Ultrasound biomicroscopy of Chinese eyes with iridocorneal endothelial syndrome

M Zhang, J Chen, L Liang, A M Laties, Z Liu

Aim: To document the ultrasound biomicroscopic (UBM) findings in Chinese patients with iridocorneal endothelial (ICE) syndrome.

Methods: 21 patients with ICE syndrome and 15 normal subjects underwent UBM. UBM findings of anterior segment were compared between normal subjects and three clinical types of ICE syndrome: progressive iris atrophy (PIA), Chandler’s syndrome (CS), and Cogan-Reese syndrome (CRS).

Results: Central anterior chamber depth was significantly less in patients with ICE syndrome (2.25 (SD 0.32) mm) than in normal subjects (2.76 (0.32) mm). Peripheral anterior synechiae were observed in all the ICE patients by UBM. Three out of four CRS subjects showed an ‘arborised’ shape of iridocorneal angle. Two eyes out of 10 with CS presented bridge-shaped synechiae. A membrane-like mound was observed in iridocorneal angle in two patients: one with CRS and one with CS. UBM was found to be more effective in detecting peripheral anterior synechiae (PAS) and iris atrophy than slit lamp microscopy and gonioscopy, mainly because of corneal oedema in patients with CS. Four out of 11 patients with unilateral ICE syndrome had shallow or closed anterior chamber angles in their fellow eyes. Two of them successfully responded to laser peripheral iridotomy.

Conclusions: UBM is an effective method to reveal the anterior segment features and provides a useful tool in the diagnosis of ICE syndrome. Different subtypes of ICE syndrome may have different UBM manifestations. UBM can help to identify angle closure in the fellow eye of unilateral ICE syndromes.

Iridocorneal endothelial (ICE) syndrome is a rare disease characterised by corneal endothelial abnormality, peripheral anterior synechiae (PAS), iris stromal abnormalities, and secondary glaucoma. ICE syndrome can be subdivided into progressive iris atrophy (PIA), Chandler’s syndrome (CS), and Cogan-Reese syndrome (CRS). Without proper treatment, blindness follows corneal oedema and secondary glaucoma in many cases. The prevalence of glaucoma associated with ICE syndrome ranges from 46% to 82%. In most cases, the glaucoma is refractory, requiring multiple medications and surgical procedures. Although patients with ICE syndrome have distinctive clinical features, diagnosis proves difficult in some cases. For instance, Laganowski et al reported that 68% of the ICE patients with glaucoma who were operated on had PAS with ICE syndrome. Lack of awareness of this relatively rare disorder is one explanation for misdiagnosis. Another may be that diagnosis is hindered by corneal oedema obscuring the anterior chamber angle.

Ultrasound biomicroscopy (UBM) has a significant role in ocular imaging in recent years. It has allowed progress in the study of glaucoma and has contributed to a better understanding of the mechanisms of angle closure in glaucoma. In addition, UBM has been used to study structural alterations in many other pathological conditions such as aniridia, ocular trauma, and so on. UBM has proved to be useful for evaluating the status of surgical procedures such as laser iridotomy. In particular, it has permitted visualisation of the anterior chamber where gonioscopy is not feasible.

PATIENTS AND METHODS

Patients

The records of the patients diagnosed with ICE syndrome and seen at both the glaucoma department and the cornea department in the Zhongshan Ophthalmic Center, Sun Yat-sen University between January 1998 and February 2003 were reviewed retrospectively. Twenty one patients with ICE syndrome who underwent UBM before any surgical procedure were included in this study. Patients with a history of ocular trauma or uveitis were excluded. The diagnosis and the classification of ICE syndrome of different subtypes were determined by the examining physician. Inclusion criteria were “hammered silver” appearance of posterior corneal surface or corneal oedema that precluded visualisation of the posterior cornea, and characteristic iris stromal abnormalities including PAS, corectopia, iris holes, or multiple iris nodules. Patients were classified into three clinical variants based on iris changes. Progressive iris atrophy was diagnosed in patients with iris stromal atrophy and distortion with or without iris holes. Those with multiple iris nodules were classified as CRS. CS was indicated by the presence of corneal abnormalities typical of ICE but with minimal or no iris stromal atrophy.

Among 21 patients, 10 patients (11 eyes) were examined for the affected eye and seven patients (seven eyes) were examined for both affected and the fellow eyes. The remaining four patients (four eyes) had surgery before receiving UBM examination. Their fellow eyes received UBM examination during follow up, so only the UBM records for the fellow eyes for these four patients were.

