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Case Report

Novel Surgical Treatment of an Intraretinal Juxtapapillary Hemangioblastoma Using Intraocular Diathermy Forceps: A Case Report

Koen A. van Overdam[a, b] Anass Hajjaj[c] Lisette M. Smid[b] Emine Kiliç[c] Jan H. de Jong[a]

[a]The Rotterdam Eye Hospital, Rotterdam, The Netherlands; [b]Rotterdam Ophthalmic Institute, Rotterdam, The Netherlands; [c]Department of Ophthalmology, Erasmus Medical Centre, Rotterdam, The Netherlands

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Novel surgical treatment · Juxtapapillary retinal hemangioblastoma · Sessile growth pattern · Von Hippel-Lindau disease · Intraocular diathermy forceps · Case report

Abstract
The surgical treatment of intraretinal juxtapapillary retinal hemangioblastomas (JRHs) was previously contraindicated because of the significant risk of collateral damage to the macula and optic nerve. This case report discusses the effectiveness and safety of a novel surgical technique using intraocular bipolar diathermy forceps to coagulate feeder and draining blood vessels of an intraretinal JRH. The patient suffered from bilateral retinal hemangioblastomas with loss of visual function in one eye and the development of an intraretinal JRH in the other eye. Despite intensive treatment with intravitreal bevacizumab and subconjunctival triamcinolone acetonide, growth of the intraretinal JRH continued, macular exudation worsened, and visual acuity decreased. Surgical treatment was undertaken in which, first, the feeder and draining vessels of the JRH were identified by comparing the retinal imaging of the JRH with the imaging before the emergence of the JRH 4 years earlier. Then, retinal incisions were made above the blood vessels and parallel to the nerve fibers during a pars plana vitrectomy. Lastly, these vessels were lifted above the retinal surface and coagulated using intraocular diathermy forceps. Postoperatively, macular edema reduced, and visual acuity increased and remained stable for about 6 months. Using intraocular diathermy forceps, this case report demonstrates effective and safe intraretinal JRH blood vessel coagulation above the retinal surface. This novel surgical approach was able to

Correspondence to:
Koen A. van Overdam, k.vanoverdam@oogziekenhuis.nl

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delay the deterioration of visual acuity due to tumor growth and exudation in this patient. This suggests that coagulation with intraocular diathermy forceps can be considered an additional surgical treatment option for JRHs, especially those with an intraretinal growth pattern.

Introduction

Retinal hemangioblastomas are benign vascular tumors, which may occur isolated but are mostly present in association with von Hippel-Lindau (VHL) disease. Retinal hemangioblastomas are usually progressive, and without treatment, exudation, and vitreous traction will lead to vision loss [1]. Peripheral retinal hemangioblastomas (PRHs) can be treated with various treatment modalities, resulting in an overall eradication rate of 87% of cases [2]. Juxtapapillary retinal hemangioblastomas (JRHs), which represent 15% of cases, are more difficult to treat than PRHs since they are close to vulnerable and vital structures. Three distinct growth patterns of JRHs have been described: endophytic, sessile, and exophytic, representing the depth localization in the superficial, middle, and outer layers of the retina, respectively. Current treatment options for JRHs are limited to anti-vascular endothelial growth factor (anti-VEGF), corticosteroids, photodynamic therapy (PDT), and vitreoretinal surgery, with varying degrees of success depending on the characteristics of the JRH [1, 3].

Surgical feeder and draining vessel ligation and/or tumor removal have only been reported in the literature for PRHs [4] and JRHs with an endophytic, superficial growth pattern [1, 3, 5–7]. Novel techniques are needed for the surgical treatment of JRHs located in the deeper layers of the retina. Interruption of the efferent and afferent blood vessels using diathermy could be an effective option. However, with the conventional point-shaped intraocular diathermy probe, coagulation and compression are only possible from one side of the blood vessel, which increases the need for high energy levels and the risk of substantial collateral damage and insufficient closure leading to incomplete tumor destruction and higher risk of intra- and postoperative hemorrhage in case subsequent tumor excision is performed [4]. Previously, we developed intraocular bipolar diathermy forceps, which can apply mechanical compression and coagulation of the blood vessel from two sides between the forceps' jaws, exerting minimal pressure on the underlying tissue and requiring less coagulation energy leading to less collateral damage [8, 9].

