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Rare and severe complications following surgical treatment of retinopathy of prematurity according to the vitrectomy method – case report

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ABSTRACT

Introduction: Retinopathy of preterm infants is a serious condition that can lead to various complications, such as severe vision loss, blindness, and other sequelae of progressive disease in premature infants. In this paper, we report the complication of ciliary body hernias resulting from high intraocular pressure in the afflicted eye combined with secondary glaucoma after vitrectomy due to retinopathy of prematurity (ROP), a condition previously not described in the literature (PubMed or Google Scholar from 2014–2022).

Material and methods: The infant underwent photocoagulation treatment twice due to ROP due to ROP stage 4/5. At 4th months of life, the baby underwent posterior vitrectomy with lensectomy, with the final injection of sodium hyaluronate to the vitreous chamber. The child did not suffer from any autoimmune diseases or keratitis. The only risk factors included photocoagulation and vitrectomy with the reconstruction of both the anterior chambers and the pupil.

Results: Following posterior vitrectomy, the child manifested multiple complications, such as hernia of the ciliary body, secondary glaucoma, leucoma, hemorrhage to the anterior eye chamber, keratomalacia, and advanced keratopathy. Autoimmune diseases, avitaminosis, the inflammatory of the cornea (of no iatrogenic etiology) and viral or bacterial infections were excluded. Nevertheless, positive bacterial cultures from natural body orifices obtained in routine examinations during hospitalization could cause a severe course of ROP as well as complicated outcomes of surgical treatment.

Conclusions: Vitrectomy is the last resort therapeutic option (ROP stage 4A, 4B, 5), as it might result in keratopathy, cataract, glaucoma, strabismus, or severe hyperopia. Due to severe damage to the eye structures that may occur after surgical vitrectomy in premature infants in the course of ROP, this technique should only be used by experienced vitrectomists with great care and caution, especially in extremely low-birthweight children.

Keywords: retinopathy of prematurity; corneal malacia; iris hernia; ciliary hernia; vitrectomy; secondary glaucoma.

INTRODUCTION

Retinopathy of prematurity (ROP) is a serious condition which can lead to various complications such as severe vision loss, blindness, and other repercussions of progressing disease in prematurely delivered infants. It has been estimated that the number of children who had lost their vision because of untreated or improperly treated ROP varies between 30,000–50,000 cases worldwide [1, 2]. In Poland, ROP was diagnosed in 19.3% of generally examined newborns in 2003–2012 [3], among whom 43% of extremely low-weight newborns delivered <29 hebdomas graviditatis (Hbd) and 23% of newborns delivered between 29–31 Hbd [4]. In the last 5 years (2016–2021) the incidence of ROP in Poland has varied between 12.2% (2017) and 35% (2020) [5].

There are 2 main phases of the development of ROP, namely vasoconstrictive phase I (during exposure to hyperoxia) and vasoproliferative phase II (dilatation, neoproliferation) vascular endothelial growth factor-depended (VEGF-depended) [6]. Currently, the most commonly used treatment methods include laser photocoagulation as well as intravitreal injections of anti-VEGF agents depending on the stage of the disease [7]. Retinopathy of prematurity can be associated with deteriorated visual acuity and unfavorable structural malformations such as macular fold, retinal detachment, retrolental mass, and refractive errors such as myopia and astigmatism [7, 8].

Apart from progressing retinal disease, the side effects of the used therapy also need to be taken under consideration, although it is rather rarely observed. As far as diode laser therapy is concerned, the most common complications include hyphema (1.6%), keratopathy (0.6%) [9], and strabismus (16.1%) or retinal detachment (5.0%) [10]. The last resort therapeutic option is vitrectomy (ROP stage 4A, 4B, 5), as it might result in keratopathy (11–19%), cataract (8–29%), strabismus (21–29%) or severe hyperopia (0–53%) [11]. One should bear in mind that the onset of ocular complications is caused not only by the choice of the treatment approach but also by the clinical condition of the premature infant (including Hbd at premature delivery), ROP stage, and concomitant diseases [12].

