A Review of Intravitreal Treatment Alternatives Used as an Adjunctive Therapy in Coats' Disease

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AIM: To review the intravitreal treatment alternatives used as an adjunctive therapy in Coats’ disease.

METHODS: A comprehensive literature search in the databases of Pubmed and Cochrane Library was conducted in July 2015 to obtain all manuscripts related to Coats’ disease and intravitreal treatment. Results: Among 71 search results, 34 relevant studies, predominately in the form of case reports and small case series were included. These were evaluated in detail and summarized in this report.

CONCLUSIONS: There is a growing body of literature on the use of intravitreal agents as an adjunctive treatment for Coats’ disease. However, there is still open questions, particularly regarding the drug choice and long-term safety. Coming years will ascertain the place of intravitreal pharmacotherapy, which may find a niche in the treatment armamentarium of Coats’ disease.

Key words: Bevacizumab; Coats’ disease; Dexamethasone implant; Laser photocoagulation; Ozurdex; Pegaptanib; Ranibizumab


INTRODUCTION

Coats’ disease was first described in 1908 by George Coats as a retinal vascular disorder characterized by retinal telangiectasia and severe intraretinal and subretinal exudation[1]. It mainly affects young male individuals during the childhood and presents mostly unilateral. However, Coats’ disease can also present in adults and bilaterally[2]. Its prevalence is estimated as <1:100.000[3].

The pathogenesis of Coats’ disease is still somewhat unclear. Black et al[4], suggested that Coats’ telangiectasia could be secondary to somatic mutation in the NDP gene, which results in the deficiency of Norrin within the developing retina. A vessel malformation and breakdown of the blood-retinal barrier at the endothelial level are thought to be the main pathological process of Coats’ disease. Weakening of the vessel wall structure leads to the formation of telangiectasia and aneurysms, peripheral capillary dropout, progressive intraretinal and/or subretinal exudation and retinal detachment[5]. In recent years angiogenic cytokines such as vascular endothelial growth factor (VEGF), were also investigated in Coats’ disease.

CLINICAL FEATURES, DIAGNOSIS AND CLASSIFICATION

The most common presenting signs and symptoms are leukocoria, strabismus and decreased vision[6]. Sometimes asymptomatic children are recognized during routine ophthalmoscopy. In the early phase, the anterior segment is usually inconspicuous. Ciliary injection, corneal edema, ruberosis iridis can only be seen in advanced disease due to retinal detachment and neovascular glaucoma. Typical funduscopic
findings of Coats’ disease are retinal vascular changes such as telangiectasia, microaneurysms, calibre variations, tortuosity and intraretinal and/or subretinal exudates (Figure 1a and b). Progressive subretinal exudation can lead to a total retinal detachment and several related complications[7].

In the majority of cases it is possible to establish the diagnosis with the clinical examination alone. Fluorescein angiography (FA) is an important diagnostic tool, which can demonstrate the vascular abnormalities, breakdown of the inner blood-retinal barrier and capillary dropout. Imaging modalities, like ultrasound, computerized tomography and magnetic resonance imaging, can be helpful in the differential diagnosis in difficult cases[9].

Shields et al[8] have classified the Coats’ disease into 5 stages as follows: only retinal telangiectasia in stage 1; telangiectasia and exudation in stage 2 (2A:extrafoveal exudation; 2B:foveal exudation); exudative retinal detachment (RD) in stage 3 (3A:subtotal RD; 3B:total RD); total RD with glaucoma in stage 4; and advanced end-stage disease defined as stage 5. This classification seems to be helpful for the therapeutic management and for prediction of prognosis.

**TREATMENT**

There are several treatment modalities for the Coats’ disease, depending on the disease stage during the initial presentation. The primary objective is to obliterate the abnormal vasculature and eradicate the nonperfused retinal areas. This management aims at reducing the exudation and capillary dropout and thereby preserving the vision (Figure 2 a, b, c, d).