The intraocular diathermy forceps have been used to treat diabetic tractional retinal detachment to prevent vitreous hemorrhage after tractional membrane removal [9]. These diathermy forceps are not commercially available; they were developed by modifying a single-use 23-gauge ILM-peeling forceps (Vitreq, Vierpolders, the Netherlands). The emitting electrode was connected to one half of the core and the return electrode to the other half, with one jaw of the forceps attached to each half of the core and both halves electrically insulated from each other and from the shaft that enclosed them [8]. In this case report, we aim to discuss the effectiveness and safety of a novel surgical technique in a patient with JRH with a sessile growth pattern, using further developed intraocular bipolar diathermy forceps whose jaws, apart from the gripping areas, were also insulated.

Case Report

In 2016, a 46-year-old woman with VHL disease was referred to our institution because of multiple large PRHs in all quadrants with tractional and exudative retinal detachment in the superior quadrants in the right eye. Despite laser- and cryotherapy, the visual acuity of the left

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eye has been completely compromised since 1994 due to a tractional and exudative retinal detachment caused by multiple PRHs. At presentation at the Rotterdam Eye Hospital, the visual acuity of the right eye was 1.0 decimal (Snellen). Previous treatment of the right eye included laser photocoagulation and cryotherapy of the PRHs in 1994 and laser photocoagulation in 2014. Figure 1 gives an overview of treatments performed for the patient's right eye in the Rotterdam Eye Hospital (Fig. 1, upper part) and the treatment outcome from May 2016 to September 2021 (Fig. 1, lower part).

A vitrectomy with silicone oil tamponade was performed in July 2016, including posterior vitreous detachment induction, vitreous base shaving, and removal of the tractional membranes. Triamcinolone acetonide (Kenacort-A; Bristol-Myers Squibb, New York, NY, USA), with a concentration of 20 mg/mL after removal of the preservatives from the suspension and dilution with BSS, was used for vitreous visualization at the vitreous base and for detection of vitreoschisis-induced vitreous cortex remnants (VCR) posterior to the vitreous base. VCR were present over the entire retinal surface and only removed from the superior quadrants and the macula, together with the tractional membranes and macular internal limiting membrane. After 2 months, all PRHs were excised during a second surgery with silicone tamponade and laser photocoagulation at the vitreous base and around the excision sites. At the end of each surgery, intravitreal bevacizumab (1.25 mg/0.05 mL; Avastin, Roche Pharma AG, Grenzach-Wyhlen, Germany) and subconjunctival triamcinolone acetonide were administered. There were no intra- and postoperative complications associated with these treatments.

A third surgery was planned 2 months later for silicone oil removal. However, a newly formed juxtapapillary retinal hemangioma (JRH) was discovered just before the third surgery. Visual acuity had decreased to 0.6 decimal, mostly due to macular edema leaking from the JRH. A sessile growth pattern (i.e., in the middle layers of the retina) was demonstrated with optical coherence tomography angiography [10]. The tumor was located in the papillomacular bundle; hence, laser photocoagulation and PDT were considered inappropriate treatment modalities. Also, surgical coagulation, ligation, or excision during the third surgery were deemed to cause unacceptable collateral damage to the retinal tissues. Therefore, after silicone oil removal, the patient was repeatedly treated with intravitreal bevacizumab and subconjunctival triamcinolone acetonide at an interval of approximately 2 months.

