Annals of Clinical Case Reports

Case Report
Published: 13 Mar, 2020

Macular Telangiectasia Type 2 in Association with Down Syndrome

*Rabiee B[1,2] and Fishman GA[1,2]**

[1]Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, USA

[2]The Pangere Center for Inherited Retinal Diseases, The Chicago Lighthouse, USA

Abstract

Purpose: Macular Telangiectasia (MacTel) type 2 is an idiopathic condition characterized by juxtafoveolar telangiectatic vessels, retinal crystalline deposits, right-angle venules, and intraretinal pigment plaques. The purpose of this study was to report a case of MacTel type 2 with concomitant Down syndrome, and discuss the possibility of an association between these two conditions, backed up by previous studies on the diseases metabolic abnormalities.

Observations: A 33-year-old Caucasian male with Down syndrome, who presented with increasing visual difficulty in both near and distance, underwent a complete ophthalmic examination, color fundus photography, Optical Coherence Tomography (OCT) and near-infrared fundus reflectance imaging. Prominent clinical findings suggesting IJFT included bull's eye-appearing hypopigmentary lesions in maculae, bilateral parafoveal pigment depositions, and bilateral right angle venules. Near-infrared reflectance imaging showed intraretinal telangiectasia, and OCT imaging showed bilateral disruption of the ellipsoid within the foveal region.

Conclusion and Importance: A possible explanation for an association between MacTel type 2 and Down syndrome could be underlying peripheral neuropathy and degeneration due to genetic and metabolic abnormalities, defects in the serine/glycine metabolic pathways, as well as angiogenesis regulation system. A detailed and comprehensive retinal examination of Down syndrome patients could help further investigation on a possible association between these two diseases.

Keywords: Macular telangiectasia type 2; Down syndrome; Juxtafoveal telangiectasis

OPEN ACCESS

Correspondence:
Gerald A Fishman, The Pangere Center for Inherited Retinal Diseases, The Chicago Lighthouse, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, 1850 West Roosevelt Road, Chicago, IL 60608, USA, Tel: +1-312-997-3646; E-mail: gerafish@uic.edu

Received Date: *20 Feb 2020*
Accepted Date: *09 Mar 2020*
Published Date: *13 Mar 2020*

Citation:
Rabiee B, Fishman GA. Macular Telangiectasia Type 2 in Association with Down Syndrome. Ann Clin Case Rep. 2020; 5: 1809.

ISSN: 2474-1655

Introduction

Macular telangiectasia (MacTel) type 2 is an idiopathic bilateral condition with alterations of the macular capillary network as well as neurosensory atrophy [1]. Characteristic findings include juxtafoveolar telangiectatic vessels, retinal crystalline deposits, right-angle venules, and intraretinal pigment plaques. Visual loss can often occur, and treatment is controversial.

The first description of the disease was presented by Gass et al. [2], and subsequently Gass and Boldi [3] classified this condition under idiopathic juxtafoveolar telangiectasia type 2A. During the past decade, there has been notable progress in characterizing the disease and understanding its pathophysiology. It is now assumed that MacTel type 2 is a neurodegenerative disease with vascular alterations [1]. Recent genetic studies demonstrated that MacTel type 2 is a complex disease with specific involved pathways. Significant associations were identified at three independent loci at 5q14.3, 2q34, and 1p12 [4]. The 5q14.3 locus is associated with retinal vascular diameter variations, and the 2q34 and 1p12 loci are involved in the glycine/serine metabolic pathway [4]. Further investigation of this pathway demonstrated that a mutation affecting serine metabolism could lead to a MacTel type-2 phenotype [5].

In this case report, we describe a patient with MacTel type 2 and concomitant Down syndrome.

Case Presentation

A 33-year-old Caucasian male with Down syndrome presented with increasing difficulty in his distance visual acuity for one year. He could no longer recognize faces at a distance, but had no difficulty with peripheral, color or night vision. Medical and family history was noncontributory.