Shields et al[8] proposed a stepwise therapy approach according to their classification:

- Patients in stage 1 can be followed conservatively or abnormal vessels can be treated by photoocoagulation.
- Stage 2 disease should be managed with cryo- and/or laser ablation depending on the severity and localisation.
- Cryoablation is preferable in stage 3 if the detachment is shallow. Surgical reattachment may be required if the retina is bullously detached.
- In stage 4, eyes are with ocular pain due to glaucoma and enucleation can be required.
- In Stage 5, eyes are generally blind but comfortable and don’t require aggressive treatment.

In the last decade, intravitreal pharmacotheraphy played an important role in ophthalmic practice. Vascular endothelial growth factor inhibitors and corticosteroids are established treatment options in many retinal vascular diseases, like diabetic retinopathy and retinal vein occlusion.

On the other hand, retinopathy of prematurity (ROP) is the most common retinal vascular disorder in childhood. And especially in this field, VEGF inhibitors have come widespread in use[11, 12]. However, there are significant concerns regarding their long-term safety[13, 14].

This study reviews the therapeutic value of intravitreal agents used as an adjunctive therapeutic option in Coats’ disease.

**VEGF Inhibitors (Bevacizumab, Ranibizumab, Pegaptanib, Afibercept)**

Vascular endothelial growth factor is one of the most important intraocular angiogenic cytokines, which influences the vascular permeability[15]. Markedly elevated VEGF levels were measured in Coats’ disease. He et al[16], analysed the VEGF levels from subretinal fluid in patients with Coats’ disease and compared it with the eyes with rhegmatogenous retinal detachment. Mean intraocular VEGF level in eyes with Coats’ disease was 2,394.5 pg/mL, compared to 15.3 pg/mL in eyes with rhegmatogenous retinal detachment. In one of these cases with stage 2B Coats’ disease intravitreal bevacizumab was administered, which provided a significant reduction in macular edema and VEGF level, while visual acuity was also improved. Kase et al[17] analyzed VEGF and VEGF-receptor (VEGFR) expression in enucleated eyes with Coats’ disease. They found a significant immunoreactivity for VEGF and VEGFR-2 in macrophages and endothelia of abnormal vessels, where VEGFR-1 and VEGFR-3 were not expressed. A relatively larger and controlled study by Zhao et al[18] also revealed a correlation between VEGF level in aqueous humour and disease severity.

A few anecdotal case reports showed some promising clinical results with the use of anti-VEGFs, Sun et al[19], reported of a 2-year-old boy with stage 4 Coats’ disease, who had undergone an unsuccessful scleral buckle surgery with cryotherapy. A dramatic response was obtained after two intravitreal pegaptanib injections. The pre-treatment VEGF concentration in aqueous humour was 908 pg/ml and reduced to 167 pg/mL after the treatment. Kaul et al[20], reported a similar good outcome with pegaptanib as an adjunctive treatment after laser photocoagulation and cryotherapy in a 16-year-old girl.

**Figure 1** a: Color fundus photography of a 20-year-old male patient with Coats’ disease in stage 2B (right eye), showing the retinal telangiectasia (blue arrow) and yellow subretinal exudates (green arrow). b: Oblique Axial OCT-image showing the severe serous retinal detachment and irregular hyperreflectivity corresponding to subretinal exudates (white arrows).