Abbreviations: ACD, anterior chamber depth; BCVA, best corrected visual acuity; CS, Chandler’s syndrome; CRS, Cogan-Reese syndrome; ICE syndrome, iridocorneal endothelial syndrome; PACG, primary angle closure glaucoma; PAS, peripheral anterior synechiae; PIA, progressive iris atrophy; UBM, ultrasound biomicroscopy
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BCVA, best corrected visual acuity; C/D, cup-disc ratio; PAS, peripheral anterior synechiae; ACD, anterior chamber depth; PIA, progressive iris atrophy; CS, Chandler’s syndrome; CRS, Cogan-Reese syndrome; b, bullous keratopathy; NA, not accessed, CF, counting fingers; HM, hand motion.

*Patient had myopia (−10D). †Patient had hyperopia.
included in this study. Among 18 affected eyes that received UBM, four eyes were diagnosed as having PIA, 12 eyes as having CS, and four eyes as having CRS. The profiles of the patients are summarised in tables 1 and 2.

Fifteen healthy subjects served as normal controls. Of 15 normal subjects, all had open anterior chamber angle, normal intraocular pressure, no known ocular abnormalities, and a manifest refractive error of –3.00 dioptres or less of myopia, and less than 2.00 dioptres of astigmatism with a best corrected visual acuity of 20/20 or better (11 with normal refractive power, and four with myopia).

Ultrasound biomicroscopy
Scanning was performed using the Zeiss-Humphrey ultrasound biomicroscope Model 840 (Humphrey-Zeiss, San Leandro, CA, USA). This instrument consisted of a 50 MHz transducer probe, allowing 4–5 mm tissue penetration and approximately 50 μm resolution. The examinations were performed with the patient in the supine position. After surface anaesthesia, eyes were studied using an eyecup, filled with 2% methylcellulose as a coupling medium. UBM was performed to scan over the central cornea and central anterior chamber, then in 8–12 sectors of the limbal circumference. The anterior chamber depth was calculated from the distance between the corneal endothelium and the anterior lens surface. All UBM examinations were carried out by a single examiner.

Statistical analysis
The statistical analysis was processed by SPSS 10.0 software (SPSS Inc, Chicago, IL, USA). Data were expressed as mean (SD). Independent samples t test and χ² test were used to compare the anterior chamber depth between ICE patients and normal controls, as well as age and sex. A one way analysis of variance (ANOVA) test or χ² or Fisher’s exact test was performed to compare the measurements among the three clinical variants. Statistical significance was considered significant if p<0.05.

RESULTS
Clinical data
Patient profiles
Among 21 patients (22 eyes) with ICE syndrome, one patient was found to have CS in the right eye and PIA in the left eye. The remaining 20 presented with unilateral disease. There were 10 men and 11 women. The average age at the time of diagnosis was 49 (SD 13) years (range 33–80 years). For the normal controls, the mean age was 43 (16) years (range 17–70 years). There were nine males and six females. The age and sex of normal subjects were similar to patients with ICE syndrome (age: t = 1.344, p = 0.189; sex: χ² = 0.161, p = 0.688). Figure 1 showed slit lamp examination findings of patients with PIA (fig 1A) or CS (fig 1B).

Eyes with ICE syndrome
Ultrasound biomicroscopy data were obtained in 18 eyes (17 patients) with ICE syndrome. The patient profiles are shown in table 1. Best corrected visual acuity was usually poorer in patients with CS than with PIA or CRS. Intraocular pressure (IOP) was obtained by averaging three repeated measurements using non-contact tonometer. The intraocular pressure (IOP) in eyes with ICE syndrome varied widely, ranging from 7.4–59.1 mm Hg. Nine eyes had an IOP higher than 21 mm Hg. All CS patients had severe corneal oedema and the fundus was not accessible. Two PIA patients and three CRS patients showed advanced cupping of the optic nerve (C/D ≥0.6). Peripheral anterior synechiae were observed by slit lamp biomicroscopy in 13/18 eyes and iris atrophy was observed in 12/18 eyes with ICE syndrome. Gonioscopy revealed PAS in all patients with PIA or CRS. Patients with CS were not examined by gonioscopy because of the severe corneal oedema. Three of four PIA patients and all CRS patients received surgery, either a trabeculectomy or an aqueous shunt or in some instance both. All patients with CS received at least once penetrating keratoplasty with or without trabeculectomy.

Contralateral eye of unilateral ICE syndrome
Contralateral eyes of 11 unilateral ICE patients were examined with UBM. The patient profiles are shown in table 2. The BCVA was 20/30 in two eyes and 20/20 in nine eyes. The average IOP was 15.1 (2.2) mm Hg (range 10.2–18.0). Four patients had shallow anterior chamber, and no

Table 2  Patient profiles with iridocorneal endothelial syndrome (the fellow eyes)

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All data come from the fellow eyes except the diagnosis. Patients 2, 7, 8, 11, 14, 15, and 16 received UBM in both eyes. *Patient had myopia. †Patient had hyperopia.
anterior segment abnormality was found in the remaining seven patients. No patient showed advanced cupping of optic nerve.