In 2017, new PRHs developed in the temporal inferior quadrant and later in the nasal inferior quadrant, which could not be effectively treated with laser photocoagulation. Consequently, tumor growth continued, and tractional membranes formed, requiring additional surgery. At the end of 2017, vitrectomy with tumor excision, membrane peeling, and silicone oil tamponade were performed, followed by silicone oil removal 3 months later. In the meantime, the JRH grew slowly despite the treatment with bevacizumab and triamcinolone acetonide. Therefore, during additional surgeries in 2018, two attempts were made to coagulate the JRH feeder vessel with conventional diathermy probes, but the depth of the vessel and the use of low energy to limit collateral damage made effective blood vessel compression and coagulation impossible. In 2019 and 2020, three sessions of laser photocoagulation of new PRHs in the superior temporal quadrant were performed. Meanwhile, the growth of the JRH continued.

Novel Surgical Technique with Intraocular Diathermy Forceps

Despite all treatment efforts, macular edema returned, and visual acuity slowly declined to 0.15 decimal in mid-2020. Because of tumor growth, exudation, and bleeding, in September 2020, a new surgical technique was applied by the first author, in which intraocular bipolar diathermy forceps were used to coagulate feeder (Fig. 2a–f) and draining vessels (Fig. 2g–l) above the retinal surface (see also the online suppl. Video; for all online suppl. material, see https://doi.org/10.1159/000530687). These blood vessels were chosen by comparing fundus

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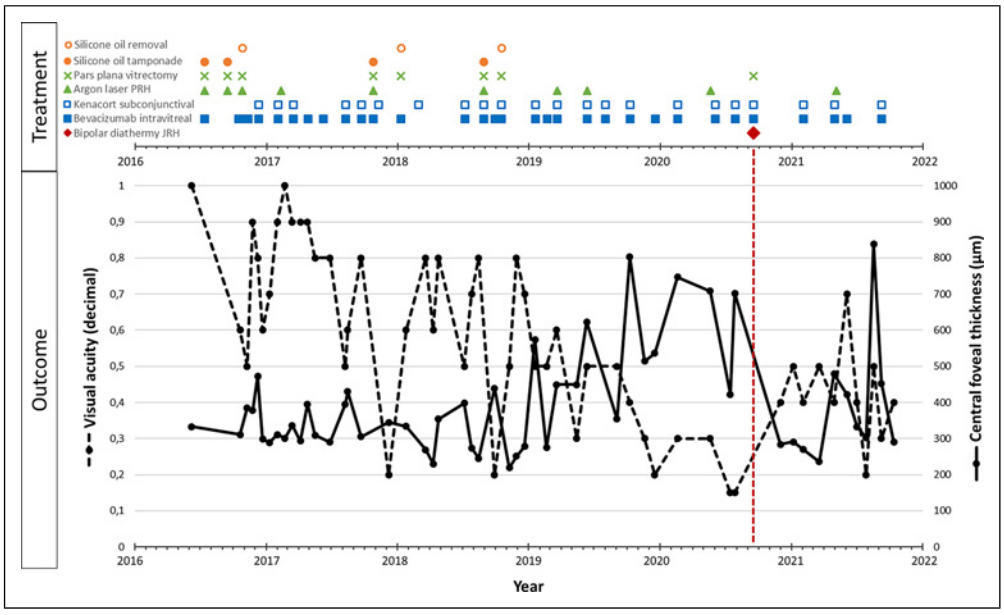

Fig. 1. Overview of treatment (upper part) and outcome of treatment (lower part) of the peripheral retinal hemangioblastoma (PRH) and juxtapapillary retinal hemangioblastoma (JRH) between 2016 and 2022. As the outcome of treatment, the course of best corrected visual acuity (black dashed line) and central foveal thickness (black solid line) pre- and postoperatively are presented. The red dotted line indicates the timepoint of application of the novel surgical technique in which intraocular bipolar diathermy of the feeder and draining vessel of the JRH was performed.