**Figure 2** a: Pretreatment color fundus picture of a 35-year-old male, who was treated with a single session of laser photococoagulation. Teleangectasia, sausage-like calibre variations, subretinal yellow exudations are seen. b: Fundus fluorescein angiography, showing the lightbulb hyperfluorescence and large areas of retinal nonperfusion. c and d: Posttreatment appearance; occluded teleangectasia, scattered laser scars and partial resorption of subretinal exudates.
The most commonly used VEGF inhibitor in Coats’ disease is bevacizumab, a whole VEGF antibody. Table 1 gives a summary of the previous publications on bevacizumab and ranibizumab in Coats’ disease. In a recent retrospective case series by Villegas et al.[21], treatment outcomes of 24 children with Coats’ disease were discussed. All 24 children received intravitreal bevacizumab injections (mean 4.6; range 2-9 number) and laser treatment (mean 7.4; range 3-15 sessions) during a mean follow-up of 22.4 months. With a relatively standardized treatment protocol they achieved a complete resolution of exudative retinal detachment with anatomic improvement in all 24 children. No case of neovascular glaucoma was noted and thereby no enucleation was required. Unfortunately, the clinical staging and functional outcomes were not given in this work. Ray et al.[22], reviewed the clinical course of their treated children with Coats’ disease over the last decade. Ten patients who received adjunctive intravitreal bevacizumab were compared with 10 severity-matched patients treated only with ablative therapy. All patients in the bevacizumab group were successfully treated, while the ablative therapy failed in two patients of the control group and even one of these required enucleation. Zheng et al.[23], reported the treatment outcomes of 14 paediatric and five adult patients with Coats’ disease. Most of them were in stage 3A and 3B. All patients were initially treated with a single dose of intravitreal bevacizumab. Follow-up treatments, such as laser photocoagulation, cryotherapy, surgery, and reinjection of bevacizumab, were performed as needed. After a follow-up of at least 6 months, all of the paediatric patients showed a resolution of subretinal fluid and exudation, and regression of the telangectasia. No patient experienced an ocular or systemic adverse event attributable to the intravitreal bevacizumab administration. Fibrotic vitreoretinal changes were present in two adult patients at the initial presentation even before the intravitreal treatment. Increase in tractional forces was observed following the intravitreal anti-VEGF injections in other retinal vascular diseases.[24-26]. Jonas et al.[26] suggested that this is probably related to the involution of neovascular tissue due to rapid decrease of VEGF levels. After evaluating their data, Ramasubramanian and Shields[27] suggested to be prudent in the use of bevacizumab in patients with Coats’ disease. Their retrospective case series comprised of 8 children, who were treated with adjunctive intravitreal bevacizumab in addition to cryotherapy (n=8; 100%) and laser photocoagulation (n=4; 50%). They observed vitreoretinal fibrosis in the 4 patients (50%), which was not present initially. To the best of our knowledge this is the only paper reporting a high rate of vitreoretinal fibrosis in eyes with Coats’ disease. It should be taken into account that all patients in this series were treated with at least one cryotherapy session. Thereby, the role of intravitreal anti-VEGF causing an increase in the traction seems to be still somewhat uncertain. Experience with ranibizumab is limited in Coats’ disease when compared to bevacizumab (Table1). In the largest published case series, Gaillard et al[28] treated 9 patients with severe Coats’ disease in stage 3B (5 eyes) and stage 4 (4 eyes) with adjunctive intravitreal ranibizumab in addition to conventional ablative therapy. They observed a progressive retinal reattachment in all cases on an average of 2 months after the injection, which facilitated further treatments, like cryotherapy and laser photocoagulation. In two third of these patients a single intravitreal ranibizumab injection was sufficient (mean: 1.77 inj.; range: 1-4). Despite the relatively advanced presenting stage, anatomical success could be achieved in 8 of 9 patients, showing a similar positive effect as bevacizumab without any systemic adverse event. These eyes developed no late recurrence during a mean follow-up of 50 months. The temporary effect of VEGF inhibitors should be considered, too. Several studies demonstrated later ROP recurrences, treated with intravitreal VEGF antibodies alone, compared to conventional laser therapy in ROP.[29,30]. Unlike ROP, ablative treatments cannot be waived in Coats’ disease. Nevertheless it remains uncertain, whether VEGF antibodies can induce late recurrences in Coats’ disease, because the present comparative studies did not focus on this aspect. However it should be taken into account and experience should be expanded, accordingly.