Best corrected visual acuity was 20/200 OD and 20/100 OS. In the clinical examination, pupils were reactive and ocular motility was full. There was an intermittent alternating esotropia. Ocular

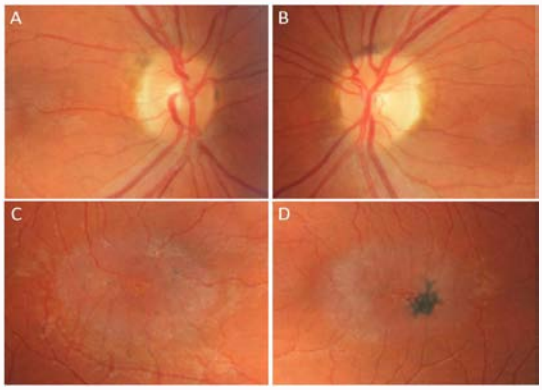

Figure 1: Color fundus images of the patient's right, A) and C) and left, B) and D) eyes showing a high number of vessels crossing the margin of the optic nerve,macular hypopigmentation and pigment clumping. Pigment depositions are visible bilaterally, most prominantly in the left eye temporal to the fovea, which is a charachteristic finding for type 2A idiopatic juxtafoveolar retinal telangiectasis.

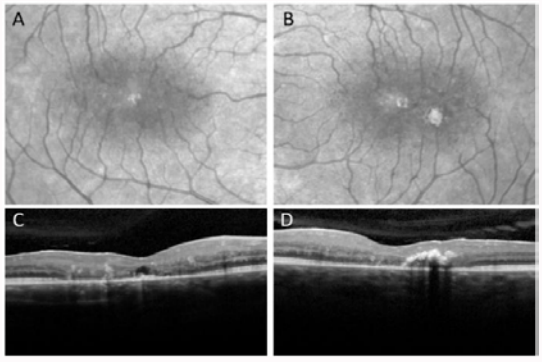

Figure 2: Near-infrared reflectance images of the patient's right, (A) and left (B) eyes showing macular intraretinal telangiectasis. Optical coherence tomograms of the right (C) and left (D) eyes showing bilateral disruption of ellipsoid, with macular thickening. Note the migration of melanin pigment into the inner retinal layers (small round infrared reflections), a specific finding for type 2A idiopathic juxtafoveolar retinal telangiectasis.

pressures where 14 OD and 15 OS. The right cornea showed inferior stain near the limbus which was not evident in the left. The anterior chambers were clear. Other findings included bilateral Brushfield spots on the iris, punctate cortical opacities both anterior and posteriorly in the lens of each eye, a mildly fibrillary vitreous, with no evidence of macular hemorrhage or exudate. A bilateral increase in vascular branches crossing the optic disc was present (Figure 1). Bull's eye-appearing hypopigmentary lesions were evident in both maculae, with bilateral temporal parafoveal pigment depositions (Figure 1). Right angle venules were noted both temporally and superiorly in each eye. Near-infrared reflectance imaging showed intraretinal telangiectasia, and OCT imaging showed disruption of the ellipsoid within the foveal region bilaterally, in addition to thickening of the macula (Figure 2). The patient's overall findings were consistent with MacTel type 2.

Discussion

Although the concurrence of MacTel type 2 and Down syndrome in this patient may be coincidental, it could suggest a previously unrecognized association between the two conditions in some patients. The presented patient interestingly has a severe phenotype despite his young age. Investigators have studied macular abnormalities in Down syndrome patients during the past decade. O'Brien et al. [6] demonstrated that the central subfield thickness for the full retina and inner and outer retinal layers were all significantly greater in the Down syndrome children compared to a control group, suggesting an abnormal macular development in children with Down syndrome. In line with this study, Mangalesh et al. [7] found abnormal foveal morphology and persistence of inner retinal layers using OCT in Down syndrome children.

Recent studies also tie Down syndrome with peripheral neuropathy and degeneration due to genetic and metabolic abnormalities [8,9]. For instance, Patel et al. [8] found that abnormal increase in a regulator of calcineurin 1 -an endogenous inhibitor of the calcineurin phosphatase that is triplicated in Down syndrome- impairs neurotrophic support of neurons by inhibiting endocytosis of the nerve growth factor receptor TrkA. Furthermore, investigators have shown metabolic abnormalities involving the serine/glycine pathway in Down syndrome patients [10,11]. Given the neurodegenerative nature of MacTel type 2 and recent discoveries regarding serine/glycine pathway abnormalities in MacTel patients, it would be of potential value to further investigate the possibility of an association between the two diseases.