In this article, the authors present a 3-year-old child with severe and very rare complications following ROP stage $^4/_5$ treatment, including 2 laser photocoagulation procedures, and vitrectomy. This case report is unique and one of a kind among other publications found on PubMed or Google Scholar (2014–2022), as it presents the severe and unexpected complications after vitrectomy procedure with ROP, such as hernias of the ciliary body, and hernia of the iris due to secondary glaucoma. It refers to the complications following the last resort treatment approach, as well as the consequence of the disease itself.

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CASE REPORT

A premature male newborn in breech position with nuchal cord was spontaneously delivered (vaginal delivery) at 26th week by a 30-year-old woman with gestational diabetes G1 and premature rupture of membranes. The infant's birth weight was 920 g (Apgar 1, 3, 3). The delivery period was complicated by asphyxia and lung failure associated with pneumonia, dyspnoea, intraventricular hemorrhage, periventricular leucomalacia, and necrotizing enterocolitis. The infant required cardiopulmonary resuscitation, synchronized intermittent mandatory ventilation and continuous positive airway pressure for 54 days after birth, eventually leading to chronic lung disease. The newborn underwent 8 blood transfusions due to severe anemia. There were no hepatitis B virus or cytomegalovirus (CMV) infections. Intrauterine infection was detected in the form of positive smears from all available natural orifices. The anal swab was positive for *Escherichia coli* extended-spectrum beta-lactamases (ESBL), *Enterobacter cloace* ESBL, *Klebsiella oxytoca* ESBL and tracheal aspirate was positive for *Serratia fonticola* ESBL. The blood cultures derived from umbilical vein and central venous catheter were negative. The samples derived from saliva, urine, and spinal fluid were negative as well.

A 4 months of age, the infant was diagnosed with cholestasis and given appropriate treatment. Differential diagnoses included alfa-1-antitrypsine deficiency, tyrosinemia, other metabolic diseases, sub adrenal insufficiency, urinary tract infections, malabsorptions syndrome, parasitic diseases, gastrointestinal diseases, and toxoplasmosis, other, rubella, CMV, herpes infections. All of them were ruled out. At 8 months, the baby suffered from hepatic failure, eventually leading to intracranial hemorrhage. This was the rationale for performing frontal craniotomy, followed by the evacuation of the hemorrhage. It was not until then that the baby was diagnosed with impaired psycho-motor development, psychomotor development disorder, visual analyser disorder, microcephaly, and low muscle tone.

At the age of 2, the diagnoses of West syndrome and cerebral palsy manifested with left hemiparesis were confirmed. Because of the episodes of epilepsy the boy was treated with intravenous immunotherapy. There was a suspicion of familial intrahepatic cholestasis. He also underwent multiple surgeries such as small bowel resection, endoscopic cholangiopancreatography and 2 bilateral inguinal hernia surgeries. Vitamin A and E levels were within a normal range. Coagulation did not reveal any abnormalities. The low levels of vitamin D and K were supplemented orally (vitamin A: 528.2 ng/mL, vitamin E: 0.5 ug/mL, 25-vitamin D: 10.2 ng/mL – deficiency).

Furthermore, the infant underwent the diode-laser photocoagulation treatment, for the 1st time as a 2-month-old (34 Hbd) baby and for the 2nd time 3 weeks later (37 Hbd) due to ROP (ROP 3 and a plus sign). Despite the 2 photocoagulation procedures, ROP stage 4/5 in the right eye (without plus) and stage 4 (with evidence of plus) in the left eye were diagnosed which required surgical posterior vitrectomy with lensectomy with final injection of sodium hyaluronate to the vitreous chamber, to the right and the left eye respectively in 4th month of its life (Fig. 1, 2). After the aforementioned procedures, the ophthalmic examination revealed pupil sphincter tear, postoperative cavities of the iris with aphakic eye, shallow anterior chamber (Fig. 3) and increased intraocular pressure (up to 50 mmHg), with cloudy cornea and grey reflex of eye fundus, confirmed as complete retinal detachment in ultrasonography (USG) – Figure 4. Furthermore, peripheral corneal lesions with haze and thinning of their thickness were observed in both eyes. Softening and corneal malacia was also noted. They were accompanied by severe ciliary hyperemia in the form of a dark-red dilated vascular network lying around the corneal rim and neovascularization. Localised hernias of the ciliary body (which subsequently underwent epithelialization) and a hyphema were reported at 10 o'clock and 12 o'clock in the left eye (at slerocorneal junction). The colliquative necrosis of the peripheral part of the cornea was suspected (it made it impossible to examine the eye fundus of the right eye).

