

## **Efficacy and Safety Profile of Bevacizumab as Primary Treatment in Coats Disease**

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**Received:** May 14, 2018; **Published:** August 30, 2018

### **Abstract**

**Background:** Coats disease is an idiopathic retinal vascular disorder that is more commonly reported in children between 6 - 8 years old, although it can be seen on earlier ages or in adults. The purpose of this case report is to present an adult individual with late Coats disease, with typical exudative retinitis, telangiectasia and pigmentary epithelium detachment, and show the efficacy of the primary treatment with intravitreal anti-VEGF (Vascular Endothelial Growth Factor) injection associated with ablative argon laser photocoagulation.

**Case Presentation:** A male patient with 31 years old presented with complaints of low visual acuity on the left eye (20/400), whose fundus exam had retinal exudation, telangiectasia, focal fibrosis and pigmentary epithelium detachment. Four Intravitreal injection of Bevacizumab were performed along with two sessions of ablative argon laser photocoagulation on a period of four months. On the post injection course, the edema reduced rapidly, no adverse events were seen and the pigmentary epithelium detachment resolved. His visual acuity remained the same mainly because of the central subretinal fibrosis and the recently formed epiretinal membrane. However, all of the other complications of the disease, including neovascular glaucoma and phthisis bulbi were avoided.

**Conclusion:** Intravitreal injection of Anti-VEGF may be safe and effective on adults as primary treatment of the intraretinal edema and exudation in Coats Disease, associated with adjunctive ablative photocoagulation laser as needed.

**Keywords:** *Coats Disease; Intravitreal Bevacizumab; Retinal Telangiectasias; Exudative Retinal Detachment*

### **Introduction**

Coats Disease, also known as retinal telangiectasia, is an idiopathic retinal vascular disorder characterized by exudation, telangiectasia and intraretinal edema. In more advanced cases can evolve to exudative retinal detachment, secondary glaucoma and painful phthisis [1]. It is more common in males (approximately 75% of the cases) and 95% of the cases are unilateral [2]. While there are reports of the disease in adults, the vast majority is diagnosed in early ages typically from 6 to 8 years old [3,4]. There are differences in disease manifestations in adults, including limited area of involvement, slower apparent progression of disease, and hemorrhage near larger vascular dilatations [3]. Although there is no known hereditary component, there is some evidence to suggest that Coats' disease is caused by a somatic mutation of the Norrie disease protein (NDP) gene [5].

