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Ocular Manifestations in a Patient with Collagen Type IV Alpha 1 (*COL4A1*) Mutation

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Abstract **Case Report**

A 10-days-old girl with fetal ventricular dilatation was referred for ophthalmological evaluation. Magnetic resonance imaging detected dilatation of the lateral ventricles with porencephaly and intracranial hemorrhages in the occipital lobe. Funduscopy revealed increased tortuosity of the retinal arterioles, arteriovenous anastomosis and intraretinal hemorrhage. Exome sequencing revealed a known mutation, c. 2253G>A, p. (Gly555Arg) in collagen type IV alpha 1 (*COL4A1*). During the follow-up period, posterior subcapsular cataract was progressed in the left eye. This is the youngest patient with *COL4A1* mutation documented by fundus photographs to be reported. Fundus examination was useful in visualizing retinal vascular changes in patients with *COL4A1* mutation.

Keywords: Collagen type IV alpha 1 (*COL4A1*), Retinal arteriolar tortuousity, Arteriovenous anastomosis, Intraretinal hemorrhage.

INTRODUCTION

Mutations in collagen type IV alpha 1 (*COL4A1*) have recently been identified in both a mouse model and families with porencephaly, a rare autosomal dominant condition characterized by cystic brain cavities and cerebral white-matter lesions [1-7]. *COL4A1* mutations have also been found in a single family with small-vessel disease affecting the brain and the eye [1-11]. Here, we describe a 10-days-old girl with *COL4A1* mutation.

Case Report

A 10-days-old girl with fetal ventricular dilatation was referred for ophthalmological evaluation. Magnetic resonance imaging detected dilatation of the lateral ventricles with porencephaly and intracranial hemorrhages in the occipital lobe. Funduscopy revealed increased tortuosity of the second-order retinal arterioles (white arrow), although the first-order arteries and venous system were normal appearance (Figure-1). In addition, arteriovenous anastomosis (yellow arrows) and intraretinal hemorrhage (white arrow head) were also observed. Exome sequencing revealed a known mutation, c. 2253G>A, p. (Gly555Arg) in collagen type IV alpha 1 (*COL4A1*). During the follow-up period, posterior subcapsular cataract was progressed in the left eye.

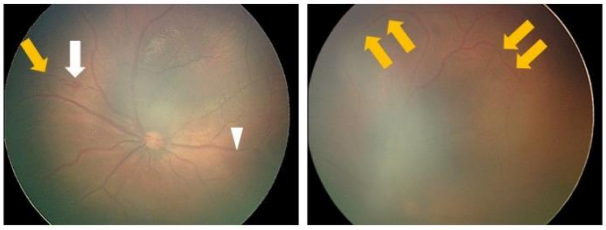

Fig-1: Fundus photographs in the left eye

DISCUSSION

The recognized ocular manifestations with *COL4A1* mutations include cataract, retinal arteriolar tortuousity, strabismus, iris hypoplasia, posterior embryotoxon, corneal opacity, retinal hemorrhage, optic atrophy, microcornea, microphthalmos, glaucoma, high myopia, reduced cone and rod responses, nystagmus, optic coloboma, retinal detachment and hypermetropia [8-11].

Patients with a *COL4A1* mutation have an increased risk for intracranial hemorrhage because of disrupted integrity in the vascular basement membrane due to the mutation [1-7]. To the authors' knowledge, this is the youngest patient with *COL4A1* mutation documented by fundus photographs to be reported. Fundus examination was useful in visualizing retinal vascular changes in patients with *COL4A1* mutation.

CONCLUSION

Although our report is based solely on a patient with *COL4A1* mutation, pediatric neurologists should be aware of an undiagnosed *COL4A1* mutation when a patient presents with retinal vascular changes, such as increased tortuosity, arteriovenous anastomosis and intraretinal hemorrhage.

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REFERENCES

1. Plaisier E, Gribouval O, Alamowitch S, Mougenot B, Prost C, Verpont MC, Marro B, Desmettre T, Cohen SY, Roullet E, Dracon M. COL4A1 mutations and hereditary angiopathy, nephropathy, aneurysms, and muscle cramps. New England Journal of Medicine. 2007 Dec 27;357(26):2687-95.
2. Alavi MV, Mao M, Pawlikowski BT, Kvezereli M, Duncan JL, Libby RT, John SW, Gould DB. Col4a1 mutations cause progressive retinal neovascular defects and retinopathy. Scientific reports. 2016 Jan 27;6:18602.
3. Vahedi K, Massin P, Guichard JP, Miocque S, Polivka M, Goutieres F, Dress D, Chapon F, Ruchoux MM, Riant F, Joutel A. Hereditary infantile hemiparesis, retinal arteriolar tortuosity, and leukoencephalopathy. Neurology. 2003 Jan 14;60(1):57-63.
4. Weng YC, Sonni A, Labelle-Dumais C, de Leau M, Kauffman WB, Jeanne M, Biffi A, Greenberg SM, Rosand J, Gould DB. COL4A1 mutations in patients with sporadic late-onset intracerebral hemorrhage. Annals of neurology. 2012 Apr;71(4):470-477.
5. Yoneda Y, Haginoya K, Kato M, Osaka H, Yokochi K, Arai H, Kakita A, Yamamoto T, Otsuki Y, Shimizu SI, Wada T. Phenotypic spectrum of COL4A1 mutations: porencephaly to schizencephaly. Annals of neurology. 2013 Jan;73(1):48-57.
6. Vahedi K, Kubis N, Boukobza M, Arnoult M, Massin P, Tournier-Lasserve E, Bousser MG. COL4A1 mutation in a patient with sporadic, recurrent intracerebral hemorrhage. Stroke. 2007 May 1;38(5):1461-1464.
7. Gould DB, Phalan FC, van Mil SE, Sundberg JP, Vahedi K, Massin P, Bousser MG, Heutink P, Miner JH, Tournier-Lasserve E, John SW. Role of COL4A1 in small-vessel disease and hemorrhagic stroke. New England Journal of Medicine. 2006 Apr 6;354(14):1489-1496.
8. Meuwissen ME, Halley DJ, Smit LS, Lequin MH, Cobben JM, De Coo R, Van Harssel J, Sallevelt S, Woldringh G, Van Der Knaap MS, De Vries LS. The expanding phenotype of COL4A1 and COL4A2 mutations: clinical data on 13 newly identified families and a review of the literature. Genetics in Medicine. 2015 Nov;17(11):843-853.
9. Rødahl E, Knappskog PM, Majewski J, Johansson S, Telstad W, Kråkenes J, Boman H. Variants of anterior segment dysgenesis and cerebral involvement in a large family with a novel COL4A1 mutation. American journal of ophthalmology. 2013 May 1;155(5):946-53.
10. Shah S, Ellard S, Kneen R, Lim M, Osborne N, Rankin J, Stoodley N, Van der Knaap M, Whitney A, Jardine P. Childhood presentation of COL4A1 mutations. Developmental Medicine & Child Neurology. 2012 Jun;54(6):569-74.
11. Coupry I, Sibon I, Mortemousque B, Rouanet F, Mine M, Goizet C. Ophthalmological features associated with COL4A1 mutations. Archives of ophthalmology. 2010 Apr 1;128(4):483-9.