High-resolution, three-dimensional, and contrast-enhanced ultrasonographic findings in diseases of the eye[☆]

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KEYWORDS

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Abstract *Objectives:* To review the contrast-enhanced ultrasound (CEUS) and 3D ultrasound findings (3D-US) in various pathologies involving the eye and orbit and to compare them with high-resolution US (HRUS) findings.

Background: CEUS is a valid diagnostic tool for study several districts. There are numerous pathological conditions of the eye in which CEUS can be very helpful or detrimental.

Image Findings: We review a wide range of ocular lesions, traumatic (retinal and choroidal detachments) and malignant (choroidal melanoma, tumors inside and outside the muscle cone) evaluated alternatively with CEUS and 3D and compare these findings with those obtained with HRUS. Dysthyroid orbitopathy is not included in this review.

Conclusion: CEUS plays a central role in the differentiation of detached retina (vascular) and vitreous membranes (avascular). It is also helpful in the assessment of tumor of the eye, in planning treatment for choroidal melanoma, and in assessing orbital masses for neovascularization. HRUS is highly effective in the detection of traumatic and non-traumatic lesions of the eye, but it is less effective for the assessment of orbital lesions. The 3D module has increased the diagnostic value of CEUS. CEUS is cost-effective and can be used when CT and MR cannot be performed.

Sommario *Obiettivi:* Illustrare i reperti ecocontrastografici (CEUS) e di ecografia in tre dimensioni (3D) di un ampio spettro di patologie del globo oculare, confrontandole con l'ecografia ad alta risoluzione (HRUS).

Introduzione: La CEUS è un valido strumento nella valutazione di numerosi distretti corporei. Nella patologia del bulbo oculare esistono una serie di situazioni in cui la CEUS può essere di-
rimente o molto utile.

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Imaging: In questo lavoro presentiamo uno spettro di lesioni traumatiche (distacchi di retina e della coroide) e di patologia maligna del bulbo oculare (melanoma della coroide, tumori intra ed extra conali) valutate con CEUS ed ecografia 3D. I risultati sono stati confrontati con HRUS. L'orbitopatiadistroidea è stata esclusa dal presente studio.

Conclusione: CEUS gioca un ruolo centrale nella diagnosi differenziale tra distacchi di retina (vascolari) e membrane vitreali (avascolari). Inoltre CEUS è molto utile nella valutazione dei tumori bulbari, nel percorso terapeutico del melanoma della coroide e nella valutazione della neovascolarizzazione delle lesioni orbitarie. HRUS è molto efficace nel riconoscimento di lesioni traumatiche e non traumatiche, ma non è utile nella valutazione delle lesioni della parete dell'orbita. L'utilizzo delle ricostruzioni 3D ha aumentato la confidenza diagnostica della CEUS. Infine, CEUS ha un ottimo rapporto costo-beneficio e può essere utilizzata quando la TC e la RM non possono essere eseguite.

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Introduction

Ultrasound has long been used to evaluate pathology of the ocular bulb or eyeball [1–3]. In particular, the development of new techniques such as contrast-enhanced ultrasound (CEUS) and three-dimensional reformatting (3D) of US images has firmly established the validity of this method in the field of ophthalmology. The objectives of our study were to examine the possible applications of CEUS and 3D-US reconstructions in the study of lesions involving the eyeball or orbit (in particular, retinal detachment and neoplastic lesions) and to compare these new methods with conventional ultrasound in the field of ophthalmology.

Examination technique

Normal anatomical findings and color Doppler evaluation

The examination is performed with the patient lying on the table in the supine position. The eyes are closed and the lids

covered with a thick layer of sterile gel. Evaluation of eye movements may be useful for diagnosis, and to this end the patients may be asked to follow the movements of a penlight or other light source with the contralateral eye. For optimal exploration of the chambers of the eye and the orbit, high-frequency, high-resolution probes are needed (a minimum of

Fig. 1 Normal anatomy of the eye, axial scan. AC = anterior chamber, L = lens, I = iris, CB = ciliary body, V = vitreous humor, S = sclera; ON = optic nerve.

Fig. 2 The easiest vessels to evaluate are those located at the end of the optic nerve. The ophthalmic artery (arrow) is located medially to the optic nerve and has a high resistance. The superior ophthalmic vein is located in the superomedial quadrant of the orbit and can be visualized in 90% of patients. It has continuous, low-resistance flow. The inferior ophthalmic vein is a smaller-caliber vessel and for this reason it is visualized less frequently. The central retinal artery and vein run parallel to the center of the distal segment of the optic nerve. Ultrasound diagnosis of complete detachment of the retina is generally easy because the retina remains anchored to its two attachment points (the optic nerve posteriorly and the ora serrata anteriorly).