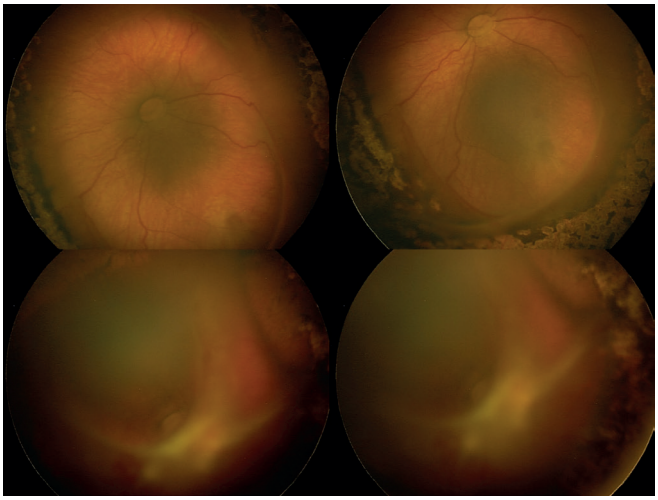

FIGURE 1. Eye fundus following the 2 retinal photocoagulation procedures (the right and the left eye)

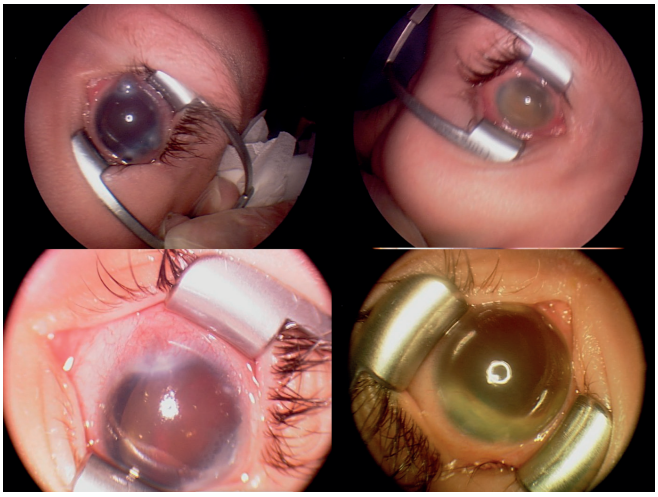

FIGURE 2. Image of the anterior eye segment after vitrectomy. Visible are numerous hernias of the cornea and ciliary body, corneal haze, and the peripheral and paracentral part of the corneal softening