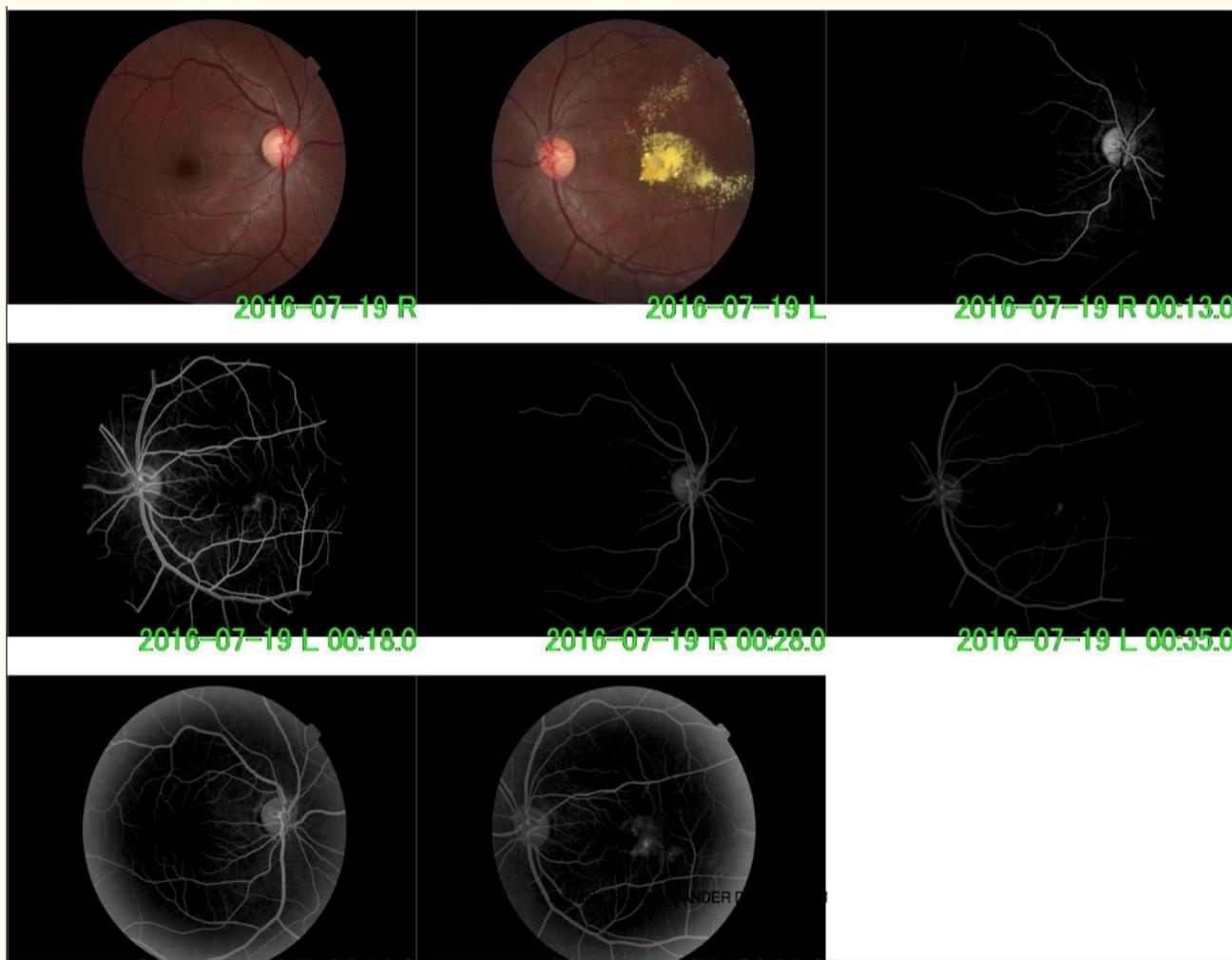
The symptoms include decreased and blurred vision, leukocoria, strabismus and floaters. The diagnosis is made with a fundoscopic exam, fundus photography and angiography to provide optimal status and localization of the vascular abnormalities.

Although not needed for diagnostic purposes, Optical Coherence Tomography (OCT) is useful for evaluation of intraretinal edema and to monitorize the response to therapy [6,7]. Treatment is made with laser ablative procedures and more recently with anti-VEGF [8,9]. In cases of retinal detachment, vitreoretinal surgery may be needed [10]. Cryotherapy has also been used in cases of extensive exudation and subtotal retinal detachment. This report describes a patient with late Coats Disease and evaluates the safety and efficacy of the primary treatment with intravitreal anti-VEGF injections of Bevacizumab.

