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Case Series

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Iridocorneal Endothelial Syndrome Management is tough but Never Impossible. A Case Series Study

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Abstract

Purpose: To document and describe clinical manifestations and management approaches to patients diagnosed with Iridocorneal Endothelial (ICE) syndrome presenting at the Glaucoma Department, Chittagong Eye Infirmary and Training Complex, Chittagong, Bangladesh.

Design: A hospital-based prospective observational case series review. Participants: 25 patients who were diagnosed as ICE syndrome from November 2007 to October 2009.

Method: Patient particulars, history with main causes of hospital presentations were recorded. Ophthalmic examination details including tonometry, slit lamp examination, gonioscopy, indirect ophthalmoscopy, visual fluid examination and management given were documented. Similar relevant details were recorded for three follow up periods on all patients extending over a total period of 12 months.

Main outcome measure: Significant observations, pattern or associations within the cohort.

Results: 25 patients were included in the study. There were 15 female and 10 male patients. All 25 cases were unilateral. The mean age of the patients was 41 ± 15.27 years. Among them 15(60%) had pre-treatment visual acuity between 6/9 – 6/18 and 10(40%) had 6/24 – 6/60). Improved visual acuity was observed one year after starting treatment. 21 patients (84%) presented with eccentric pupil (corectopia), 9 patients (36%) with peripheral anterior synechiae, 6 patients (32%) with iris atrophy, 6 patients (24%) with mild corneal oedema, 3 patients (12%) with ectropion uveae, 2 patients (8%) with polyconic and 11 patients (44%) presented with pigmentary changes over iris (like diffuse iris naevus). Mean IOP at presentation was 24.08 ±14.3 mmHg and that of last follow-up was 17.38 ± 7.57 mmHg. IOP was controlled with 2 – 3 topical anti glaucoma medications in 8 patients (32%); with only observation in 5 patients (20%) and with surgical intervention in 12 patients (48%).

Conclusion: Although ICE syndrome is a refractory glaucoma, control of Intraocular Pressure (IOP) and preservation of visual acuity were seen in 52% of cases which had conservative management with topical medications and observation. Patients not responding to medical management needed surgery for the control of intraocular pressure.

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Introduction

ICE syndrome is typically a unilateral condition characterized by a corneal endothelial abnormality that is variably associated with corneal oedema, anterior chamber angle changes, alterations in the iris and secondary glaucoma. The disorder is usually diagnosed in early adulthood and is more common in females than in males. The spectrum of ICE syndrome is divided into Chandler's syndrome, essential (progressive) iris atrophy, and the Cogan–Reese (iris naevus) syndrome based primarily on the changes in the iris. Although clinically the distinction may be important, the three sub-types of ICE syndrome may more accurately be regarded as different manifestations of the same disease process. The subtypes of ICE syndrome are linked by the presence of an abnormal corneal endothelial cell layer. These cells have the capacity to migrate across the trabecular meshwork and onto the surface of the iris. Contracture of this layer results in iris changes, Peripheral Anterior Synechiae (PAS) and glaucoma. The glaucoma is presumed to be secondary to angle closure or a membrane covering the trabecular meshwork. The rate of glaucoma associated with ICE syndrome has been reported to range from 46% to 82%.[1-4] Previous studies have suggested that essential iris atrophy has a more refractory glaucoma than Chandler's syndrome.

The glaucoma associated with ICE syndrome often is difficult to treat [1,4,5]. Medical therapy is usually limited to aqueous suppressants and often becomes ineffective.4 Laser trabeculoplasty is ineffective. The success rate of filtering surgery is also believed to be lower than with most other forms of glaucoma. A few smaller studies on secondary glaucoma in ICE patients have looked at the outcomes since the introduction of antifibrotics agents and Glaucoma Drainage Implant (GDI) surgery, but these studies have had limited follow-up [6,7]. The purpose of the current study is to describe clinical manifestations and management outcomes of patients who were diagnosed as ICE syndrome at the Glaucoma Department, Chittagong Eye Infirmary and Training Complex, Chittagong, Bangladesh.

Methods

This is a hospital-based combined non-concurrent and concurrent prospective cohort study of all cases presenting to the glaucoma clinic with a diagnosis of ICE syndrome. Cases were identified throughout a two-year period from November 1st 2007 to October 31st 2009. All patients were reviewed by a single consultant.

