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Difficulties in treatment of iridocorneal endothelial syndrome - case report

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Abstract

The iridocorneal endothelial syndrome manifests in three clinical types: Chandler syndrome, progressive iris atrophy, and Cogan-Reese syndrome. It is caused by the presence of abnormal corneal endothelium on the iris stroma and anterior chamber angle leading to usually unilateral, progressive iris atrophy, glaucoma, and/or corneal edema. The etiology is yet unclear. It affects mostly young adults, mostly females. Management of iridocorneal endothelial syndrome is complex: conservative and surgical, depending on the stage of the disease and intensity of present symptoms. A 30-year-old female with a medical history of the iridocorneal endothelial syndrome was reported to the Ophthalmology Department for consultation. Slit-lamp examination revealed iris atrophy and superior-nasal corectopia in the left eye. On gonioscopy, the angle was wide open in the right eye, but there were iridocorneal adhesions and incomplete angle-closure in the left eye. The patient was provided with maximum local therapy consisting of three anti-glaucoma medications. On later check-ups, the patient presented corneal edema and increased intraocular pressure. She was qualified to ExPress mini shunt trabeculectomy with mitomycin C. Two years later, a patient came to the clinic because of increased values of intraocular pressure (up to 59 mmHg), slit-lamp examination showed that the ExPress implant was congested with fragments of the corneal endothelial cells. Thanks to YAG iridotomy the implant was recanalized.

Running title: Iridocorneal endothelial syndrome - a case report

Keywords: iridocorneal endothelial syndrome, glaucoma, progressive iris atrophy

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Introduction

An iridocorneal endothelial syndrome is a group of rare diseases in which abnormal corneal endothelial cells are present on the iris stroma and anterior chamber angle [1–5]. One can distinguish three clinical variants of the syndrome: Chandler syndrome, progressive iris atrophy, and Cogan-Reese syndrome [3,6]. Its etiology is yet unclear [1,7]. It mostly affects adult women [5–8]. The manifestation of the syndrome is usually unilateral and includes elevation of intraocular pressure, defects of the cornea (corneal edema, epithelial bullae), corectopia, ectropion uvea, and atrophy of iris stroma [2,6,7]. Treatment of iridocorneal endothelial syndrome is difficult because its course is progressive [9]. This paper aims to present a multiplex treatment of a female with a rare variant, progressive iris atrophy.

Case report

A 30-year-old female reported to the Ophthalmology Department for consultation. In the past, she was diagnosed with the iridocorneal endothelial syndrome (ICE). On ophthalmic examination, her best-corrected visual acuity (BCVA) in both eyes was 0,9 on Snellen charts. The intraocular pressure (IOP) was 24 mmHg in the left eye and 18 mmHg in the right eye. Slit-lamp examination revealed iris atrophy and superior-nasal corectopia in the left eye (OS), right eye appeared normal (**Fig. 1**). On gonioscopy, the angle was wide open in the right eye, but there were iridocorneal adhesions and incomplete angle-closure in the left eye. On the funduscopic examination; the cup to disc ratio was 0,5, the optic disc was pink, the dull foveal reflex was noticed in the left eye, and the right eye was normal. The patient was provided with maximum local therapy consisting of dorzolamide (40mg) + timolol (20mg) (Rozacom) 2 times a day, brimonidine (2 mg/ml) (Alphagan) 2 times a day, and travoprost (40 ug) + timolol (5mg) (Duotrav) once a day, all in eyedrops. On the follow-up after 6 weeks, the IOP OS measures from the last weeks were around 30-42 mmHg. The patient was qualified for the Ex-PRESS mini shunt trabeculectomy with mitomycin C (MMC). On the check-up, 18 months after the surgery BCVA OS was 0,8 and IOP OS equaled 5 mmHg. Slit-lamp examination showed bullous keratopathy in the left eye. The right eye was normal. The patient has been prescribed an ophthalmic solution with osmotic action (Terso) 4 times per day combined with dexpanthenol in gel (Corneregel) at night. Two years after the surgery (02.11.2020) the patient presented to the clinic again because of the increased IOP OS up to 59 mmHg. The BCVA OS was 0,06, and IOP OS equaled 28 mmHg. Slit lamp examination showed that the ExPress implant was congested with fragments of the IPE cells at the 12 o' clock position. YAG laser iridotomy was applied which reduced IOP OS to 12 mmHg. On the follow-up one year later the implant was permeable and IOP OS was 8 mmHg. The bullous keratopathy, in the left eye, resolved, but there was a corneal opacity present.