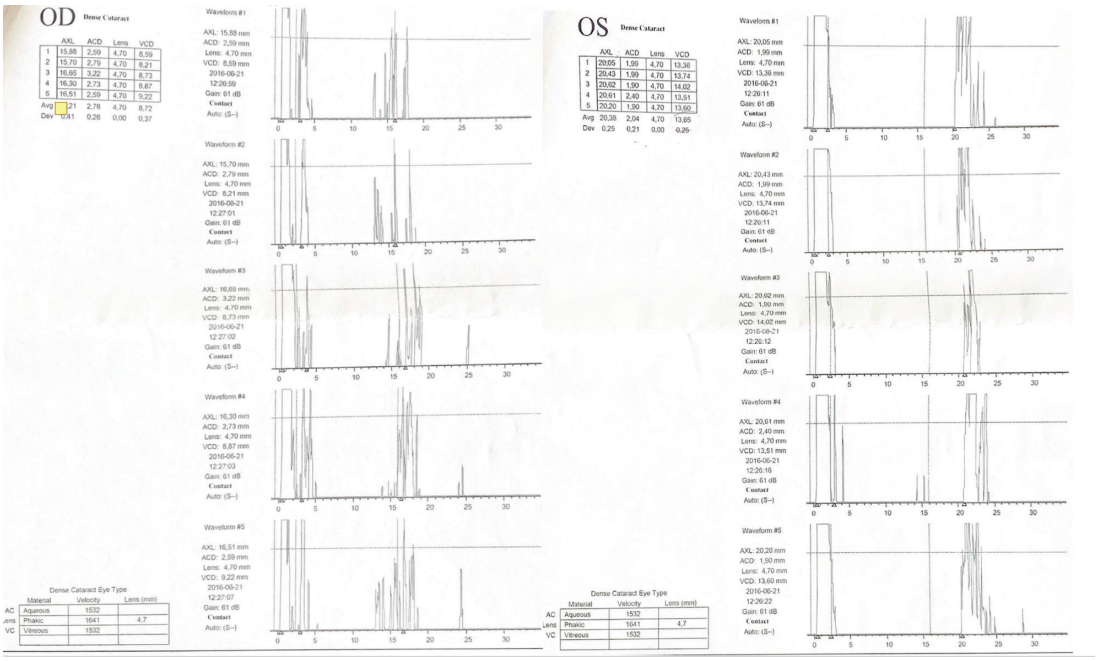

FIGURE 3. Measurement of the axial length of the right and left eyeballs

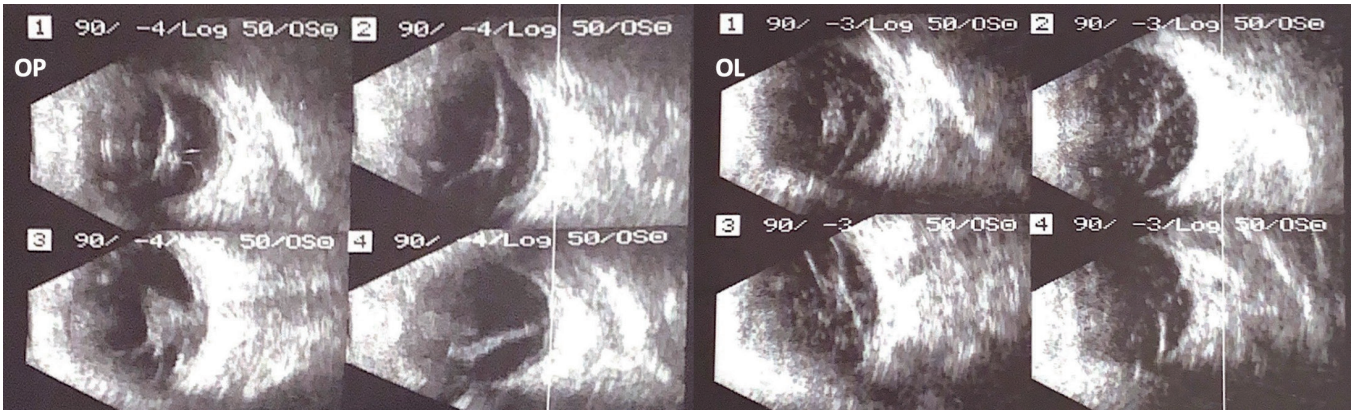

FIGURE 4. Retinal detachment with secondary proliferations in vitreus in USGB examination

The secondary glaucoma was treated with drugs reducing elevated intraocular pressure (dorzolamide, tymolol, latanoprost), which also lead to a decrease of the ciliary body hernias in the left eye. Eventually, the intraocular pressure was stabilized at 17.2 mmHg. The child developed horizontal nystagmus, strabismus, amblyopia, and hyperopia in the operated left eye (right eye: +1.5/–2.0 D and left eye: +20/–3.0 D), which underwent correction. At the age of 2 years, the child underwent an assessment of the functional function of the optic nerve and visual evoked responses (VER) test, which showed residual P 1,2,3 waves in the right eye and preserved P1 and P3 waves with a residual P2 wave in the eye left (Fig. 5).

DISCUSSION

Retinopathy of prematurity is the most common cause of vision loss in children, defined as vision <1.3 according to logMAR scale (3/60 according to Snellen tables) according to the World Health Organization [13]. According to the latest Polish guidelines concerning ROP, the treatment of choice is diode or ion laser photocoagulation, as well as anti-VEGF injections, depending on the examined retinal condition and the severity of the disease, whilst the detachment of the retina should be treated with vitrectomy [14].

