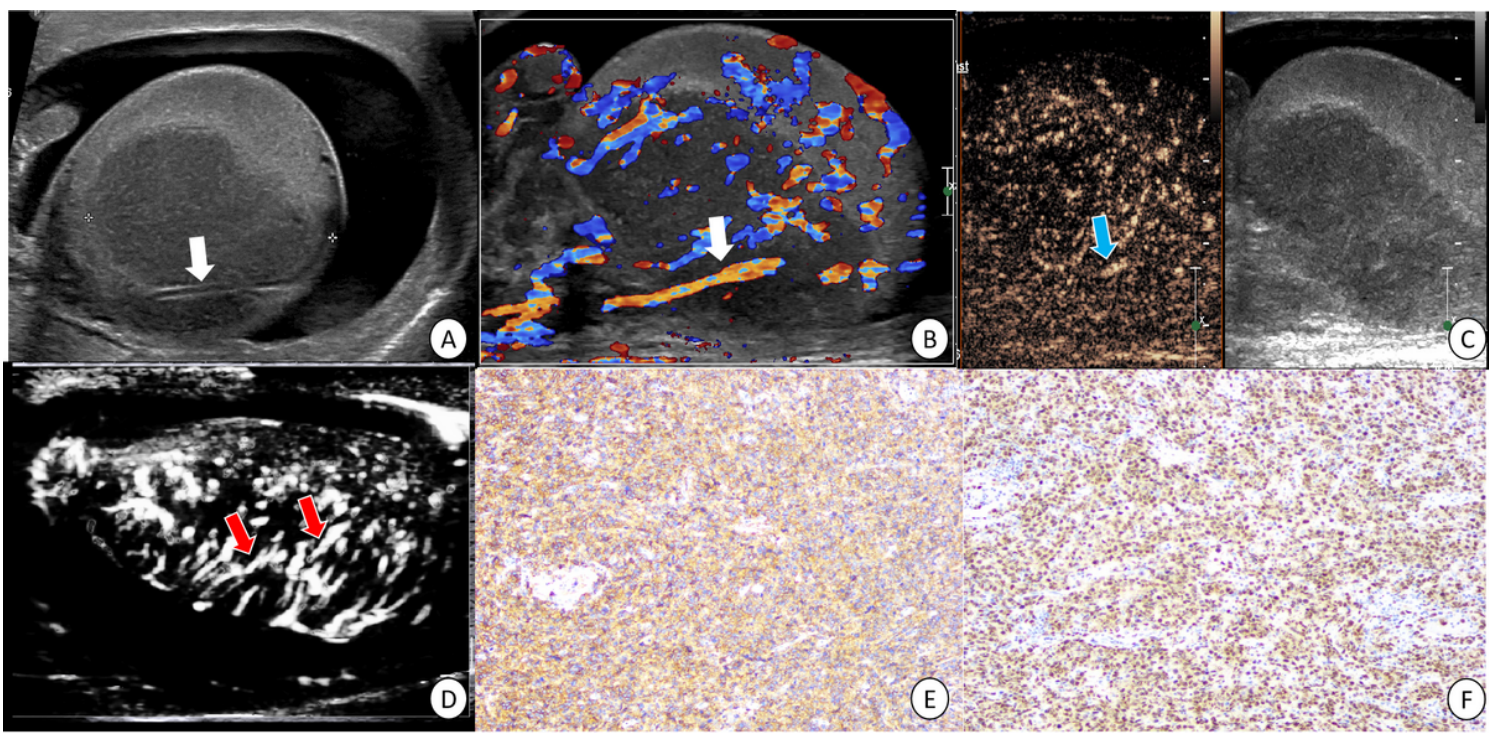

Figure 1

A diffuse large B-cell lymphoma of right testis in a 91-year-old patient proven after orchiectomy. White arrows showed the straight vessel pattern in grey-scale US(A) and CDFI(B) image. The lesion showed increased

enhancement with enlarged range on contrast-enhanced ultrasound(C). Blue arrow presented the linear nonbranching in CEUS image(C). Red arrows showed linear nonbranching pattern in microvascular US image(D) . Tumor cells were positive for CD20(+) (E) and PAX5(+) (F) by immunohistochemistry.