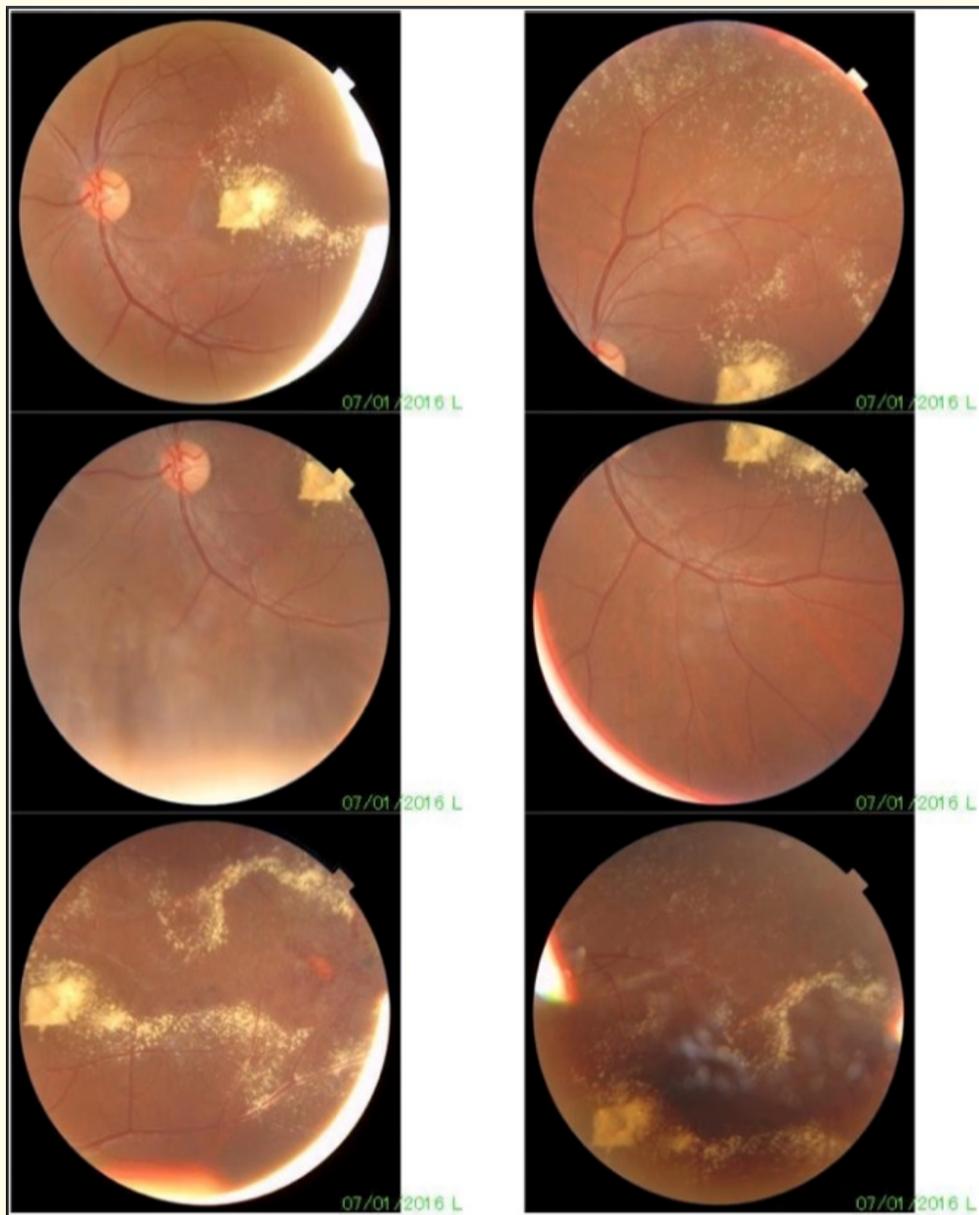
**Case Presentation**

A 31 years old patient presented with complaints of low visual acuity on the left eye, associated with floaters, which started and maintained over the past 6 months. The patient also reported that he had a recent photo taken 1 month prior to the appointment, where his left eye had a white reflex that was not seen on the contralateral eye. He did not report any other illnesses and had healthy living habits. There was no history of trauma and no cases of blindness or other ocular problems on his family. Visual acuity was 20/20 on right eye (OD) and 20/200 on left eye (OS). Nothing atypical on the slit lamp biomicroscopy examination and intraocular pressure was 16 mmHg OD and 15 mmHg OS.