A common finding in Down syndrome is a high number of vessels crossing the margin of the optic nerve [12], as seen in this case. This has been attributed to the mild systemic angiogenesis deficiency associated with Down syndrome [13]. As a result of high endostatin levels in trisomy 21, bulbous expansion of the hyaloid vessels is down regulated, causing the retinal vessels to branch closer to the optic disc center and create an abnormally crowded vascular pattern on the disc [13]. Furthermore, atrioventricular septal defects in Down syndrome has been associated with abnormalities in the Vascular Endothelial Growth Factor-A (VEGF-A) pathway [14]. This pathway is crucial in endothelial cell functions involved with angiogenesis, including proliferation, migration, survival, and new vessel formation [15]. The abnormalities in the vascular system in Down syndrome patients could partially contribute to the vascular alterations seen in MacTel type 2.

Conclusion

This manuscript highlights certain similarities between the pathophysiology in MacTel type 2 and Down syndrome. We recognize that there could be other, yet unknown pathways contributing to the pathophysiology of MacTel as well. It is notable that in early stages, the clinical findings of MacTel type 2 can are very subtle, and mild changes in the macula might not always be appreciated as possible primary changes of MacTel. A detailed and comprehensive retinal examination of Down syndrome patients could help define an association between these two diseases.

Patient Consent

Informed consent was obtained from the patient and legal guardian to publish this report. This report does not contain any personal information that could lead to the identification of the patient.

References

1. Issa PC, Gillies MC, Chew EY, Bird AC, Heeren TFC, Peto T, et al. Macular telangiectasia type 2. Prog retin eye res. 2013;34:49-77.

2. Gass J. Stereoscopic atlas of macular diseases. St. Louis ets. CV Mosby Co. 1977.

3. Gass JDM, Blodi BA. Idiopathic juxtafoveolar retinal telangiectasis: Update of classification and follow-up study. Ophthalmology. 1993;100(10):1536-46.

4. Scerri TS, Quaglieri A, Cai C, Zernant J, Matsunami N, Baird L, et al. Genome-wide analyses identify common variants associated with macular telangiectasia type 2. Nat genet. 2017;49(4):559-67.

5. Gantner ML, Eade K, Wallace M, Handzlik MK, Fallon R, Trombley J, et al. Serine and lipid metabolism in macular disease and peripheral neuropathy. N Engl J Med. 2019;381(15):1422-33.

6. O'Brien S, Wang J, Smith HA, Donaldson DL, Haider KM, Roberts GJ, et al. Macular structural characteristics in children with Down syndrome. Graefes Arch Clin Exp Ophthalmol. 2015;253(12):2317-23.

7. Mangalesh S, Vinekar A, Jayadev C, Kemmanu V, Bhat M, Sivakumar M, et al. Spectral Domain optical coherence tomography in detecting sub-clinical retinal findings in Asian Indian children with Down Syndrome. Curr Eyr Res. 2019;44(8):901-7.

8. Patel A, Yamashita N, Ascano M, Bodmer D, Boehm E, Bodkin-Clarke C, et al. RCAN1 links impaired neurotrophin trafficking to aberrant development of the sympathetic nervous system in Down syndrome. Nat Commun. 2015;6:10119.

9. Watson-Scales S, Kalmar B, Lana-Elola E, Gibbins D, La Russa F, Wiseman F, et al. Analysis of motor dysfunction in Down syndrome reveals motor neuron degeneration. PLoS genet. 2018;14(5):e1007383.

10. Orozco JS, Hertz-Picciotto I, Abbeduto L, Slupsky CM. Metabolomics analysis of children with autism, idiopathic-developmental delays and Down syndrome. Translational psychiatry. 2019;9(1)1-15.

11. Pogribna M, Melnyk S, Pogribny I, Chango A, Yi P, James SJ. Homocysteine metabolism in children with Down syndrome: *In vitro* modulation. Am J Hum Genet. 2001;69(1):88-95.

12. Williams EJ, McCormick AQ, Tischler B. Retinal vessels in Down's syndrome. Arch Ophthalmol. 1973;89(4):269-71.

13. Parsa C, Almer Z. Supranumerary optic disc vessels may indicate reduced systemic angiogenesis in Down syndrome. Br J Ophthalmol. 2008;92(3):432-3.

14. Ackerman C, Locke AE, Feingold E, Reshey B, Espana K, Thusberg J, et al. An excess of deleterious variants in VEGF-A pathway genes in Down-syndrome-associated atrioventricular septal defects. Am J Hum Genet. 2012;91(4):646-59.

15. Abhinand CS, Raju R, Soumya SJ, Arya PS, Sudhakaran PR. VEGF-A/VEGFR2 signaling network in endothelial cells relevant to angiogenesis. J Cell Commun Signal. 2016;10(4):347-54.