Review article

Retinal detachment in Stickler syndrome: A review of surgical outcomes and prognosis

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Abstract

Stickler syndrome is an inherited disorder of the collagen connective tissues with ophthalmic, orofacial, auditory, and articular manifestations. The risk of retinal detachment in Stickler syndrome is very high, and it is considered to be the most common cause of retinal detachment in children. Repair of retinal detachment in Stickler syndrome is challenging with variability in surgical and visual outcomes. Early diagnosis, close follow up and prompt intervention is necessary to prevent serious complication of retinal detachment and visual loss. Here we are reviewing the retinal detachment in Stickler syndrome, surgical outcomes and prognosis.

Keywords:
Stickler syndrome, retinal detachment in Stickler syndrome, prognosis of Stickler retinal detachment.

الملخص

خلفية:
متلازمة ستيكلر هي اضطراب وراثي للأنسجة الضامة للكولاجين مع وجود مظاهر وتغيرات في العيون، ومنطقة الفم، والقناة السمعية، وكذلك المفاصل. إن خطر انفصال الشبكية في مرضى متلازمة ستيكلر مرتفع للغاية، ويعتبر السبب الأكثر شيوعًا لانفصال الشبكية عند الأطفال. عملية إصلاح انفصال الشبكية في متلازمة ستيكلر تمثل تحديًا مع وجود تباين في النتائج الجراحية والبصرية. يعد التشخيص المبكر والمتابعة عن كثب والتدخل الفوري ضروريين لمنع المضاعفات الخطيرة لانفصال الشبكية وفقدان البصر. في هذه المادة تمت مراجعة انفصال الشبكية في متلازمة ستيكلر وكذلك النتائج الجراحية والتشخيص

Introduction:

Stickler syndrome (also known as hereditary arthro-ophthalmopathy) was first described by Stickler et al in 1965 [1]. It is an inherited progressive disorder of the collagen connective tissues with multi-systemic association. It is predominantly presented with ophthalmic, orofacial, auditory, and articular manifestations. The incidence of Stickler syndrome is estimated of about 1:7500 to 1:10000 live births, and it is considered to be the most common cause of inherited and childhood retinal detachment [2, 3, 4].

Genetic findings:

Stickler syndrome is a disorder caused by gene mutations affecting the formation of different types of collagen (types II, IX, and XI). These proteins are involved in building and function of the eye, articular and hyaline cartilages, and other connective tissues [5]. Because of genetic heterogeneity, there is diversity of phenotypes, and affected individuals present with variable expression. There are at least five subgroups of Stickler syndrome, based on its underlying genetic collagen defect [3, 6, 7, 8, 9, 10, 11]. Autosomal dominant forms of Stickler syndrome caused by mutation in COL2A1 gene(type I), COL11A1 gene (type II), and COL11A2 gene(-type III ,non-ocular form). While, mutation in COL9A1 gene(type IV) and COL9A2 gene(-type V) are the autosomal recessive forms of Stickler syndrome [7, 9, 11, 12, 13, 14]. Type I Stickler

syndrome is the most common type, affecting more than 80% of patients [6, 15].

Clinical features and diagnosis:

Ocular manifestations present in 95% of Stickler syndrome patients include, congenital abnormality of vitreous, high myopia , anterior chamber drainage abnormality with high risk glaucoma , cortical cataract, and retinal lattice degeneration with high risk of retina breaks formation [16,17]. Non-ocular findings include orofacial malformation (e.g. maxillofacial hypoplasia and cleft palate), hearing loss, as well as numerous skeletal malformations(e.g. premature osteoarthritis, epiphyseal dysplasia and joint hypermobility [18,19,20]. Although diagnosis of Stickler syndrome is confirmed by genetic analysis, careful systemic examination is essential and continue to have a major role for clinical suspicion and to help in genetic screening [6].

Rhegmatogenous retinal detachment(RRD) in Stickler syndrome:

Rhegmatogenous retinal detachment (RRD) is caused by a retina break which permit accumulation of fluid in the potential space between neuroretinal layers and the retinal pigment epithelium (RPE), and potentially leading to vision loss. RRD risk in Stickler syndrome patient is very high, and it was reported that over 50% to 65% of clinical diagnosis patient of one of the Stickler syndromes had retinal detachment [16, 17, 21, 22]. The risk reach to 70% of genetically confirmed type 1 Stickler syndrome, and almost 50% of them had bilateral detachment [21]. In type 2 Stickler syndrome, the percentage of retinal detachment is less and it was suggested to be between 40–50% of patients [23].