In 2014–2017, the best available treatment method for ROP was laser therapy. It was performed twice in our patient because of the severity of ROP and the treatment resistance. The complications of the applied therapies are consistent with the reports from the literature, including: corneal opacity, strabismus, iris atrophy, refractive abnormalities and iris synechia (caused by the inflammation associated with laser treatment or inadvertent damage caused by laser photocoagulation), cataract, hyphema, vitreous hemorrhage, glaucoma, progression of tractional retinal detachment, retinal tears (as a result of the excessive laser energy or traction), macular edema, retinal detachment, retinal vessel occlusion, decreased night and color vision, decreased contrast sensitivity, visual field constriction, anterior ischemic syndrome, and phthisis [8, 15]. The prevalence of the most common complications is presented in Table 1.

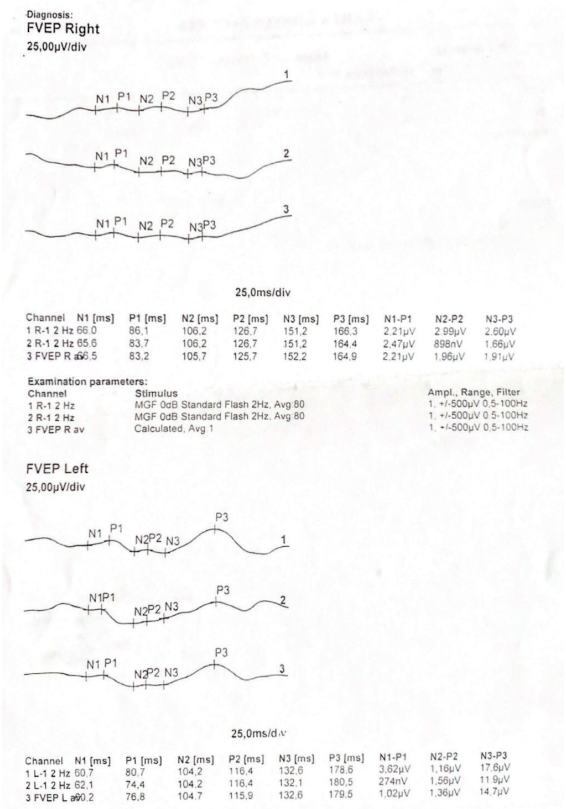

FIGURE 5. Electrophysiological examination – flash visual evoked potentials test

TABLE 1. Complications of laser photocoagulation treatment

Complications	Prevalence (%)
Strabismus operation	16.1
Retinal detachment	5.0
Macular dragging	4.3
Pale disc without known neurological defects	3.1
Glaucoma	1.2
Cataract	0.6
Vitreous hemorrhage	0.6

In their study, Morrison et al. conclude that the most frequent complication of laser therapy was hyphema (1.6%), and keratopathy (0.6%) – ASF [9], whereas Kang et al. find that retinal detachment comprises 5.0% of the reported complications [10]. The aforementioned manifestations were present in the medical history of our patient, and the retinal detachment required the vitreoretinal surgery. Probably, positive bacterial cultures for anal swab (*Escherichia coli* ESBL, *Enterobacter cloacae* ESBL, *Klebsiella oxytoca* ESBL) and tracheal aspirate (*Serratia fonticola* ESBL) during hospitalization could cause a severe course of ROP as well as complicated outcomes for surgical treatment. The vitrectomy is the last resort therapeutic treatment approach for ROP stage 4A, 4B, 5, when other therapeutic approach are unsuccessful, and the progression of the disease does inevitably lead to blindness. It is, however, not a perfect option, as it might be complicated by keratopathy (11–19%), cataract (8–29%), strabismus (21–29%), severe hyperopia (0–53%) or the cloudy cornea (ROP 4A – 11% vs. ROP 5 – 19%), which was concluded in the study of Karacorlu et al. [11]. Surgical procedures, especially in the group of low-weight premature infants, should be performed with great caution due to the easy damage to the eye structures during surgical maneuvers increased by the eye ischemia syndrome that accompanies large surgical procedures.