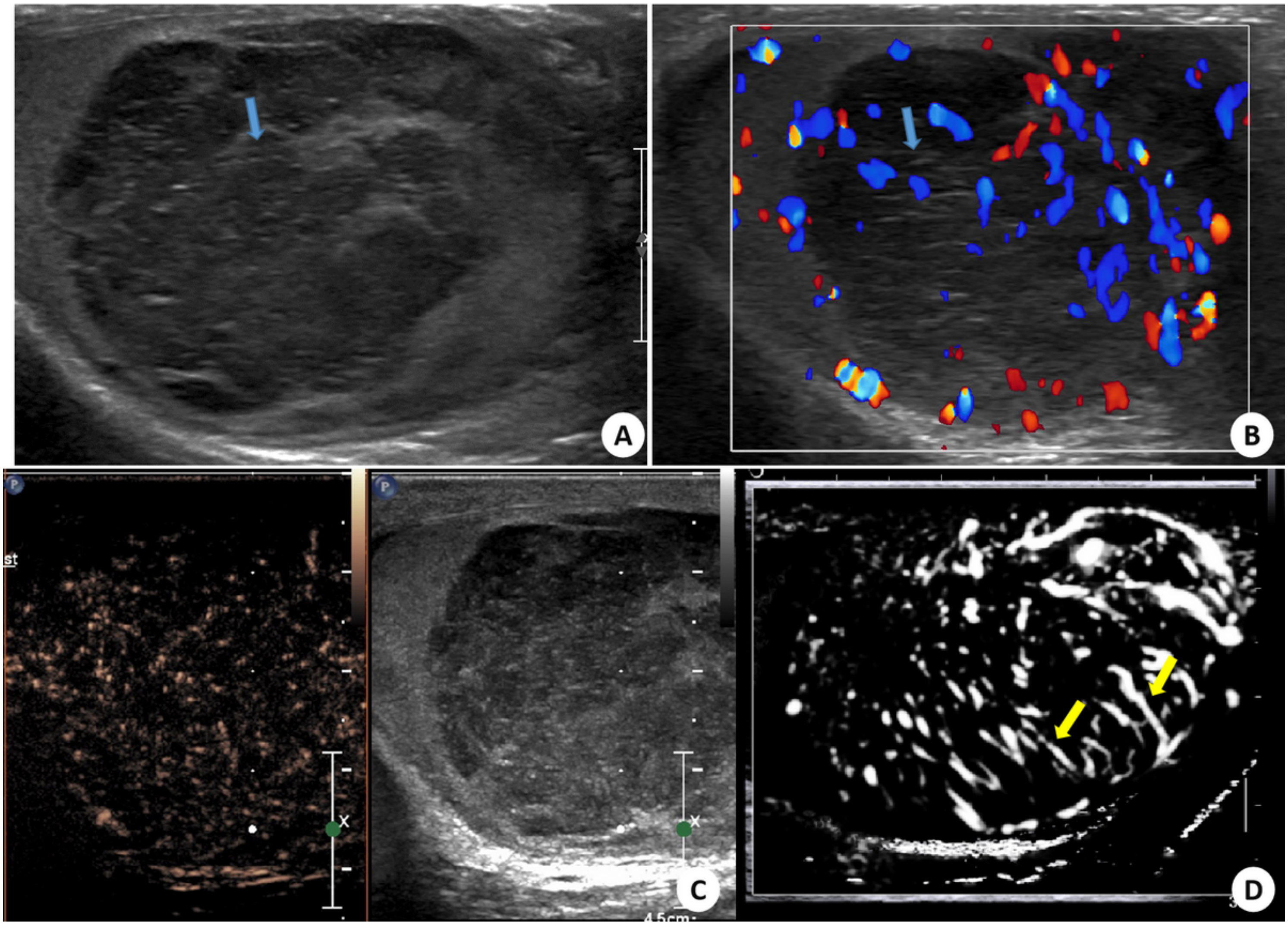

Figure 2

A diffuse large B-cell lymphoma of right testis in a 46-year-old patient diagnosed after orchiectomy. Blue arrow indicated the linear echogenic strands in grey-scale US(A) and CDFI(B) images. The increased enhancement with enlarged range was also seen in CEUS image(C). Yellow arrows(D) indicated the straight and parallel vascular sign on microvascular ultrasonographic image.