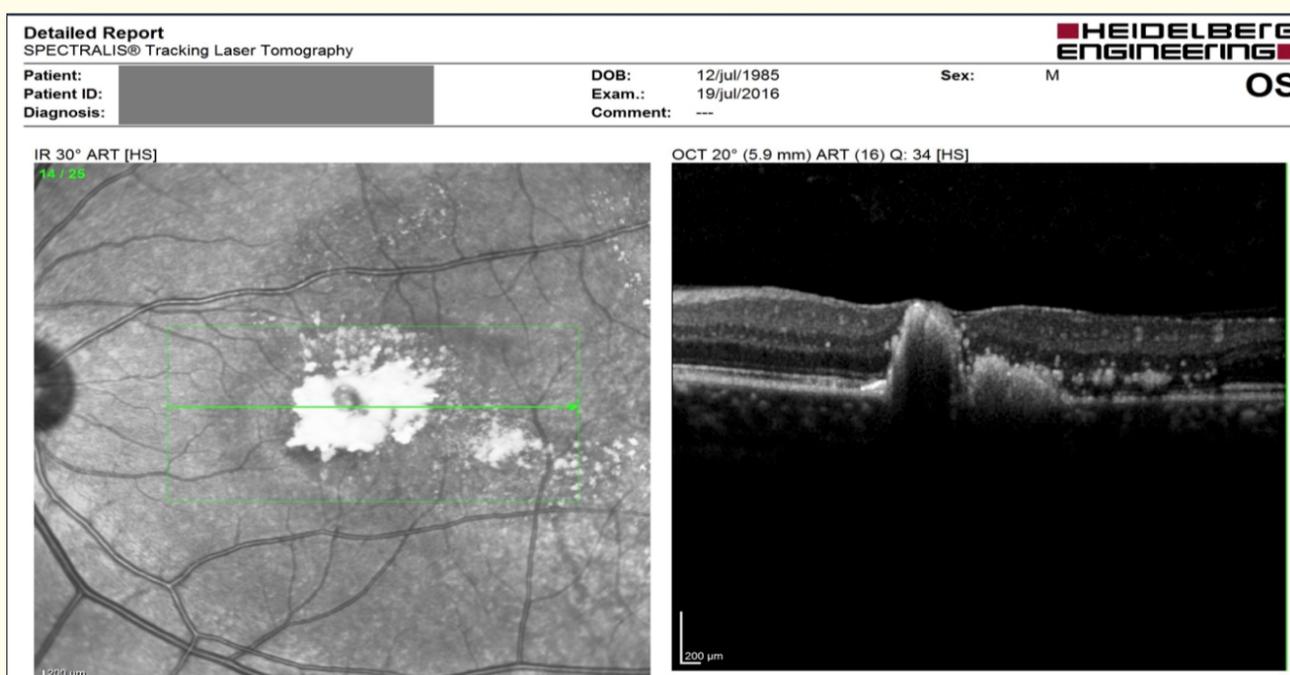
Fundus examination and angiography revealed dense and diffuse exudation, inferior temporal telangiectasia and intraretinal edema (Figure 1 and 2). Optical Coherence Tomography revealed a Pigmentary Epithelium Detachment associated with edema (Figure 3). Hemo-gram and other routine blood tests were done, showing no apparent changes.



**Figure 1:** First Fluorescein Angiography Legend: Fluorescein Angiography of the patient showing late leak and diffuse subretinal fibrosis.



**Figure 2:** First Retinography Legend: Fundus photographs showing diffuse exudation, central subretinal fibrosis, and inferior temporal telangiectasias.



**Figure 3:** OCT before treatment Legend: Horizontal Linear SD OCT scan of the left eye prior to anti VEGF treatment. Dense foveal exudation with RPE detachment in central macula.