Among the aforementioned problems, cornea-related complications are especially significant. In our patient, the corneal malacia (progressive decay of stroma of cornea) and keratopathy. Malacia is caused by the progression go the ulcer and frequently leads to permanent lost of vision. In the presented patient, it was probably triggered by the intraocular vitrectomy. The malacia following the cataract removal (the child had the lens removed), as a result of residual parts of the lens left in the anterior chamber, persistent corneal edema or longterm administration of non-steroidal anti-inflammatory drugs (NSAIDs) after the surgery [16, 17]. Among other causes increasing the chances of the malacia, are infections (particularly *Pseudomonas aeruginosa*), autoimmune inflammations, corneal injuries, chemical burn, and iatrogenic injuries [17, 18, 19, 20].

The available literature contains only 1 article concerning 4 clinical cases (of 110 eyes treated for ROP) of pars plana vitrectomy complicated by an infective (mainly coagulase-negative *Staphylococci* and *Stenotrophamonas*) corneal ulcer has been published. It was established that such complication is present more frequently after vitrectomy (33.3%) when compared to laser therapy (4.08%) whilst the cloudy cornea was observed in 10–90% among the pediatric patients undergoing the treatment [21].

The other potential causes may include avitaminosis (vitamin A and vitamin B12 deficiency), medications (steroids, NSAIDs, local anesthetics), or inflammation of the anterior layer of the eye [22]. Zhang et al. demonstrated that vitamin A deficiency might lead to the cloudy cornea and eventually, complete blindness [23]. Wadhwani and Singh reported the 2 cases of newborns who developed keratomalacia and the consecutive lost of vision [24]. The therapeutic options include intensive hydration of the cornea with substances without preservatives. Nevertheless, the additional measures involve the closure of the lacrimal puncture, bandage contact lenses, tarsorrhaphy, autologous plasma eye drops and systemic tetracycline antibiotics. If the disease progresses despite the use of medical treatment, the use of amnion or keratoplasty might be indispensable.

The hernia of the iris is a condition in which the iris trespasses the wound area. It can be a result of the injury or perforation of the corneal ulcer. The intraoperative floppy iris syndrome (IFIS) might lead to the development of hernia following the surgery of the cataract or trabeculectomy. The mechanism behind this complication is associated with the use of adrenergic antagonists, even after discontinuation before the surgical procedure. Severe IFIS is most effectively managed with iris retractors, hooks, or expanders [25].

The peripheral hernia of the iris with preserved anterior eye chamber can be managed with the administration of

acetylcholine into the anterior eye chamber with the simultaneous subtle pressure exerted on the iris. The central hernia of the iris is treated with epinephrine and viscoelastic material into the anterior eye chamber, that can lead to the repositioning of the retina due to the mechanical force. If the necrosis of the trapped part of the iris occurs (usually after 24–26 h), it should be subsequently removed at the level of the corneal surface. The postoperative wound should be managed propylene suture 10-0, cyanoacrylate glue, and bandage contact lenses. In more severe cases the amnion or the corneal transplant should be sutured. Glaucoma affects some patients with ROP and it may be a detrimental effect of immature anterior chamber development, the treatment for ROP or ROP itself. Lenis et al. published a case of glaucoma secondary to the diode laser therapy of ROP. The authors confirmed the elevated intraocular pressure as well as an attenuated anterior chamber [26], as was the case in our patient. In their research, Celik et al. compared the general ophthalmic parameters between children treated with laser therapy and children qualified for the conservative treatment – the results indicated that the prevalence of an attenuated anterior chamber was comparable in both groups [27].

CONCLUSIONS

This case report is an example of the severe ophthalmic complications following the treatment of advanced ROP by vitrectomy. Autoimmune diseases, avitaminosis, the inflammatory of the cornea (of no iatrogenic etiology) and viral or bacterial infections were excluded. Nevertheless, positive bacterial cultures from natural body orifices obtained in routine examinations during hospitalization could cause a severe course of ROP as well as complicated outcomes of surgical treatment. Vitrectomy is the last treatment option for ROP grade 4A, 4B, 5. Due to severe damage to the eye structures that can occur after surgical vitrectomy in premature babies, this technique should only be used only by experienced vitrectomists and with great caution, especially in children with very low birth weight.

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