examination and fluorescence angiography imaging of 4 years and 2 months before surgery (Fig. 3a, b). A newly formed feeder vessel and draining vessel were identified and elected for coagulation (Fig. 2a, g). During a 23-gauge pars plana vitrectomy, retinal incisions were made just above and as deep as the feeder and draining vessel using a bent stiletto tip (Fig. 2b, h). Care was taken to incise parallel to blood vessels and nerve fibers, to limit collateral damage to the surrounding tissues. Using the same bent stiletto tip, the blood vessel was hooked up and pulled above the retinal surface (Fig. 2c, i). Then, the intraocular bipolar diathermy forceps were used to grab, compress, and coagulate the blood vessel above the retinal surface (see Fig. 2d–f, J–l). Both the feeder and draining vessels were successfully closed by this approach. Intravitreal bevacizumab and subconjunctival triamcinolone acetonide were administered at the end of the surgery. The procedure was completed with an air tamponade.

Postoperative Course with 12-Month Follow-Up

Postoperatively, the tumor flattened and turned pale, indicating reduced perfusion. Visual acuity increased to 0.4 decimal 3 months after surgery and to 0.5 decimal 4 months postoperatively (Fig. 1, lower part). The macular hemorrhage and exudation resolved during this period, and central foveal thickness decreased from 702 µm 2 months preoperatively to 284 µm 2 months postoperatively. However, 5 months after surgery, some cystoid macular edema returned, and visual acuity was reduced to 0.4 decimal. Therefore, intravitreal bevacizumab was readministered and repeated 7, 9, and 12 months postoperatively. In addition, subconjunctival triamcinolone acetonide was administered 5, 7, and 12 months postoperatively. At 6 months, visual acuity was 0.5 decimal, and at 12 months postoperatively, visual acuity remained stable at 0.4 decimal, despite the appearance of new blood vessels in the area of the treated JRH and the inferior edge of the optic disc. An increased thickness of a vein

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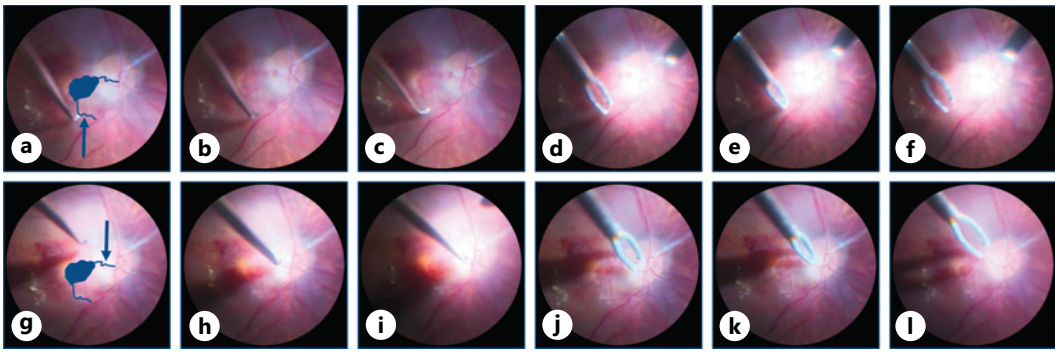

Fig. 2. Video still images illustrating the different steps of the novel surgical technique for feeder vessel (**a**–**f**) and draining vessel (**g**–**l**) coagulation of a sessile juxtapapillary retinal hemangioblastoma (JRH). Identification of the blood vessels (**a**, **g**); retinal incision above, parallel to, and as deep as the blood vessels using a bent 23-gauge stiletto tip (**b**, **h**); blood vessels pulled up just above the retinal surface with the bent stiletto tip (**c**, **i**); blood vessels visible between the open jaws of the diathermy forceps (**d**, **j**); blood vessels compressed and coagulated with closed forceps jaws above the retinal surface (**e**, **k**); closed blood vessel with limited visible retinal collateral damage after coagulation using the 23-gauge intraocular diathermy forceps (**f**, **l**).

inferior to the JRH was noticed, which now seemed to function as the main draining vessel (Fig. 3f). Therefore, the administration of intravitreal bevacizumab and subconjunctival triamcinolone acetonide was repeated. No microperimetry was performed pre- and post-operatively. However, the patient indicated that she experienced some improvement rather than deterioration in her central visual field after the surgery.