Discussion

Iridocorneal endothelial (ICE) syndrome includes the following conditions: Chandler syndrome (CS), progressive iris atrophy (PIA), and Cogan-Reese syndrome (CRS) [3,6]. Generally, ICE syndrome mostly affects adult women [5–8]. The most common variant in Whites is CS, while in Asians it is a Cogan-Reese syndrome [5,7,10]. The etiology is unclear. One of the leading hypotheses is the viral infection of HSV (Herpes Simplex Virus) or EBV (Epstein-Barr Virus). According to this, the viral genome integrates with human corneal endothelial cells (CECs). The fusion changes the morphology and activity of the cells. This allows the cells to regain the ability for mitosis. As a result, cells proliferate to form abnormal structures. The process disturbs the normal ocular anatomy leading to iris atrophy, closure of the angle, corneal edema, and

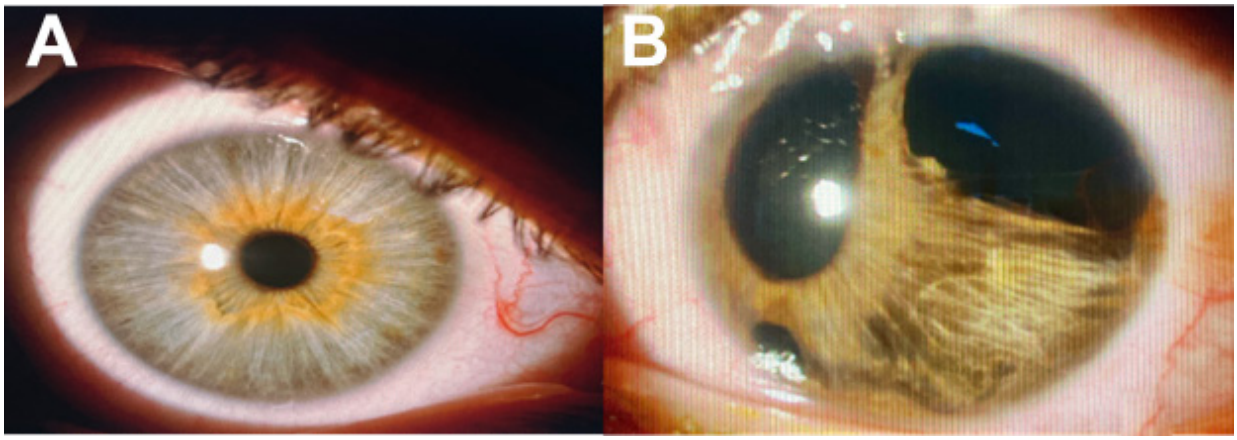


FIGURE 1 A Slit-lamp photography: right eye: normal eye without pathologies (A), left eye: iris atrophy and superior-nasal corectopia (B)