Aflibercept, a recombinant fusion protein with a VEGF-binding portion, has prevailed in treatment of retinal diseases.[31]. To the best of our knowledge, there are currently no published reports on the use of aflibercept in children, neither with Coats’ disease, nor with ROP. In a preclinical study by Tokunaga et al[32], aflibercept was used in a mouse model of oxygen-induced retinopathy. They found that Aflibercept is effective at regressing neovascularization, but they observed increased areas of avascular retina and corresponding decreased electrotoretinographic amplitudes. Today aflibercept remains to be studied carefully as an appropriate anti-VEGF agent, before of clinical application in children.

**CORTICOSTEROIDS (TRIAMCINOLONE ACETONIDE, DEXAMETHASONE IMPLANT)**

Corticosteroids influence the vascular permeability with their anti-inflammatory properties. By downregulation of local cytokines and chemokines they can fix the permeability of the outer blood-retinal barrier and promote the resorption of exudation. Thereby they found a niche in the treatment armamentarium of retinal vascular diseases.[32,33].

Triamcinolone acetonide was the first corticosteroid used intravitreally in Coats’ disease. Bergstrom et al[34], treated 5 children with Coats’ disease in stage 3A and 3B with an initial 4mg intravitreal Triamcinolone (IVTA) injection and ablative cryotherapy 4 weeks to 4 month after injection. The success in reduction of subretinal fluid was overshadowed by the high rates of intraocular pressure rise (4/5; 80%) and cataract formation (3/5; 60%). Three patients subsequently developed inoperable rhegmatogenous retinal detachments with severe proliferative vitreoretinopathy. Finally, only one of the five patients had a reattached retina without a dense cataract and with a post treatment visual acuity of 1/200.

On the contrary to this report, Othman et al[35] achieved significant visual improvement in 14 of 15 cases with stage 3 Coats’ disease, who were treated with intravitreal triamcinolone in combination with other treatment modalities, such as laser photocoagulation and/or cryotherapy. Nevertheless cataract developed in 5 patients aged between 1 and 4 years. However the follow-up was only 12 months in 4 children, which was relatively short to determine the final outcome.

A different approach, regarding the use of IVTA, was described by Ghazi et al[36]. They suggested IVTA as a single alternative to surgical drainage, rather than an adjuvant treatment option. In their case series comprised of 4 children with Coats’ disease in stage 3-4, they report an almost total resolution of subretinal fluid with a single IVTA injection. No comments were made about complications, perhaps due to the short follow-up.

Previous reports on the management of Coats’ disease with adjunctive IVTA seems to be associated with fast resorption of subretinal fluid, so that the retina is more accessible to further ablative treatments. Unfortunately, the high risk of cataract and glaucoma should be the mishaps and long-term follow-up of these patients is mandatory.
Table 1: Examples of drugs incorporated in SLN or NLC, used lipid, surfactant and preparation method.