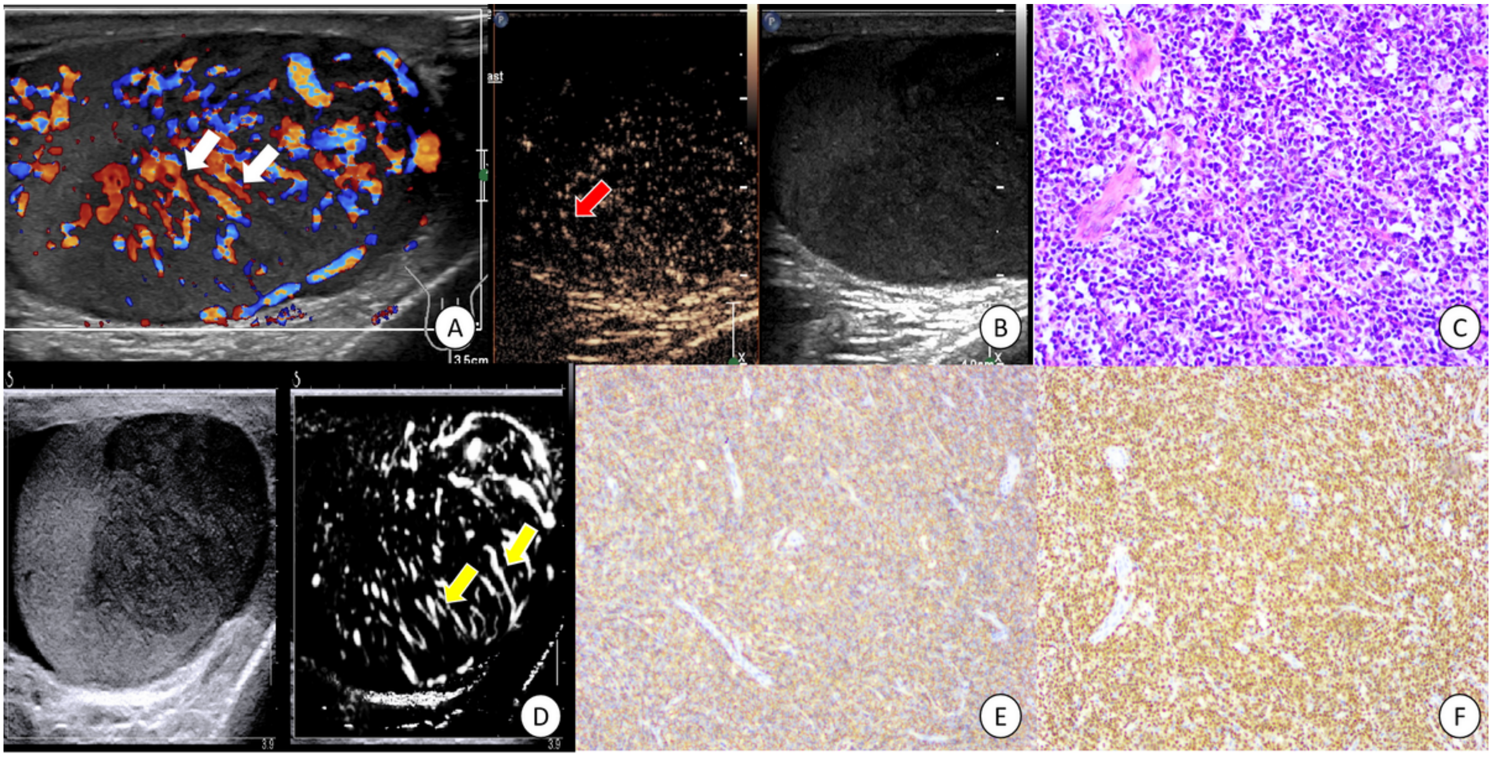

Figure 3

A diffuse large B-cell lymphoma of left testis in a 64-year-old patient. White arrows indicated the straight vessel pattern in CDFI image(A). Red arrow showed the linear nonbranching pattern in CEUS image(B). In HE*200(C), medium and large lymphocytes were diffusely distributed. Yellow arrows(D) indicated the straight and parallel vascular sign on microvascular US image. Tumor cells were positive for CD20(+) (E) and PAX5(+) (F) by immunohistochemistry.