FIGURE 2 Gonioscopy of the left eye; PAS - peripheral anterior synechiae

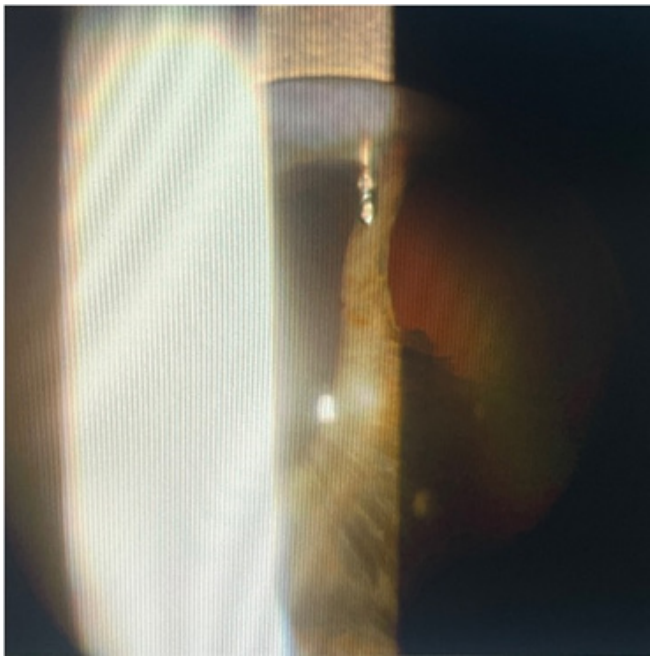


FIGURE 3 Picture showing ExPress implant

decompensation [1,7]. ICE frequently leads to glaucoma. The proliferated cells may cause obstruction of the iridocorneal angle or can constrict and pull the iris peripherally leading to peripheral anterior synechiae (PAS). In all types of ICE syndrome (CS, PIA, CRS) one can notice a cobblestone or hammered silver appearance of the corneal epithelium. It is caused by the reflection of the light from the posterior surface of the corneal cells [7]. In Chandler syndrome, most cases manifest as unilateral visual deterioration caused by the posterior corneal defects; corneal edema, epithelial bullae, and ICE cells. The iris atrophy is mild. The IOP tends to be normal. The pupil is in the central position [2,6,7]. Iridocorneal synechiae may be present but are not common for this variant [7]. Progressive iris atrophy is characterized by the formation of peripheral anterior synechiae (PAS) and extensive atrophy of the iris [8]. The focal synechiae may close the iridocorneal angle leading to elevation of IOP [3,7]. The iris is stretched by focal synechia leading to corectopia, ectropion uvea, and thinning of iris stroma with full-thickness holes formation ("stretch holes"). Corneal changes are various from corneal abnormalities to corneal edema [6,7]. Cogan-Reese syndrome presents as an extensive proliferation of corneal epithelium covering the iris and iridocorneal angle. The tension force, created by new cell formation, is usually distributed uniformly on the iris, hence does not lead to its atrophy or pupil displacement. However, rarely in CRS, one can notice nodules and mild atrophy of iris or corectopia [3,7]. Our