Details of history including the biographical details of patients (age, gender, address etc.) and clinical presentations were recorded. Ophthalmic examination was done and included visual acuity, intraocular pressure (IOP) by Goldman applanation tonometry, slitlamp examination, gonioscopy examination by Goldman 2 mirror Gonio lens, indirect ophthalmoscopic examination with 90D and 78D lens were done and documented as much as possible.

For previously diagnosed patients, their medical records were retrieved and relevant data were extracted and asked to come for follow-up as necessary. Newly diagnosed patients were duly processed and asked to return for future follow-up visits.

At least 3 follow-up data were recorded, 1 month after diagnosis of

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ICE syndrome, then 3 months and 6 months. On all visits ophthalmic exanimation was done by the same consultant.

Bleb clarity and AC depth were examined in each follow-up of all postoperative cases. After collection of data, they were then tabulated and analysed. Outcomes of management were assessed mainly with regards to IOP control. Statistical analysis was done using SPSS v 13. T-test was done to determine probability value.

Results

A total number of 25 patients with ICE syndrome were encountered during the study period. All of the cases were unilaterally affected. Of these, 14 were newly diagnosed cases and had a history of 6 month to one year and 11 were previously diagnosed. The mean age of the patient was 41 ± 15.87 years (Table 1). Among them 15 (60%) were female and 10 (40%) were male patients (Figure 1). In all age group categories females were significantly more than males (Table 1).

21 patients (84%) presented with eccentric pupil (corectopia), 9 patients (36%) with peripheral anterior synechiae (PAS), 6 patients (32%) with iris atrophy, 6 patients (24%) with mild corneal edema, 3 patients (12%) with ectropion uveae, 2 patients (18%) with polycoria and 11 patients (44%) presented with pigmentary changes over iris like diffuse iris naevus (Table 2).

Among them 15(60%) had pretreatment visual acuity between (6/9 – 6/18) and 10(40%) had (6/24 – 6/60). Improvement in visual acuity was observed one year after initiating treatment (Table 3). 15(60%) patients in the right eye and 10(40%) patients in the left eye were involved (Table 4).

At presentation 5 patients had a normal C:D ratio (0.2 – 0.5):1 with healthy neuroretinal rim and 20 patients presented with glaucomatous optic disc changes like increased C:D ratio (0.6 – 1), thinning or notching of the neuroretinal rim with corresponding visual field loss detected by HVF 24–2 and HVF 10–2 analysis (Table 5a and 5b).

Mean IOP at presentation was 24.08 ± 14.83 mmHg, at 1st follow-up was 18.48 ± 8.70 mmHg and at last follow-up was 17.38 ± 7.57 mmHg (p value = 0.001 by T-test) (Figure 2).

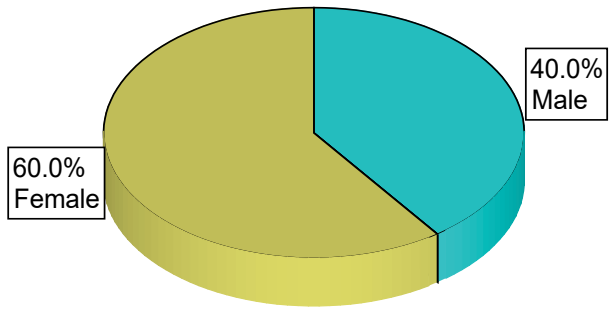

Figure 1: Gender distribution of patients.

Table 1: Gender distribution of patients in the defined age categories (p < 0.4).

Age (years)	Male	Female	Total
15-29	2	4	6 (24%)
30-45	4	6	10 (40%)
> 45	4	5	9 (36%)
Total	10	15	25 (100%)
Mean age = 41 ± 15.87 years.			

Table 2: Distribution of syndrome features.

Features	N	Percentage (%)
Corectopia	21	84
Peripheral Anterior Synechaea	9	36
Iris atrophy	8	32
Corneal edema	6	24
Very Shallow AC	4	16
Ectropion uveae	3	12
Heterochromia	2	8
Cataract	2	8
Ploycoria	2	8
Guttata	1	4
Nystagmus	1	4
Corneal scar	1	4
Posterior Subcapsular Cataract	1	4
Pigment over lens	1	4
Pigmentary changes over iris:		
Diffuse iris naevus	6	24
Iris naevus	4	16
Pigment over iris	1	4

Table 3: Pretreatment and post treatment visual acuity.