In Stickler syndrome, RRD occurs relatively early in life, often in the second and third decades of life. Giant retinal tear (GRT), which at least 3 clock-hours of peripheral retinal involvement, considered to be a major cause of retinal detachment, it predisposed by the vitreoretinal changes associated with the syndrome [5, 16, 24, 25, 26]. In different studies , they showed that retinal detachment in Stickler syndrome is caused by a single retinal break in about 18% of cases, multiple retinal breaks range between 30-50%, and in between 31-50% of cases had GRTs [25, 27]. Lattice degeneration was found in about 75% of patients of Stickler patients, which further increase the risk of retinal breaks formation [25]. 50% to 75% of Stickler syndrome patients will develop proliferative vitreoretinopathy (PVR) at any point of their life [25, 27]. PVR is a main cause of retinal detachment repair failure, it is a disease process which result in periretinal membrane formation and traction, due to the proliferation of various cells (e.g RPE, glial cells , inflammatory cells) in the vitreous and/or periretinal area in patients with rhegmatogenous retinal detachments [28,29].

Management and prognosis:

Retinal detachment repair and maintaining the final success outcome in Sticklers syndrome patient is difficult and challenging although the advancement in surgical techniques. This complexity because of multiple factors, including the presence of multiple retinal tears, GRTs, the young age of presentation, the liquefied abnormal vitreous, and the high prevalence of PVR seen in these patients [25, 27]. Scleral buckle, vitrectomy, and combined vitrectomy and scleral buckle procedures with silicon oil or gas tamponade are the surgical options for RRD repair in Stickler patients, and all show anatomical successful outcomes. Silicon oil tamponade show superiority compare to gas tampnade in the term of decrease of the recurrence rate of RRD, and it was shown that the combined vitrectomy and scleral buckle procedure with silicone oil tamponade could be the treatment of choice for treating RRD in

patients with Stickler syndrome [25, 27, 30, 31].

Outcome of visual acuity:

The visual acuity (VA) outcome after successful surgical intervention for RRD in Stickler syndrome is varies, showed improvement of VA in between 31%-63% of cases, 28%-40% of cases maintain VA, while 7%-37% showed decrease in VA [25, 27, 30]. In patients with complete re-attachment of the retina, Snellen VA was 20/200 or better in 61% to 76% of patients, and it was 20/40 or better in 16% to 45% of patients [25, 30]. There are multiple factors may impact the final visual outcome in Stickler patients, including young age of presentation, which may result in delayed diagnosis and more advanced findings, amblyopia, band keratopathy, cataract, high incidence of macula involvement and PVR changes [25, 30].

Success rate of surgery and complications:

The final success rate for retinal reattachment in Stickler syndrome patients was ranging between 75%-100% [25, 27, 30, 32]. The success rate of primary surgery was ranging between 59 % and 78 %, with an average of 63.5%,70.5% and 75% after scleral buckling with cryotherapy, pars plana vitrectomy, and combined scleral buckling and pars plana vitrectomy, respectively [25, 30, 32].The average time to re-detachment after the primary procedure was ranging between 2.6 months and 9.2 months [25, 27, 30]. The achievement of success retinal reattachment in Stickler syndrome may require multiple surgeries with average of 3.1 surgeries [27]. Most common complications noticed after retinal re-attachment surgery were proliferative vitreoretinopathy (PVR)(50-75%), cataract (26-43%), raised intraocular pressure (14-27%), band keartopathy (8-25%), epiretinal membrane (7-11%) ,and intraocular hemorrhage (1-7%) [25, 30].

Prophylactic interventions:

There are multiple prophylactic procedures were used to secure retina and to prevent retinal detachment in Sticklers patients, such as cryotherapy, laser therapy and scleral buckling. Because of safety and clinical effectiveness issues, there are no general agreement for the ideal practice and clear guidelines on prophylactic interventions. There are several studies have demonstrated that the prophylactic retinopexy is safe and markedly reduces the risk of RRDs in Stickler syndrome patients and may be eliminate the risk of bilateral retinal detachment [21, 33]. Other studies were inconclusive and showed that the final outcomes of eyes that received prophylactic retinopexy were not statistically significant differences compared with eyes that did not receive any prophylactic treatment [3, 25].