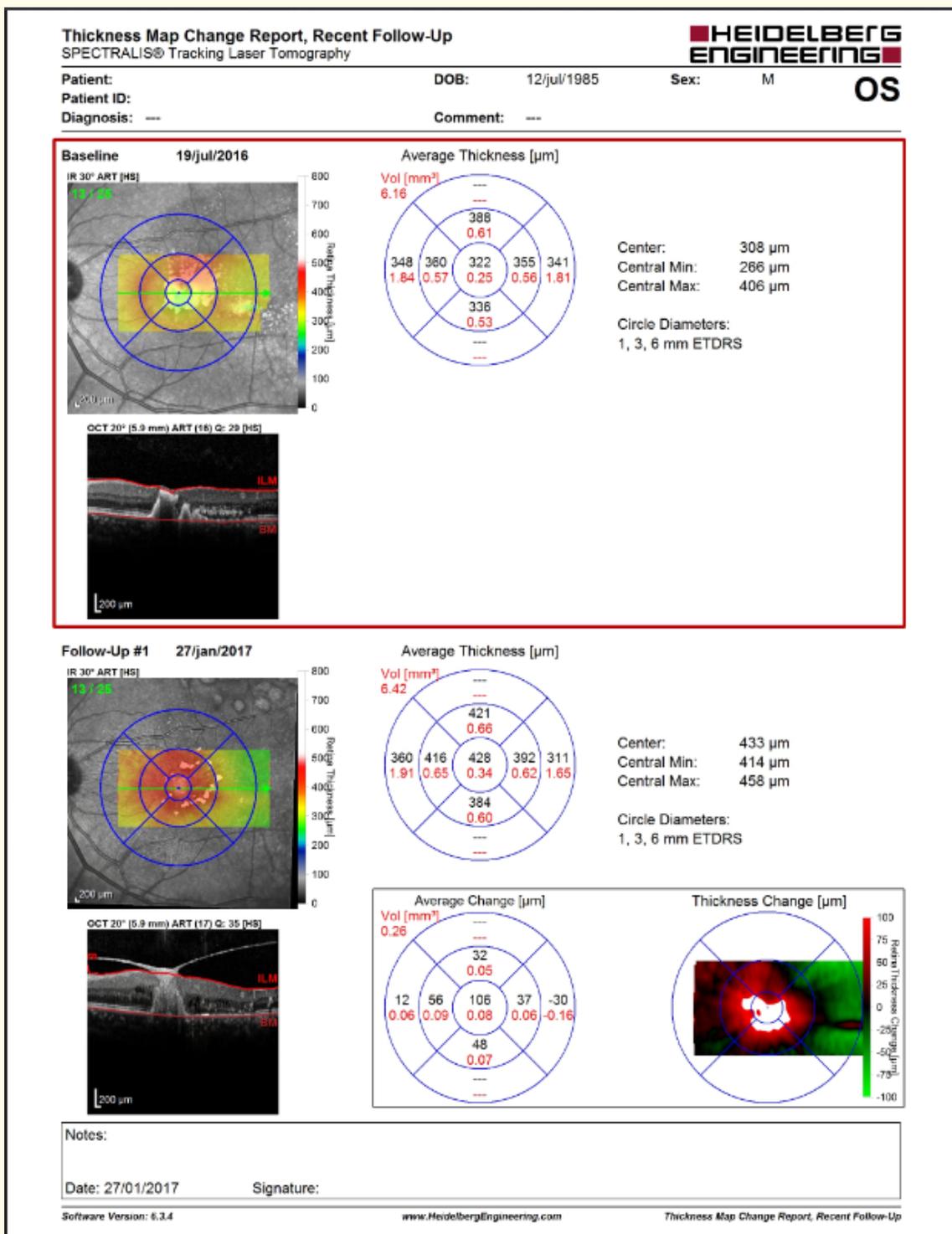
Based on the aspect of the fundus and with the exclusion of other pathologies that make differential diagnosis, the diagnosis of late Coats Disease was made.

The patient was then treated over the course of four months primarily with four intravitreal Bevacizumab injections (2.5 mg/0.1 ml) with one-month interval between them. One additional argon laser photocoagulations session was opted to be done.

The follow up was uneventful and the edema reabsorbed slowly and continually with each injection. On the third and fourth months, both the OCT and the angiography showed a drastic improvement, as the exudation and telangiectasia continued to regress. The patient evolved with an epiretinal membrane, but the choice was to not make vitreoretinal surgery (membranectomy/peeling) in this case, as the prognosis was very poor given the intense macular fibrosis (Figure 4 and 5). Best corrected visual acuity was 20/100 after the treatment. No side effects were noticed.



**Figure 4:** Angiography/retinography after treatment Legend: Improvement of the fundus after the treatment. Macular area with subretinal fibrosis, which contributed to final visual acuity.



**Figure 5:** OCT after treatment Legend: Follow up after anti VEGF treatment and laser photocoagulation. There was reduction in inner retina exudates, however a traction epiretinal membrane with increased cystoid macular edema developed. Retinal thickening and a localized sub RPE fibrosis in the foveal region prevented vision to improve significantly.