Fig. 3 Detachment of the temporal and nasal aspects of the retina, which remains attached to the optic nerve (ON).

7 MHz and as high as 50 MHz in the field of pure ophthalmology) (Fig. 1). In various pathological conditions associated with hemodynamic changes of the orbit, use of the color Doppler module can provide useful additional information (measurement of systolic and diastolic peak velocities and resistance index for the major orbital vessels) [4–6]. When intraorbital flows are being assessed, the pressure exerted with the transducer should be as light as possible to avoid provoking changes in the orbital circulation (Fig. 2).

CEUS

A 22-gauge needle is inserted into the antecubital vein of the left arm, and a second-generation contrast agent (e.g., SonoVue 4.8 mL, Bracco, Italy) is injected as a rapid bolus. The line is then flushed with 10 ml of saline to accelerate entry of the contrast medium into the blood stream. The vasculature can then be observed for about 180 s, the duration of the perfusion time prior to complete wash-out [7–11]. We generally use a 8–4 MHz microconvex transducer (iU22, PhilipsNV, Eindhoven, The Netherlands) equipped with software for the analysis of the contrast curve. We use pulse inversion technology and a side-by-side display format, in which the native B-mode image is shown in the left side of the screen and the contrast-enhanced image on the right [12].

Pathology

Retinal detachment

The retina is bounded anteriorly by the ora serrata and posteriorly by the optic disc. Retinal detachment is nothing but the separation of the neurosensory retina from the pigmented epithelium. Detachment may be idiopathic (mainly related to degeneration of the vitreous and retinal tears). In other cases, it is caused by the presence of exudative material between the neurosensory retina and pigmented epithelium (as in the case of retinopathy associated with hypertension, collagen disease, blood dyscrasias, or intraocular tumors). It can also occur as a result of traction exerted on the retina by vitreous membranes, fibrotic and/or fibrovascular vitreoretinal membranes that form following trauma, previous retinal detachments, or—as often happens—in proliferative retinopathy (diabetic retinopathy) or in retinopathy of prematurity [13].

Fig. 4 (A). Traumatic detachment of the retina (R) associated with choroidal detachment with altered organization of the membranes (arrow). ON = optic nerve. (B) Traumatic retinal detachment with choroidal detachment (C) with altered organization of membranes. The retina (arrows) is connected to the optic nerve and blood supply.

Fig. 5 (A) Hemovitreous and retinal detachment associated with vitreous membranes. B-mode US does not allow precise assessment of the damage. ON = optic nerve. (B) Contrast-enhanced study (CEUS) during the perfusional phase. (C) CEUS shows a richly vascularized retina (arrow) that can be easily differentiated from surrounding avascular membranes.

When *detachment is complete*, the retinal membrane can be seen within the vitreous body as a moderately mobile membrane bounded anteriorly by the ora serrata and posteriorly by the optic disc [13]. In this case, the anatomic boundaries and the degree of mobility of the detached

Fig. 6 Choroidal melanoma. (A) Doppler study performed before radiotherapy. (B) Evaluation of contrast prior to radiotherapy demonstrates that high vascularity of the tumor. (C) CEUS performed 5 months after radiotherapy shows persistent

Fig. 7 (A) Cyst-like appearance of lesion in the left lacrimal gland (arrow). (B) CEUS reveals the intense vascularity of the solid lesion (arrow). (C) Volumetric reconstruction provides more effective representation of the lesions relations with adjacent structures.

retina allows one to differentiate it from vitreous membranes, which are not attached to the optic disc and ora serrata and are also much more mobile [14]. Frequently, however, vitreous membranes caused by hemorrhage and blood clots in the vitreous body are associated with *partial retinal detachment*. These are not easy to identify due to the absence of anatomical relations with the optic disc and ora serrata. In addition, vitreous membranes are sometimes attached to the retina, adjacent

vascularity that is less intense than that observed during the previous study. (D) CEUS 11 months after radiotherapy reveals an almost totally avascular lesion.