Conclusion:

Stickler syndrome is an inherited disorder presented with multi-systemic manifestations and high risk of RRD. Repair of RRD in Sticklers syndrome patient is complex with highly variable in surgical and visual outcomes. Despite controversy, several studies showed that the prophylactic retinopexy is safe and markedly reduces the risk of RRDs in Stickler syndrome patients. Because of younger age of presentation, as well as the challenges of surgical procedures and visual outcomes, this emphasizes the importance of early recognizing, close follow up, and prompt intervention for preventing the severe retinal complications and visual loss in these patients.

References:

[1] Stickler GB, Belau PG, Farrell FJ, Jones JD, Pugh DG, Steinberg AG, et al. Hereditary progressive arthro-ophthalmopathy. Mayo Clin Proc. 1965;40:433–55

[2] Snead MP, Yates JR. Clinical and molecular genetics of Stickler syndrome. J Med Genet 1999 May;36(5):353-9.

[3] Carroll C, Papaioannou D, Rees A, Kaltenthaler E. The clinical effectiveness and safety of prophylactic retinal interventions to reduce the risk of retinal detachment and subsequent vision loss in adults and children with Stickler syndrome: a systematic review. Health Technol Assess. 2011 Apr;15(16):iii-xiv,1-62. doi: 10.3310/hta15160.

[4] Vandenberg P. Molecular basis of heritable connective tissue disease. Bioche Med Metabol Biol 1993 Feb;49(1):1-12.

[5] Snead MP, Mcninch AM, Poulson AV, et al. Stickler syndrome, ocular-only variants and a key diagnostic role for the ophthalmologist. Eye (Lond) 2011;25(11):1389–1400.

[6] Richards AJ, McNinch A, Martin H, et al. Stickler syndrome and the vitreous phenotype: mutations in COL2A1 and COL11A1. Hum Mutat. 2010 Jun;31(6):E1461-71. doi: 10.1002/humu.21257.

[7] Ahmad NN, Ala-Kokko L, Knowlton RG, Jimenez SA, Weaver EJ, Maguire JL, et al. Stop codon in the procollagen gene (COL2A1) in a family with the Stickler syndrome (arthro-ophthalmopathy). Proc Natl Acad Sci USA. 1991;88:6624–6627.

[8] Sirko-Osadsa DA, Murray MA, Scott JA, Lavery MA, Warman ML, Robin NH. Stickler syndrome without eye involvement is caused by mutations in COL11A2, the gene encoding the alpha2(XI) chain of type XI collagen. J Pediatr. 1998;132:368–371.

[9] Van Camp G, Snoeckx RL, Hilgert N, van den Ende J, Fukuoka H, Wagatsuma M, et al. A new autosomal recessive form of Stickler syndrome is caused by a mutation in the COL9A1 gene. Am J Hum Genet. 2006;79:449–457.

[10] Baker S, Booth C, Fillman C, Shapiro M, Blair MP, Hyland JC, et al. A loss of function mutation in the COL9A2 gene cause autosomal recessive Stickler syndrome. Am J Med Genet A. 2011;155 (7:1668–1672.

[11] Richards AJ, Martin S, Yates JRW, Baguley DM, Pope FM, Scott JD, et al. COL2A1 exon 2 mutations: relevance to the Stickler and Wagner syndromes. Br J Ophthalmol. 2000;84:364–371.

[12] Goyal M , Kapoor S , Ikegawa S , Nishimura G. Stickler Syndrome Type 1 with Short Stature and Atypical Ocular Manifestations. Case Rep Pediatr. 2016;2016:3198597. doi: 10.1155/2016/3198597. Epub 2016 Nov 28.

[13] Ahmad NN, McDonald-McGinn DM, Dixon P, Zackai EH, Tasman WS. PCR assay confirms diagnosis in syndrome with variably expressed phenotype: mutation detection in Stickler syndrome. J Med Genet. 1996 Aug; 33(8): 678–681.

[14] Vikkula M, Mariman EC, Lui VC, Zhidkova NI, Tiller GE, Goldring MB, van Beersum SE, de Waal Malefijt MC, van den Hoogen FH, Ropers HH. et al. Autosomal dominant and recessive osteochondrodysplasias associated with the COL11A2 locus. Cell. 1995;80(3):431–437.