<table>
<thead>
<tr>
<th>Bevacizumab</th>
<th>Author / Year</th>
<th>Study design</th>
<th>Number of eyes</th>
<th>Mean age</th>
<th>Disease stage</th>
<th>Number of IVI</th>
<th>Intervention</th>
<th>Anatomic success</th>
<th>Functional results (BCVA)</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venkatesh et al [45] (2008)</td>
<td>Case series</td>
<td>2</td>
<td>15 years</td>
<td>2/2</td>
<td>1/1</td>
<td>IV Bevacizumab + Laser photocoagulation (after 6 weeks)</td>
<td>Stabilization of the disease</td>
<td>HM; 20/800</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Alvarex-Rivera et al [46] (2008)</td>
<td>Case report</td>
<td>1</td>
<td>10 years</td>
<td>2</td>
<td>1</td>
<td>IV Bevacizumab alone</td>
<td>Reduction of subretinal fluid and redistribution of the exudates</td>
<td>CF at 1m</td>
<td>n.a.</td>
<td></td>
</tr>
<tr>
<td>Entecart et al [47] (2009)</td>
<td>Case report</td>
<td>1</td>
<td>13 years</td>
<td>2</td>
<td>3</td>
<td>3 consecutive IV Bevacizumab inj. with 6-weeks interval</td>
<td>Significant reduction of macular edema and exudation, partial regression of peripheral vascular lesions</td>
<td>20/20</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Kaul et al [20] (2010)</td>
<td>Case series</td>
<td>2</td>
<td>7; 2 years</td>
<td>3B; 3B</td>
<td>1;1</td>
<td>1) SRF drainage + SF6 injection + IV Bevacizumab 2) External needle drainage of the SRF and laser photocoagulation followed by injection of SF6 and intravitreal bevacizumab</td>
<td>1) Reattachment of the retina and reduction of telangiectasia and exudation 2) Marked improvement in the retinal exudation and telangiectasia with reattachment of the posterior pole</td>
<td>CF at 2m</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Zhao et al [18] (2010)</td>
<td>Case report</td>
<td>1</td>
<td>3 years</td>
<td>3B</td>
<td>4</td>
<td>IV Bevacizumab alone</td>
<td>Anatomical success with decrease of subretinal exudates and fluid</td>
<td>20/125</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Ramsabramanian et al [27] (2011)</td>
<td>Case series</td>
<td>8</td>
<td>88 months</td>
<td>1-5</td>
<td>1-4</td>
<td>IV Bevacizumab (%100; n=8) + cryotherapy (%100; n=8) + laser (%50; n=4)</td>
<td>Resolution of retinopathy (n=8, 100%), Resolution of retinal exudation (n=6, 75%), Vitreous fibrosis (n=4, 50%)</td>
<td>n.a.</td>
<td>n.a.</td>
<td></td>
</tr>
<tr>
<td>Ray et al [22] (2012)</td>
<td>Case series</td>
<td>10</td>
<td>15.4 months</td>
<td>n.a.</td>
<td>1-3</td>
<td>IV Bevacizumab + cryotherapy (n=9) + laser (n=4)</td>
<td>Resolved exudative detachment in all cases (n:10)</td>
<td>n.a.</td>
<td>15.4</td>
<td></td>
</tr>
<tr>
<td>Lin et al [48] (2013)</td>
<td>Case series</td>
<td>6</td>
<td>7 years</td>
<td>2B-3B</td>
<td>1-4</td>
<td>IV Bevacizumab monthly until the SRF completely resolved + Laser/ cryotherapy</td>
<td>Resolution of subretinal exudation (5/6)</td>
<td>LP - 0.8</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Raoof et al [49] (2013)</td>
<td>Case report</td>
<td>1</td>
<td>34 years</td>
<td>2A</td>
<td>2</td>
<td>IV Bevacizumab + Pascal laser photocoagulation</td>
<td>Complete regression</td>
<td>1.2</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Zhang et al [23] (2013)</td>
<td>Case series</td>
<td>14 children, 5 adults</td>
<td>6-9 years (children), 33.6 years (adults)</td>
<td>2-3B</td>
<td>1-5</td>
<td>Initial IV Bevacizumab + Laser photocoagulation (n=24)</td>
<td>Resolution of SRF and exudation, and regression of the telangiectasia (n=19)</td>
<td>Significant improvement in children</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Villegas et al [21] (2014)</td>
<td>Case series</td>
<td>24</td>
<td>62 months</td>
<td>n.a.</td>
<td>4-6</td>
<td>IV Bevacizumab + laser photocoagulation (in all cases)</td>
<td>Resolution of exudative retinal detachment, ablation of vascular telangiectasia, and anatomic improvement of the retina (n=24)</td>
<td>n.a.</td>
<td>22.4</td>
<td></td>
</tr>
<tr>
<td>Kodama et al [50] (2014)</td>
<td>Case series</td>
<td>2</td>
<td>13 years</td>
<td>3A, 3A</td>
<td>1.1</td>
<td>Initial laser photocoagulation, IV Bevacizumab + laser during recurrence</td>
<td>Resolution of serous retinal detachment</td>
<td>1.0 and 0.7</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Fiorentezis et al [51] (2015)</td>
<td>Case report</td>
<td>1</td>
<td>22 months</td>
<td>3A</td>
<td>6</td>
<td>IV Bevacizumab + cryotherapy + laser</td>
<td>Retinal reattachment, resolution of subretinal exudates</td>
<td>0.8</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Ranibizumab</td>
<td>Gaillard et al [28] (2014)</td>
<td>Case series</td>
<td>9</td>
<td>13 months</td>
<td>3B-4</td>
<td>1-4</td>
<td>IV Ranibizumab + laser + cryotherapy</td>
<td>Globe survival with anatomical success in 8 of the 9 eyes</td>
<td>no LP – 0.063</td>
<td>50</td>
</tr>
<tr>
<td>Lin et al [48] (2013)</td>
<td>Case report</td>
<td>1</td>
<td>9 years</td>
<td>2B</td>
<td>4</td>
<td>4x IV Ranibizumab, 1x IV Bevacizumab, 1x cryotherapy, 7x laser</td>
<td>Retinal reattachment, resolution of subretinal exudates</td>
<td>0.8</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Teh et al [32] (2014)</td>
<td>Case report</td>
<td>1</td>
<td>20 years</td>
<td>2B</td>
<td>1</td>
<td>3x IV Ranibizumab + 1x cryotherapy + 1x laser</td>
<td>Reduction in telangiectatic vessels and resorption of intra retinal and subretinal exudates</td>
<td>0.1</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