Fig. 8 Periorbital lesion. (A) B-mode US shows a cyst-like lesion (asterisk). The characteristics and location of the lesion are suggestive of a mucocele. G = eye. (B) In another scan plane, the lesion exhibits a complex cyst-like appearance (asterisk). (C) Color Doppler reveals the limited vascularity of the lesion (asterisk). (D) CEUS reveals a richly vascularized lesion (left image).

to the optic disc or the ora serrata, and this can lead to errors in diagnosis. In a preliminary study by Wong et al. [4], errors in distinguishing vitreous membranes from detached retinas occurred at a rate of 17%. More recently, Han et al. showed a misdiagnosis rate of 22% when B-mode ultrasound alone was used [7]. When there is hemovitreous associated with vitreous membranes and retinal detachment, color Doppler has been shown to improve the differential diagnosis by revealing the increased vascularity of the retina and the avascular nature of the vitreous membranes [4,7]. Han reported a sensitivity of 57% for color Doppler in highlighting the vasculature of the retina, which is significantly lower than that previously reported by Wong (100%). This difference is justified in part by size differences in the cohorts examined in the two studies and the criteria used to enroll them. The value of power Doppler in this setting has proved to be rather modest because the significant artifacts produced by vitreous membranes are not easy to distinguish from true flow signals. In short, in differentiating retinal detachment and vitreous membranes, Han reported diagnostic accuracies of 78% for B-mode ultrasound alone, 81% for color Doppler, and 59% for power Doppler [7]. The use of first-generation ultrasound contrast agents significantly improved sonographic identification of retinal detachment, increasing its sensitivity from 57% to 93% [7]. In our hands, the use of second-generation contrast agents and dedicated algorithms has allowed the identification of retinal detachment with a sensitivity of 100% (Figs. 3–5).

Tumors of the eye

Ultrasound is the first-line imaging method for the evaluation of tumors of the eye [15–19]. Color Doppler has been used to differentiate choroidal melanoma, choroidal nevus, and hemorrhages [16].

Choroidal melanomas, along with melanomas of the ciliary body, are uveal melanomas, the most common primary intraocular malignant tumor diagnosed in adults. Most choroidal melanomas are poorly pigmented or amelanotic. They are one of the causes of secondary retinal detachment. On color Doppler they appear as high vascularized lesions. Metastases usually present with a similar vascular pattern. These lesions are extremely rare, and are more frequent in adults than in children. They usually originate from primary tumors of the breast, lung, kidney, stomach, prostate, or skin (cutaneous melanoma). In our limited experience with these tumors, CEUS effectively revealed the high vascularity of choroidal melanomas of the choroid, allowing them to be differentiated from choroidal nevi, which are usually indistinguishable from melanoma on ultrasound. CEUS was also effective for monitoring responses to conservative treatment with radiotherapy, showing the gradual reduction of the lesion's blood supply (Fig. 6).

Tumors of the orbit

The primary malignancies of the orbit include vascular lesions such as cavernous hemangioma, lymphangioma, and hemangiopericytoma [15,18]. These are usually round, well-defined lesions with low to medium echogenicity relative to the adjacent connective tissue.

Hemangiopericytoma is also a vascular tumor of the orbit. Compared with hemangiomas, it is a less common tumor and characterized by the prevalence of pericytes rather than endothelial cells. On ultrasound, it is indistinguishable from hemangioma. Unfortunately, color Doppler is of little use in the study of these tumors. Blood flow is slow within these lesions, and for this reason it is not always possible to demonstrate venous flow. As highly vascular lesions, *meningiomas of the optic nerve* and *lymphomas* are well visualized on CEUS but not on B-mode ultrasound. With the latter method, meningiomas resemble vascular tumors (with variable hypoechogenicity and round shape), while lymphomas, which are poorly encapsulated, present blurred, irregular margins and are not well delineated from adjacent tissue. Because of their high cellularity and limited stromal content, these tumors appear markedly hypoechoic and have a cystic-like appearance (Figs. 7 and 8).

Conclusions

High-resolution US was highly effective in detecting traumatic and non-traumatic lesions of the eye, but it is not very efficient in the evaluation of orbital lesions. CEUS proved to be cost-effective and therefore suitable for cases in which it is not possible to use CT or MRI techniques. CEUS plays an essential role in the differential diagnosis of retinal detachment (in which the retina is vascularized) and vitreous membrane (which appear rather avascular). In addition, the method was found useful CEUS in the evaluation of ocular tumors in the therapeutic management for what concerns the choroid melanoma and assessment of neovascularization of orbital tumors.

Conflict of interest statement

The authors have no conflict of interest.

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