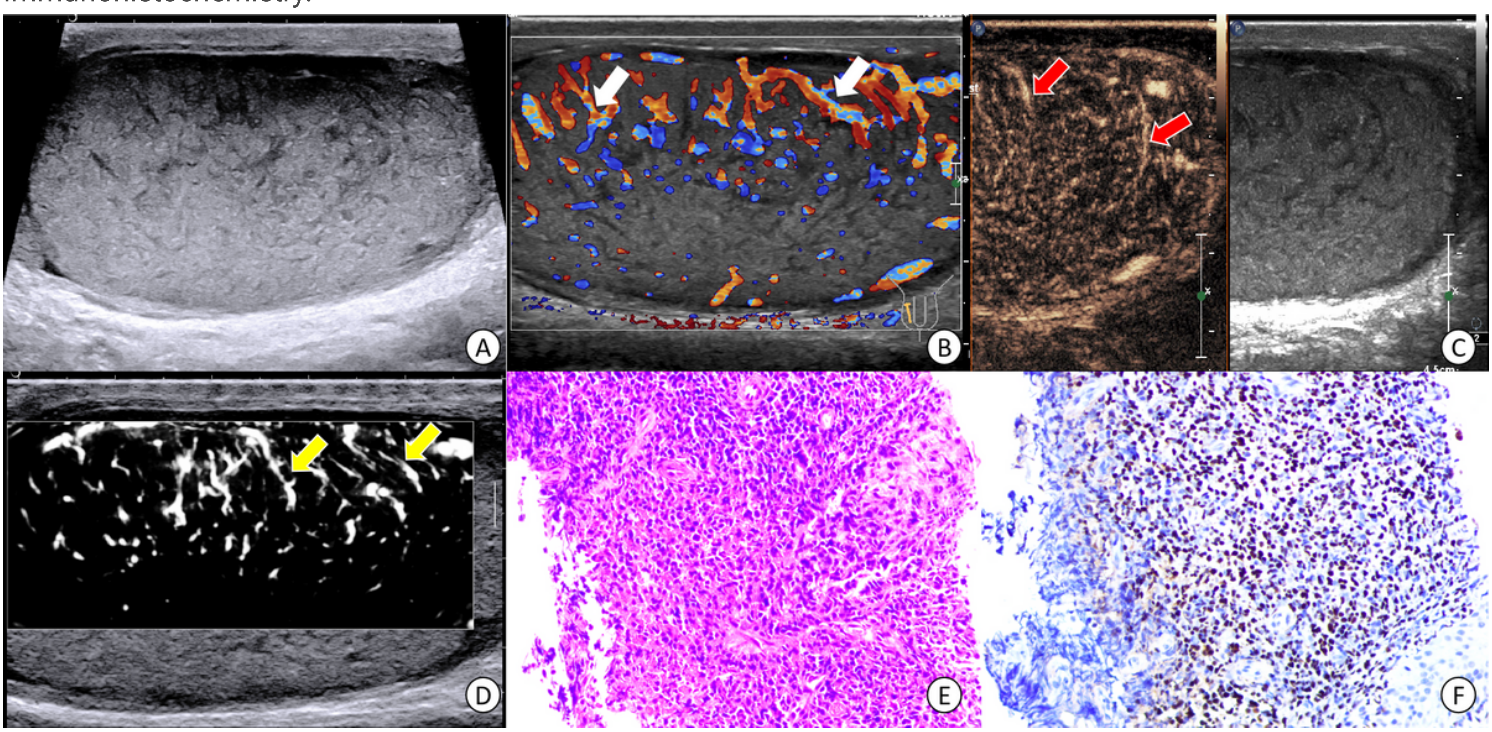

Figure 4

Images from a 31-year-old patient with histological proven extra-nodal NK/T cell lymphoma by core-needle biopsy of right testis. Multiple diffuse hypoechoic lesions were detected and the straight vessel pattern was seen in grey-scale US(A). White arrows indicated the straight vessel pattern in CDFI image(B). Red arrows showed the linear nonbranching pattern in CEUS image(C). Yellow arrows(D) indicated the straight and parallel vascular sign on microvascular US image. Diffuse distributed lymphocytes were seen in HE*200(E). Tumor cells were positive for EBER(+) (F) by immunohistochemistry.