IV: intravitreal; n.a.: not available; LP: light perception; CF: counting finger; IVI: intravitreal injection; SRF: subretinal fluid; *Combination treatments with different medications were excluded.
Table 2 Summary of reports on intravitreal triamcinolone and Ozurdex in Coats’ disease.

<table>
<thead>
<tr>
<th>Author / Study Type</th>
<th>Disease Stage</th>
<th>Mean Age</th>
<th>Number of Patients</th>
<th>Number of Interventions</th>
<th>Adverse Events</th>
<th>Functional Outcome</th>
<th>Follow-up (months)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bergstrom et al.[36]</td>
<td>3B</td>
<td>6.4 years</td>
<td>5</td>
<td>2</td>
<td>None</td>
<td>NLP-1/200</td>
<td>12.6</td>
<td>Almost total resolution of SRF within 4 weeks</td>
</tr>
<tr>
<td>Ghazi et al.[38]</td>
<td>3B-4</td>
<td>3.25 years</td>
<td>4</td>
<td>3</td>
<td>None</td>
<td>N.a.</td>
<td>34</td>
<td>No short term complications</td>
</tr>
<tr>
<td>Kimura et al.[53]</td>
<td>3A</td>
<td>7 years</td>
<td>1</td>
<td>3</td>
<td>IOP increase (1/15; %7); cataract formation in 1 case</td>
<td>34</td>
<td>Transient pressure rise</td>
<td>12</td>
</tr>
<tr>
<td>Othman et al.[37]</td>
<td>3A, 3B</td>
<td>32 years</td>
<td>1</td>
<td>1</td>
<td>Cataract (3/5; 60%)</td>
<td>34</td>
<td>Transient pressure rise</td>
<td>12</td>
</tr>
<tr>
<td>Ozurdex implant</td>
<td>3A</td>
<td>7 years</td>
<td>1</td>
<td>1</td>
<td>No ocular complications</td>
<td>34</td>
<td>No ocular complications</td>
<td>12</td>
</tr>
<tr>
<td>Saatci et al.[43]</td>
<td>3A</td>
<td>7 years</td>
<td>1</td>
<td>1</td>
<td>Cataract (3/5; 60%)</td>
<td>34</td>
<td>No ocular complications</td>
<td>12</td>
</tr>
<tr>
<td>Martinez-Castillo et al.[44]</td>
<td>3A, 3B</td>
<td>7 years</td>
<td>1</td>
<td>1</td>
<td>No ocular complications</td>
<td>34</td>
<td>No ocular complications</td>
<td>12</td>
</tr>
</tbody>
</table>