Discussion

This case report demonstrates the effective and safe coagulation of feeder and draining blood vessels of an intraretinal JRH, resulting in a delay of visual acuity deterioration due to tumor growth and exudation in this patient. Currently, the treatment of juxtapapillary hemangioblastoma is challenging. Vitreoretinal surgery is only considered when the JRH causes symptoms, develops vitreoretinal complications like epiretinal membrane and retinal detachment, or has an endophytic growth pattern [1, 3, 5–7]. Excision of these tumors or ligation of the feeder vessels is not possible without causing significant collateral damage to the retina in the papillomacular bundle or the optic nerve. Therefore, especially in cases of JRHs with sessile or exophytic growth patterns, alternative treatment options are primarily needed. Watchful waiting can be considered if the JRH is small and not symptomatic because JRH may remain stable for longer periods of time compared to extrapapillary lesions, and spontaneous regression has been reported [11–13]. For small, symptomatic lesions without vitreoretinal complications, injections with anti-vascular growth factors are advised. Elevated ocular VEGF levels have been measured in VHL patients with retinal hemangioblastomas [14, 15]. Anti-VEGF treatment reduces the permeability of retinal hemangioblastoma and thereby reducing exudation, and may also inhibit the development of new hemangiomas [1, 16, 17]. However, exudation returns after cessation of anti-VEGF treatment, requiring repeated injections. Besides, when macular edema is severe, a combination with subconjunctival corticosteroid injections may be more effective [18]. The case currently reported demonstrates that intraocular anti-VEGF injections combined with subconjunctival corticosteroids were not sufficient to prevent the growth of the JRH and loss of visual acuity [10].

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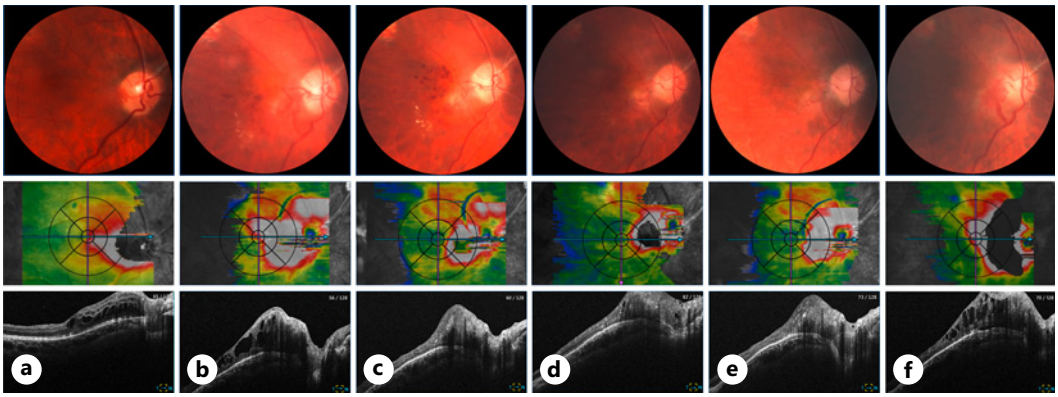