VA	Pre-treatment	Post-treatment
	N(%)	N(%)
6/6 – 6/18	15 (60)	20 (80)
6/24 – 6/60	10 (40)	5 (20)
Total	**25 (100)**	**25 (100)**

Table 4: Laterality of the disease.

Eye	N	Percentage
Right	15	60
Left	10	40
Total	**25**	**100**

Table 5 (A): Distribution of C:D ratio.

Cup Disc Ratio	N	Percent
0.2:1	1	4
0.4:1	2	8
0.5:1	2	8
0.6:1	2	8
0.7:1	5	20
0.8:1	4	16
0.9:1	4	16
1:01	5	20
Total	25	100

Table 5 (B): Distribution of visual field defect.

Cup Disc ratio	N	HVF	N
0.6:1	2	Superior arcuate scotoma	**2**
0.7:1	7	Inferior arcuate scotoma	**2**
			3
		Superior arcuate scotoma	
0.8:1	4	Double arcuate scotoma	**4**
0.9:1	4	Double arcuate scotoma	**2**
		Tubular field	**2**
0.10:1	5	Tubular field	**5**

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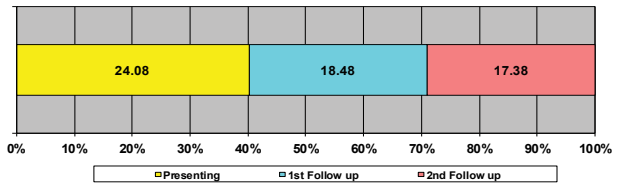

Figure 2: Intraocular pressure at different follow-up.

Table 6: Treatment options for controlled IOP.

Mode of treatment	Frequency	Percent (%)
Drug	8	32
Surgery	12	48
Observation	5	20
Total	**25**	**100**

Intraocular pressure was controlled by medication in 8(32%) patients. Among them 6 patients were with topical timolol maleate 0.5% (twice a day) and Brimonidine tartrate 0.2% eye drop(thrice a day). In 2 patients travoprost (0.004%) (once daily at night)was added with to the previously mentioned two drops.

5 patients (20%) presented with normal intraocular pressure. They are still on observation. Those patients (N=12; 48%) in whom IOP was not controlled with 2 or 3 medications and with advance visual field loss IOP was controlled with filtration surgery that is Trabeculectomy or Trabeculectomy and Cataract Surgery. Mitomycin– C was used in all cases during filtration surgery. 1 patient needed penetrating keratoplasty for corneal opacity (Table 6).

Discussion

Iridocorneal endothelial (ICE) syndrome is a spectrum of conditions affecting the eye. Iris naevus (Cogan-Reese) syndrome, Chandler's syndrome and essential iris atrophy are all manifestations of the disease spectrum. Associated ocular pathology includes glaucoma as well as corneal and iris changes. Iris changes may manifest as stromal atrophy, corectopia, pseudopolycoria and the induced nodular irregularity of iris naevus syndrome, created by evaginations of iris stroma through holes in the multilaminar membrane that covers the iris in this condition. In any case in which the pupil is displaced or enlarged or if the stroma is insufficient to block light, glare and other unwanted optical phenomena may occur.

Diagnosis of ICE syndrome is based on abnormalities in the corneal endothelium, distortion of the pupil with ectropion uveae, thickening of the iris stroma with increased pigmentation, iris atrophy, peripheral anterior synechiae, glaucoma and unilaterality of disease [8]. Most of our cases had iris abnormalities like corectopia, peripheral anterior synechiae, iris atrophy, diffuse iris nevus and iris atrophy which are predominant a noted in another study [8]. Among the three clinical variants, Cogan-Reese syndrome and progressive iris atrophy have been suggested to induce more severe glaucoma [9-11]. In our study those patient who presented with high IOP and advanced glaucomatous disc and field changes were associated with multiple iris abnormalities, both atrophic and pigmentary (Figure 3).

ICE syndrome has been suggested to affect primarily one eye. However bilateral cases have also been reported [12,13]. In recent years there is growing evidence about the sub clinical abnormalities of the fellow eye [14]. In our study all cases were unilateral and no abnormalities were detected in the other eye.