[15] Robin NH, Moran RT, Warman M, Ala-Kokko L. Stickler syndrome. In: Pagon RA, Adam MP, Bird TD, et al, eds. GeneReviews [database online]. Seattle: University of Washington, Seattle; Updated November 3, 2011.

[16] Parma ES, Korkko J, Hagler WS, Ala-Kokko L. Radial perivascular retinal degeneration: a key to the clinical diagnosis of an ocular variant of stickler syndrome with minimal or no systemic manifestations. Am J Ophthalmol. 2002;134(5):728–734.

[17] Stickler GB, Hughes W, Houchin P. Clinical features of hereditary progressive arthro-ophthalmopathy (Stickler syndrome): a survey. Genet Med. 2001;3:192–196.

[18] Bowling EL, Brown MD, Trundle TV. The Stickler syndrome: case reports and literature review. Optometry. 2000 Mar;71(3):177-82.

[19] Rose PS, Levy HP, Liberfarb RM, Davis J, Szymko-Bennett Y, Rubin BI, et al. Stickler syndrome: clinical characteristics and diagnostic criteria. Am J Med Genet. 2005;138A (3:199–207.

[20] Rose PS, Ahn NU, Levy HP, Ahn UM, Davis J, Liberfarb RM, et al. Thoracolumbar spinal abnormalities in Stickler syndrome. Spine. 2001;26:403–409.

[21] Ang A, Poulson AV, Goodburn SF, Richards AJ, Scott JD, Snead MP. Retinal detachment and prophylaxis in type 1 Stickler syndrome. Ophthalmology. 2008;115:164–168.

[22] Donoso LA, Edwards AO, Frost AT, et al. Identification of a stop codon mutation in exon 2 of the collagen 2A1 gene in a large Stickler syndrome family. Am J Ophthalmol 2002;134:720–7.

[23] Poulson AV, Hooymans J, Richards AJ, Bearcroft P, Murthy R, Baguley D, et al. Clinical features of Type 2 Stickler syndrome .J Med Genet 200441e107.

[24] Shuler M, Sullivan J, Hurley B, McNamara J. Pediatric Retina. 2011 ed. London: Springer Berlin Heidelberg; 2011. Vitreoretinal dystrophies; pp. 315–319. Kresge Reference Library. Web. 23 May 2015.

[25] Alshahrani ST, Ghazi NG, Al-Rashaed S. Rhegmatogenous retinal detachments associated to Stickler syndrome in a tertiary eye care center in Saudi Arabia. Clin Ophthalmol. 2016;10:1–6.

[26] Snead MP. Hereditary vitreoretinopathy. Eye(1996) 10:653–663.

[27] Reddy DN, Yonekawa Y, Thomas BJ, Nudleman ED, Williams GA. Long-term surgical outcomes of retinal detachment in patients with Stickler syndrome. Clin Ophthalmol. 2016; 10: 1531–1534.

[28] Sadaka A, Giuliari GP. Proliferative vitreoretinopathy: current and emerging treatments. Clin Ophthalmol. 2012; 6: 1325–1333.
[29] Pastor JC. Proliferative vitreoretinopathy: anoverview.SurvOphthalmol.1998;43(1):318.

[30] Abeysiri P, Bunce C, da Cruz L. Outcomes of surgery for retinal detachment in patients with stickler syndrome: a comparison of two sequential 20-year cohorts. Graefes Arch Clin Exp Ophthalmol. 2007;245(11):1633–1638.

[31] Pagot-Mathis V, Benouaich X, Mathis A, Rico-Lattes I, Dumoulin A. Management of complicated retinal detachment using a heavy silicone oil as temporary tamponade. J Fr Ophthalmol. 2006;29(2):137–145

[32] Billington BM, Leaver PK, McLeod D. Management of the retinal detachment in the Wagner–Stickler syndrome. Trans Ophthalmol Soc UK. 1985;104(Pt 8):875–879.

[33] Fincham GS, Pasea L, Carroll C, et al. Prevention of retinal detachment in stickler syndrome: the Cambridge prophylactic cryotherapy protocol. Ophthalmology. 2014;121(8):1588–1597.