**UBM findings of eyes with ICE**

**Corneal oedema**

Corneal oedema was detected in all the patients with CS. The corneal thickness was as great as 1.285 mm in patient 10 (fig 2C). In some cases, folds in Descemet’s membrane occurred, leading to the irregularity in the posterior corneal surface (fig 2A).

**Anterior chamber depth**

The central anterior chamber depth (ACD) was significantly less in patients with ICE (2.25 (0.32) mm) compared to normal subjects (2.76 (0.32) mm) (t = 3.240, p = 0.003, independent samples t test). The mean ACD was similar among three clinical variants (2.41 (0.14) mm for PIA, 2.11 (0.59) mm for CS, and 2.44 (0.65) mm for CRS, F = 0.730, p = 0.498, ANOVA).

**Iris atrophy**

Iris atrophy was observed in all patients except for one patient with Chandler’s syndrome. The extent of iris atrophy varied. In mild cases, the iris kept its original shape but was thinner than normal (fig 2B); in severe cases, the extensive iris atrophy, accompanied by a broad based PAS, gave the iridocorneal angle an “arborised” shape (fig 2E and F). In general, iris atrophy appeared more severe in patients with PIA or CRS than in patients with CS.

**Iridocorneal angle**

Peripheral anterior synechiae of different severity were observed in all ICE patients. In patients with CRS, three out of four eyes showed very high PAS, accompanied with extensive iris atrophy, resulting in an “arborised” shape of iridocorneal angle (fig 2E and F). These features were not found in patients with PIA or CS. Two eyes with CS presented a bridge-shaped PAS, in which the middle part of the iris adhered to the cornea, leaving the iridocorneal angle open (fig 2C and D). This was observed only in patients with CS. In two patients, a membrane-like mound was observed in iridocorneal angle (fig 3A–D).

**Comparisons among slit lamp biomicroscopy, gonioscopy, and UBM**

Peripheral anterior synechiae were detected by UBM in all 18 eyes with ICE syndrome, whereas only 13 were found to have PAS by slit lamp biomicroscopy. The difference is statistically significant (p = 0.045, Fisher’s exact test). PAS was found in all patients examined by gonioscopy; however, gonioscopy could not be achieved in CS patients with oedematous Co, cornea; Ir, iris.
proved, that this might be because the synechiae occasionally extensive PAS show minimal IOP alteration; the reason for region. When combined, these techniques can achieve a more synechiae and the details in the anterior chamber angle tool to determine the severity of peripheral anterior synechiae among the three variants. Gonioscopy has been a common features may provide additional criteria to differentiate severe synechia, was often observed in these patients. These patients with CRS compared to other two variants of ICE syndrome.16 By using UBM, we observed bridge-shaped PAS in two CS patients and both patients had normal or slightly increased IOP despite extensive PAS. This finding provides direct support for this speculation. With respect to the deposition observed in the anterior chamber, we are unsure how to explain the mound: it might be another form of PAS, or a membrane covering anterior chamber angle as proposed in the membrane theory of Campbell for the aetiology of ICE syndrome.33 However, in a retrospective study, this finding cannot be further explored to find an explanation.

ICE syndrome has been suggested to affect primarily one eye. However, bilateral cases have also been reported,22 24 In recent years, there is growing evidence about the subclinical abnormalities in the fellow eye.4 In the present study, a number of ICE patients (4/11) were found to have a narrow angle with normal IOP in the fellow eye. Perhaps it represents an ethnic anatomical difference of anterior angle in an Asian population. Studies have shown that primary angle closure glaucoma (PACG) occurs more frequently in Asians, including Chinese living in mainland China23 and Singapore,25 people in Thailand26 and Mongolia,27 than in white populations. The prevalence of PACG in Asians varies from 0.9% to 1.4% for the age over 40, compared to 0.6% in the same age group in white people.28 This may also be because of the average age of ICE patients is over 40, and the PACG prevalence increases while ageing. Therefore, more attention should be paid to the contralateral eyes in ICE patients, especially in the Asian population. In unilateral cases with a narrow angle in the fellow eyes, laser iridotomy may help to protect the contralateral eye from developing PACG.

In summary, UBM, plus gonioscopy, provides a valuable way to diagnose ICE syndrome. Different subtypes of ICE syndrome may have different UBM manifestations. UBM can help to characterise the risk of angle closure glaucoma in the fellow eye of unilateral ICE syndromes.

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