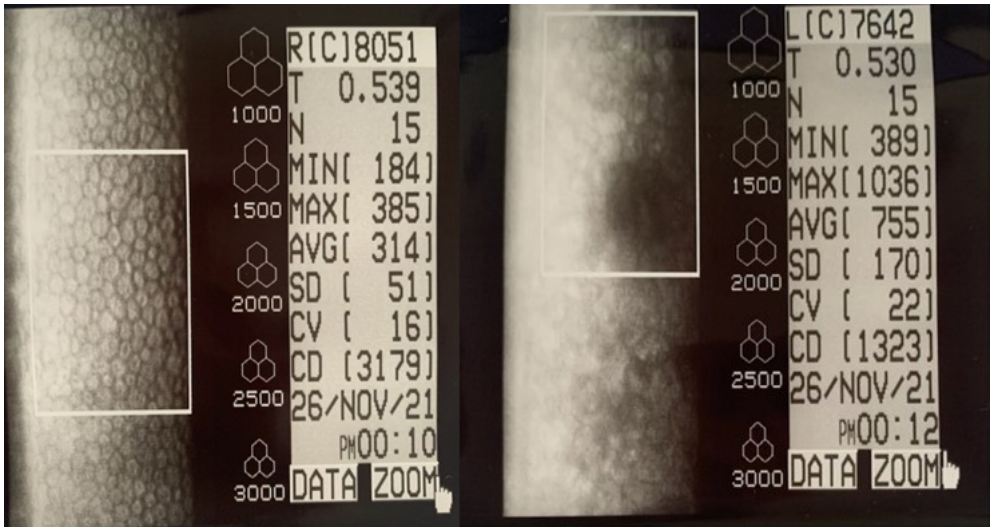


FIGURE 4 Specular microscopy of right and left eye

patient presented with iridocorneal adhesions, iris atrophy, and superior-nasal corectopia in the left eye. These findings are characteristic of progressive iris atrophy. The initial diagnosis of ICE can be made through the routine ophthalmic examination involving; the slit-lamp examination, tonometry, and gonioscopy. A slit-lamp examination may reveal a "hammered-silver" or "beaten-bronze" appearance of the endothelium, corectopia, ectropion uvea, or atrophy of iris stroma [6,7,11]. Tonometry enables the detection of the eventual increase of IOP. Gonioscopy may reveal abnormalities in the iridocorneal angle. The most common findings are iridocorneal adhesions like peripheral anterior synechiae (PAS). Which can eventually lead to the closure of the anterior chamber angle [6]. To confirm the diagnosis one should perform specular microscopy or in vivo corneal confocal microscopy (CCM) [7]. In specular microscopy, one can assess the presence of "ICE-cells". These cells look abnormal; are large, rounded, and pleomorphic with specular reflex showing a typical "light-dark reversal" consisting of a dark surface. In the centrum, there can be present light spots. Intracellular borders are also light [6,12–14]. In vivo corneal confocal microscopy is a non-invasive tool to assess corneal cellular structures at high magnification. It is useful to detect "ICE-cells" (epithelial-like endothelial cells with hyperreflective nuclei) and corneal edema [6,15]. In patients with increased IOP, it is worth performing a fundus examination to assess the condition of the optic nerve. Moreover, optical coherence tomography (OCT) may be helpful to detect iris atrophy and iridocorneal synechiae (OCT) [6,16]. Differential diagnoses should include posterior polymorphous dystrophy (PPCD), Fuchs endothelial dystrophy, iris melanoma, Axenfeld-Rieger syndrome, inflammatory iris nodule, and aniridia [6]. The management of ICE is complex, including drugs and surgery. The initial treatment is conservative and varies according to the symptoms. Increased IOP is reduced by anti-glaucoma medications that suppress the production of aqueous humor (beta-blockers, alpha agonists, carbonic anhydrase inhibitors, typically with the addition of miotics). Prostaglandin analogs should be prescribed with caution as they may stimulate the recurrence of HSV infection. In corneal edema, patients should be given eye drops with hypertonic saline solution [6]. There is a high rate of unsuccessful conservative treatment (from 60% to 88%). That is why patients, in a later course, undergo surgical treatment [4,6,17]. One of the methods is conventional filtration surgery. However, it is less satisfactory than in other forms of glaucoma [4,18–20]. The chance of long-term treatment success, of conventional trabeculectomy in ICE, is 60% after 1 year and 40% after 2 years [6,19]. Trabeculectomy can be combined with Mitomycin C or 5-fluorouracil. These two agents suppress the proliferation of fibroblasts and increase the effectiveness of the procedure [6,18,20,21]. Lanzl study suggests that Mitomycin C provides better intermediate-term effects than 5-fluorouracil [20]. The filtration surgery can be also boosted by implant drainage devices such as Ex-PRESS implant and XEN gel stent. The devices divert the aqueous solution from the anterior chamber to the subconjunctival area. These shunt devices tend to have good intermediate-term results [22,23]. Despite a wide range of treatment options, cyclodestructive procedures such as cyclophotocoagulation are often needed because of the young age of patients and the progressive nature of the disease. Patients with advanced corneal edema can undergo penetrating keratoplasty to cease the pain and improve vision [6]. Our patient was initially provided with conservative treatment consisting of three anti-glaucoma agents. Later on, corneal edema developed and the patient was prescribed

hypertonic solution in eye drops. With time the symptoms intensified so an Ex-PRESS mini shunt trabeculectomy with Mitomycin C was performed. However, two years after the surgery IOP records were up to 59 mmHg. Slit-lamp examination revealed implant congestion by corneal endothelium. Complications and evolution of our patient's ocular disease show that management of ICE syndrome is difficult and complex.

Conclusions

ICE syndrome should be always considered in young adults (especially women) with unilateral iris atrophy, glaucoma, and/or corneal edema [6]. To diagnose ICE, one should perform a routine ophthalmic examination; slit-lamp examination, fundus examination, and tonometry. The preliminary diagnosis can be confirmed in specular microscopy and by optical coherence tomography. The treatment is complex including medications and surgery.

Ethical approval

The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration. As all of the data presented were collected during routine clinical practice without any additional clinical procedures or inclusion of patient sensitive data, no Ethical Committee approval is needed for this study.

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Conflict of interest

The authors declare they have no conflict of interest.

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