Fig. 3. Pre- and postoperative fundus photography (upper row), optical coherence tomography (OCT) thickness map (middle row), and OCT cross-section of the juxtapapillary hemangioblastoma (JRH). **a** 4 years preoperatively: decimal visual acuity (VA) 1.0, early stage juxtapapillary hemangioblastoma (JRH) with cystoid macular edema (CME) requiring regular treatment with intravitreal bevacizumab and subconjunctival triamcinolone acetonide. **b** 2 months preoperatively: VA was reduced to 0.15 with a larger JRH; some retinal hemorrhages, exudates, and more CME were retreated with bevacizumab and triamcinolone acetonide. **c** 1 month preoperatively: VA was 0.15 with less CME, more retinal hemorrhages and exudates, after which it was decided to perform the novel surgical technique. Briefly, intraocular bipolar diathermy forceps were used to grab, compress, and coagulate the feeding and draining blood vessels of the JRH during this surgery. **d** 3 months postoperatively: VA was 0.4 with much fewer retinal hemorrhages, exudates, and a whitish lesion, indicating reduced to no perfusion. **e** 6 months postoperatively: VA was 0.5 with no CME, retinal hemorrhage, and exudates 4 weeks after restarting bevacizumab and triamcinolone acetonide for CME reappearance. **f** 12 months postoperatively: VA was 0.4 with a new JRH temporal superior and a larger new or reperfused JRH temporal of the optic disc with increased CME and enlarged blood vessels temporal inferior of the optic disc.

For larger symptomatic lesions, intravitreal anti-VEGF injections can also be combined with PDT. PDT is a nonthermal, photobiochemical procedure causing selective vascular occlusion and tumor destruction, causing minimal damage to the adjacent optic nerve [19]. For these larger tumors, however, verteporfin may only be activated on the surface of the tumor, while the closure of deeper tumor vessels is not achieved [20]. Besides, other complications of PDT can occur, like transient optic disc edema, retinal vessel occlusion, optic neuropathy, vitreous hemorrhage, massive retinal detachment, and massive subretinal hemorrhage [21–23]. In the current case, the JRH was located in the papillomacular bundle, and therefore, PDT was not applied. Laser photocoagulation and cryotherapy carry an even higher risk of causing an arcuate scotoma if applied for JRH due to their proximity to the optic nerve and were, therefore, not considered in this case. The safety and efficacy of transpupillary thermotherapy, plaque radiotherapy, or proton beam radiotherapy are uncertain and, therefore, were not considered [2, 24]. Saitta et al. [1] proposed a decision tree for the treatment of JRHs, including vitreoretinal surgery, but admitted that current scientific evidence is insufficient to support the recommendations.

Since the introduction of minimally invasive sutureless transconjunctival pars plana vitrectomy (especially 25-gauge), no further surgical advancements have been reported in the treatment of JRHs [6, 7]. However, for JRHs with sessile or exophytic growth patterns worsening under conventional treatment modalities, new surgical approaches are warranted. Recently, we developed intraocular bipolar diathermy forceps to overcome the downsides of conventional diathermy. The effectivity of conventional diathermy is limited because coagulation and pressure on blood vessels are applied from one side only due to the point-shaped tip, requiring higher energy levels and causing more collateral damage. Besides, there is a lack

of view of the coagulated tissue unless the probe is removed [8, 9]. In our case, we demonstrated that intraocular bipolar diathermy forceps could be used effectively and safely to close feeder and draining vessels of an intraretinal JRH. The collateral damage was limited by making retinal incisions parallel to nerve fibers, bringing the blood vessel above the retinal surface, and coagulating the JRH blood vessels above the retinal surface with adequate visualization. In addition, intraocular diathermy forceps allow mechanical compression combined with coagulation from two sides of the blood vessel, reducing energy requirements [8]. The treatment resulted in reduced perfusion, a reduction of macular edema, and a significant improvement in visual acuity during the first 6 months after surgery.

A limitation of our approach may be that the identification and selection of the feeder and draining vessels can be difficult. In our case, the positive results during the first 6 months seem to indicate that the correct feeder and draining vessels were coagulated. Over the course of the next 6 months, however, another vein initially present seemed to have taken over the function of draining vessel (Fig. 3f). In the case of multiple feeder and draining vessels, some may be missed and, therefore, not treated, and tumor growth may continue. However, a cautious approach, like in our case, may be preferable because of the increased risk of iatrogenic damage when coagulating multiple vessels.