Ozurdex (Allergan Inc., Irvine, CA, USA) is a biodegradable dexamethasone sustained-release intravitreal implant delivering 0.7 mg of potent preservative-free dexamethasone directly within the vitreous cavity. It is approved by the FDA for the use of macular edema associated with retinal vein occlusion, noninfectious posterior uveitis and diabetic maculopathy.[34,35,39] Because of its anti-inflammatory properties with a favourable side-effect, it became an important treatment option also in childhood eye diseases.[40,41]

Lei et Lam[42], reviewed their treatment outcomes of 4 paediatric patients with macular edema, including a 4-year-old boy with Coats’ disease. He was previously treated unsuccessfully with multiple laser sessions and repeated intravitreal bevacizumab injections. After three Ozurdex implantations the macular edema decreased and visual acuity slightly improved. During the follow-up of 65 months a significant lens opacification was observed. Intraocular pressure increased only after repeated implantations, which could be satisfactorily managed with topical IOP-lowering agents.

Martinez-Castillo et al.[44], treated a patient with Coats’ disease in adulthood, initially with Ozurdex implant and observed in already 1 week a complete resolution of the exudative retinal detachment, allowing further laser photocoagulation. One year after the Ozurdex implantation the patient gained a favourable visual outcome of 20/25, without any ocular complications.

Previously, we described two children with Coats’ disease in stage 3A, where we used Ozurdex in addition to laser photocoagulation.[43] The first case, a 12-year-old boy was initially treated with 5 monthly ranibizumab injections in addition to two photocoagulation sessions. As subretinal exudation remained almost the same, we administered a single Ozurdex implantation, which contributed to resolution of the exudation. The second case was managed with indirect laser photocoagulation and a simultaneous intravitreal 0.7-mg dexamethasone implant injection. Macular exudates gradually resolved and visual acuity increased. In both cases a slight intraocular pressure rise was noted which was successfully managed with an antiglaucomatous medication. In view of these case reports, the Ozurdex implant seems to be an effective adjuvant treatment option, which can facilitate an effective ablative treatment, tighten the abnormal vessel structure and provide an acceleration of subretinal fluid resorption (Figure 3). As like with other corticosteroids, caution is advised regarding the potential risk for cataract development and intraocular pressure rise especially in young ages. The main benefit of this implant is that it requires fewer interventions in comparison to...
VEGF antibodies and requires less general anaesthesia in paediatric age. A summary of published case reports about steroids in Coats’ disease is given in table 2.

To our best knowledge; two other sustained-release fluorocinolone acetoneide devices namely Retisert (Bausch & Lomb, Rochester, NY, USA), and Iluvien (Alimera Science, Alpharetta, GA, USA) have not been administered in Coats disease so far.

CONCLUSION

Depending upon the clinical stage, several treatment modalities can be employed in patients with Coats’ disease. The hallmark of the therapy is the ablative treatment techniques (photocoagulation and cryotherapy) wherever appropriate. On the other hand, intravitreal pharmacotherapy can be used as an adjunctive treatment to ablation in order to achieve faster resolution and better visual outcome. Initially, VEGF inhibitors would likely be preferred to steroids, because of unfavourable local adverse effects, like cataract or glaucoma.

Coming years will ascertain the place of intravitreal pharmacotherapy in Coats’ disease.

CONFLICT OF INTERESTS

The authors have no conflicts of interest to declare.

REFERENCES