## Discussion and Conclusions

The prognosis depends on the extent of the disease. Therefore, treatment has to start as soon as the diagnosis is made. Photocoagulation reduces the exudation by thermal ablation of defective retinal vessels. Scheffler, *et al.* have shown that, even in the advanced presentation of the disease, aggressive and repetitive laser ablation therapy may help some patients retain useful vision or at least achieve globe salvage [11]. If more than 2 quadrants of the retina are involved, the efficacy of laser treatment may decrease. It is also necessary to keep close follow-up after thermal ablative therapy as additional treatment may be needed for late recurrences [2,12].

There are already several evidences indicating that treatment with intravitreal Anti-VEGF as primary treatment, or as adjunctive to therapy with ablative laser photocoagulation is valuable in both children and adults, as Coats Disease is being associated with increased intraocular VEGF level [13-17]. Recently, Yannuzzi, *et al.* reported a patient after a 7-year treatment of Coats Disease with Bevacizumab, showing reduced number of telangiectasias and aneurysms in serial Intravenous Fluorescein Angiography [18]. Zhao, *et al.* even reported a patient who had resolution of total retinal detachment with Bevacizumab [19].

However, Ramasubramanian, *et al.* published a retrospective analysis of eight patients with Coats Disease treated with Bevacizumab and adjunctive therapy with laser or cryotherapy [20]. The authors warned about the possibility of the development of vitreoretinal fibrosis and traction retinal detachment. In 2008, Venkatesh, *et al.* reported two older children (14 and 16 years of age) with Coats' disease treated with intravitreal Bevacizumab. Their conclusion was that, despite reduction of macular edema and exudation after injection, intravitreal injection alone may not be enough in some case [9]. On resistant patients, some authors suggest that adjunctive treatment with Intravitreal Triamcinolone can help in the regression of the subretinal fluid collection, particularly in cases of exudative retinal detachment and central macular edema [21-23].

Anti-VEGF, as shown in this case, is a viable option in terms of efficacy and safety on adult patients, particularly for the subretinal edema and exudation of the disease. In our patient, the option for a session of photocoagulation was done to further reduce exudation. Kam, *et al.* recently reported a case of rapid development of epiretinal membrane following intravitreal Bevacizumab in a 7-year old boy. The authors performed membrane peeling, with good outcomes [24]. In our case, we opted for not doing vitreoretinal surgery, as the prognosis was already very poor given the localized sub retinal fibrosis.

Further studies are necessary to establish the Anti-VEGF as primary treatment on Coats Disease, but our conclusion is that it lowers the number of ablative laser photocoagulation sessions necessary for each patient, as the edema and exudation regressed with the injections. Also, no collateral effects were seen in our patient, even with injections done with 1-month interval between them. Therefore, the use of Anti-VEGF agents might be a good option to treat patients with Coats Disease, if supplemented with ablative laser techniques as necessary.

## Financial Support

The authors have not received grant support or research funding for this study.

## Conflict of Interest

No conflicting relationship exists for any author.

## Bibliography

1. Cahill M., *et al.* "Classification of the spectrum of Coats' disease as subtypes of idiopathic retinal telangiectasis with exudation". *Acta Ophthalmologica Scandinavica* 79.6 (2001): 596-602.
2. Shields JA., *et al.* "Clinical variations and complications of Coats' disease in 150 cases: The 2000 Sanford Gifford Memorial Lecture". *American Journal of Ophthalmology* 131.5 (2001): 561-571.