Besides missed feeder and draining vessels, ongoing production of vascular growth factors in inadequately destructed tumors may lead to the development of new feeder vessels postoperatively. An early report on transretinal feeder vessel ligature found that after ligation, two new feeder vessels grew toward the retinal hemangioblastoma [25]. VHL disease not only results in overexpression of VEGF but also of platelet-derived growth factor β (PDGFβ), transforming growth factor α (TGFα), and erythropoietin [26]. These growth factors are not specifically targeted by bevacizumab or triamcinolone. Therefore, tumor growth could continue despite combining intravitreal bevacizumab, subconjunctival triamcinolone, and surgical interventions.

Ultimately, the diathermy of the feeder vessels should be applied as early as possible. However, the identification of feeder vessels is even more challenging in the early stage of JRH. Therefore, vitrectomy with draining and feeder vessel coagulation may not be considered a standalone therapy but should be combined with intraocular anti-VEGF injections, subconjunctival corticosteroid injections, and, if possible, PDT. Other potential future treatment options include systemic sunitinib and belzutifan. In a small case series, sunitinib improved hemangioblastoma-related retinal edema in patients with VHL-related retinal hemangioblastomas but, unfortunately, did not improve their visual acuity or reduce the tumor size and resulted in serious adverse events [27]. Treatment with belzutifan resulted in an improvement of all retinal hemangioblastomas found in 16 eyes in a clinical trial treating patients with renal cell carcinoma associated with VHL disease. However, belzutifan also resulted in significant adverse events [28].

The development of the tractional membranes after insufficient additional laser photocoagulation of new PRHs may be (partly) attributed to the unremoved VCR over the retinal surface in the lower quadrants during the first surgery [29, 30]. These VCR can serve as a scaffold for proliferative vitreoretinopathy (PVR) formation, and hyalocytes (resident vitreous macrophages) present in the cortical vitreous can modulate immune and inflammatory processes, initiate intraretinal gliosis, and transdifferentiate into myofibroblasts resulting in tractional membranes [29–31]. Therefore, triamcinolone acetonide-assisted visualization and removal of VCR are important for the prevention of postoperative PVR but also of tractional membrane formation after additional laser treatment or cryotherapy for new retinal hemangioblastomas [29, 30]. Disruption of the blood-retinal barrier due to laser or cryocoagulation as well as factors released by (inadequately treated) retinal hemangioblastomas may also play a role. Furthermore, regular ophthalmic evaluations are crucial for the early detection and treatment of new tumors. Laser treatment in the early stages when they are small offers the most effective intervention and minimizes the risk of complications.

Conclusions

This case report demonstrates effective and safe intraretinal JRH blood vessel coagulation above the retinal surface using intraocular diathermy forceps. This novel approach can be considered an additional surgical treatment option for JRHs, especially those with an intraretinal growth pattern. More cases of JRH should be treated with intraocular diathermy forceps coagulation to further evaluate the effectiveness and safety of this novel surgical technique. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material.

Statement of Ethics

Ethical approval is not required for this study in accordance with local guidelines. Written informed consent was obtained from the patient for the application of the described novel surgical technique and publication of the details of the medical care and any accompanying images.

Conflict of Interest Statement

Van Overdam has a patent (EP3181080A1), and the other authors have no conflicts of interest to declare.

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Authors have no funding to declare.

Author Contributions

Koen A. van Overdam: design, data acquisition and interpretation, and manuscript drafting and editing. Anass Hajjaj, Lisette M. Smid, and Emine Kiliç: manuscript reviewing and editing. Jan H. de Jong: data acquisition and interpretation and manuscript drafting and editing.

Data Availability Statement

All data generated or analyzed during this study are included in this published article and supporting images. Further inquiries can be directed to the corresponding author.

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