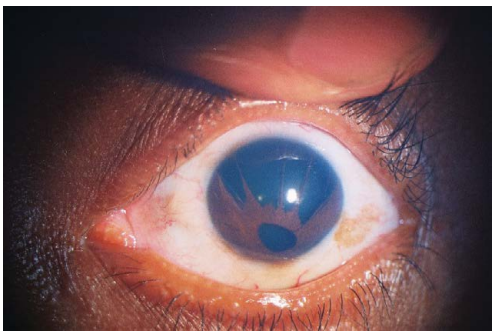

Figure 3: Showing Corectopia with diffuse iris atrophy.

To diagnose ICE syndrome slitlamp findings are enough but in cases with atypical clinical features (such as lack of iris holes or corectopia or with severe corneal edema) diagnosis of this rare disorder can be difficult. Ultrasound biomicroscopy was found to be a good tool in detecting the feature of anterior chamber angle giving detail information of PAS and iris atrophy. It has special merit when the cornea does not permit a good view by slitlamp microscopy or gonioscopy [15]. In majority of our cases the cornea was clear. There was mild corneal edema in 6 cases.

Poor vision in patients with ICE syndrome might be related to corneal edema, glaucomatous optic nerve damage, cataract formation or due to a combination of these factors [16,17]. In our study, decrease visual acuity was due to similar causes. Chandler's syndrome occurred in 7 cases. 6 patients presented with corneal oedema and 1 patient with corneal scar. The others presented with either Cogan-Reese syndrome or with iris atrophy. Teekhasaenee and Ritch [18,19] reported that Cogan-Reese syndrome was the most common form in Asian patients, while Chandler's syndrome was more common in white patients. This is consistent with our findings.

With regards to the sexual difference in patients with ICE syndrome, we found that women composed of the majority of the patient group (80%) which is in support of the description by Sherrard9 that "the typical patient is a woman". Specular microscopy is a good tool for visualizing endothelial abnormalities directly and for assisting in differential diagnosis [20]. Other causes of endothelial abnormalities are Fuch's endothelial dystrophy and posterior polymorphous dystrophy. Focal and secular microscopic examination reveals ICE cells and subtotal ICE (+) tissue in ICE syndrome.[20] It would have been better to perform specular microscopy on all of our ICE syndrome cases.

Histopathological studies have found that endothelial cells undergo epithelial changes including alterations in the desmosomal junctions, surface microvilli and increased intracytoplasmic filaments. These endothelial changes can lead to corneal edema and growth of the membrane onto the iris. Contraction of the membrane may cause peripheral anterior synechiae with secondary glaucoma and various changes in the iris [21-23]. In our study 9 patients presented with peripheral anterior synechiae of more than 1800. Many investigations have been done to investigate the causative agent or stimulus for abnormal endothelial growth in ICE syndrome. No definitive proof has been established but a relationship may exist with the herpes simplex and Epstein –Bar viruses [24]. In our study we did not attempt to investigate causative factors. Further investigations are needed to determine the causative factors.

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Glaucoma due to ICE syndrome is difficult to treat.5 Medical therapy is usually ineffective.4 Filtration surgery is needed to control intraocular pressure [4]. The success rate of filtration surgery is also believed to be lower than that with most other forms of glaucoma. [6,7] Few studies have described the success rate of filtration surgery which can be improved by using antifibrotics and glaucoma drainage implants. In 32% of our patients IOP was controlled by 2–3 antiglaucoma medications at the end the 10 months. Most of them presented at early stages of the disease. 48% needed filtration surgery with mitomycin C to control intraocular pressure and are still doing well after 10 months. Most of them have a thin polycystic functioning bleb. IOP was normal in 20% of our cases at presentation. They are still under observation.

We can not define a final success due to short term follow-up. Further long term follow-up is needed to determine the success. Attvim PT25 showed that a favourable outcome can be achieved in patients with ICE syndrome involving cornea but may require multiple procedures. Penetrating keratoplasty(PK) was done in one of our cases that presented with a corneal scar. Visual acuity was improved by 2 lines post-PK.

Conclusion

Although ICE syndrome is an established cause of refractory glaucoma, medical control of intraocular pressure can be achieved. Early diagnosis with proper examinations and investigations are needed. Explanation to the patients, proper counselling and strict follow-up is mandatory to achieve proper treatment outcomes. Glaucoma filtration surgery with antimetabolites is usually successful when done early, but may fail later on due to endothelialisation of the fistula by the abnormal corneal endothelium.

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