3. Smithen LM, et al. "Coats' disease diagnosed in adulthood". *Ophthalmology* 112.6 (2005): 1072-1078.
4. Shienbaum G and Tasman WS. "Coats' disease. A lifetime disease". *Retina* 26.4 (2006): 422-424.
5. Graeme CM, et al. "Coats' Disease of the Retina (Unilateral Retinal Telangiectasis) Caused by Somatic Mutation in the NDP Gene: A Role for Norrin in Retinal Angiogenesis". *Human Molecular Genetics* 8.11 (1999): 2031-2035.
6. Kessner R, et al. "Intraretinal exudates in Coats' disease as demonstrated by spectral-domain OCT". *Case Reports in Ophthalmology* 3.1 (2012): 11-15.
7. Gupta MP, et al. "Spectral domain optical coherence tomography findings in coats disease". *Retina* (2018).
8. Jun JH, et al. "Resolution of severe macular edema in adult Coats' disease with intravitreal triamcinolone and bevacizumab injection". *Korean Journal of Ophthalmology* 22.3 (2008): 190-193.
9. Venkatesh P, et al. "Management of Coats disease with bevacizumab in 2 patients". *Canadian Journal of Ophthalmology* 43.2 (2008): 245-246.
10. Li AS, et al. "Long-Term Outcomes of Total Exudative Retinal Detachments in Stage 3B Coats Disease". *Ophthalmology* 125.6 (2018): 887-893.
11. Scheffler Amy C, et al. "Advanced Coats Disease: Management With Repetitive Aggressive Laser Ablation Therapy". *Retina* 28.3 (2008): S38-S41.
12. Nucci P, et al. "Selective photocoagulation in coats' disease: ten-year follow-up". *European Journal of Ophthalmology* 12.6 (2002): 501-505.
13. He YG, et al. "Elevated vascular endothelial growth factor level in Coats' disease and possible therapeutic role of bevacizumab". *Graefe's Archive for Clinical and Experimental Ophthalmology* 248.10 (2010): 1519-1521.
14. Sun Y, et al. "Elevated vascular endothelial growth factor levels in Coats disease: rapid response to pegaptanib sodium". *Graefe's Archive for Clinical and Experimental Ophthalmology* 245.9 (2007): 1387-1388.
15. Zhao Q, et al. "Vascular endothelial growth factor in Coats' disease". *Acta Ophthalmologica* 92.3 (2014): e225-e228.
16. Zhang L, et al. "The efficacy of conbercept or ranibizumab intravitreal injection combined with laser therapy for Coats' disease". *Graefe's Archive for Clinical and Experimental Ophthalmology* 256.7 (2018): 1339-1346.
17. Park S, et al. "Intravitreal bevacizumab injections combined with laser photocoagulation for adult-onset Coats' disease". *Graefe's Archive for Clinical and Experimental Ophthalmology* 254.8 (2016): 1511-1517.
18. Yannuzzi NA, et al. "Flourescein Angiography Versus Optical Coherence Tomography Angiography in Macular Teleangiectasia Type I Treated With Bevacizumab Therapy". *Ophthalmic Surgery, Lasers and Imaging Retina* 48.3 (2017): 263-266.
19. Zhao T, et al. "Resolution of total retinal detachment in Coats' disease with intravitreal injection of bevacizumab". *Graefe's Archive for Clinical and Experimental Ophthalmology* 249.11 (2011): 1745-1746.
20. Ramasubramanian A and Shields CL. "Bevacizumab for Coats' disease with exudative retinal detachment and risk of vitreoretinal traction". *British Journal of Ophthalmology* 96.3 (2012): 356-359.

21. Çakır M., *et al.* "Combined intravitreal bevacizumab and triamcinolone injection in a child with Coats disease". *Journal of American Association for Pediatric Ophthalmology and Strabismus* 12.3 (2008): 309-311.
22. Böhm MR and Uhlig CE. "Use of intravitreal triamcinolone and bevacizumab in Coats' disease with central macular edema". *Graefe's Archive for Clinical and Experimental Ophthalmology* 249.7 (2011): 1099-1101.
23. Ihab Saad Othman., *et al.* "Management of lipid exudates in Coats disease by adjuvant intravitreal triamcinolone: effects and complications". *British Journal of Ophthalmology* 94.5 (2010): 606-610.
24. Kam AW., *et al.* "Rapid "epiretinal membrane" development following intravitreal bevacizumab for Coats' disease". *American Journal of Ophthalmology Case Reports* 11 (2018): 75-77.

**Volume 9 Issue 9 September 2018**

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