



## TİROİD OFTALMOPATİSİ

Ezgi KARATAŞ<sup>1</sup>

### GENEL BİLGİLER

Tiroid göz hastalığı orbita yağ dokusunu, ekstraoküler kasları ve lakrimal bezi etkileyen otoimmün inflamatuvar bir hastalıktır. Bu dokularda glikozaminoglikan birikimi ve ikincil ödem olabilmekle beraber bazı olgularda anormal kollajen üretimine sekonder fibrozis de izlenebilmektedir (1). Çoğu hastada göz kapak retraksiyonu, proptozis ve korneada ekspozure olabilir iken olguların üçte birinde ekstraoküler kaslarda ciddi tutulum ve hareketlerinde kısıtlılık, yumuşak doku ödemi ve kompresif optik nöropati gibi ciddi klinik bulgular da olabilmektedir. Bu klinikteki varyasyon hastalığın ciddiyeti olarak sınıflandırılır.

Tiroid göz hastalıkları klinik olarak bifazik eğilime sahiptir. Bu eğilimde yaklaşık olarak 18 aya varan aktif faz ve onu takip eden inaktif faz mevcuttur (**Şekil 1**).

Tiroid göz hastalığı çoğunlukla kendini sınırlayan bir klinik olmasına rağmen hayat kalitesinde en az diyabetes mellitus veya kronik obstrüktif akciğer hastalığı kadar bozulmaya yol açmaktadır (2).

Tiroid göz hastalığı insidansı kadınlarda 14/100.000 kadar olup erkeklerde bu oran beşte biri kadardır (3). Tüm yaşlarda ve cinsiyette görülebilen bu hastalık ikinci ve altıncı dekatta daha sık görülür (4).

Tiroid oftalmopati yaklaşık %90 oranında Graves hastalığı ile ve %3 oranında Hashimoto tiroiditi ile ilişkilidir. Antikorlar TSH reseptörünü veya IGF1 reseptörünü hedef olarak tiroid bezinde, orbital fibroblastlarda ve ciltte etki gösterir (3). Otoimmün tiroid hastalarının %25-50'sinde göz tutulumu beklenmektedir ve bu hastaların üçte birinde ciddi göz komplikasyonları olabilmektedir (5).

<sup>1</sup> Dr. Öğr Üyesi, Ağrı İbrahim Çeçen Üniversitesi Tıp Fakültesi Göz Hastalıkları AD., e.karatas.2015@gmail.com

Sonuç olarak tiroid oftalmopatisinde kapak retraksiyonu tedavisinde çeşitli cerrahi ve cerrahi dışı seçenekler olmakla beraber tedavi seçimi hastaya, beklentiye ve hastalığın aktivasyonuna göre değişkenlik göstermektedir.

## KAYNAKLAR

1. Bahn RS. Graves' ophthalmopathy. *N Engl J Med.* 2010;362(8):726-38. DOI: 10.1056/NEJMr-a0905750
2. Gerding MN, Terwee CB, Dekker FW, Koornneef L, Prummel MF, Wiersinga WM. Quality of life in patients with Graves' ophthalmopathy is markedly decreased: measurement by the medical outcomes study instrument. *Thyroid.* 1997;7(6):885-9. DOI: 10.1089/thy.1997.7.885
3. Pritchard J, Horst N, Cruikshank W, Smith TJ. Igs from patients with Graves' disease induce the expression of T cell chemoattractants in their fibroblasts. *J Immunol.* 2002;168(2):942-50. DOI: 10.4049/jimmunol.168.2.942
4. Pritchard J, Han R, Horst N, Cruikshank WW, Smith TJ. Immunoglobulin activation of T cell chemoattractant expression in fibroblasts from patients with Graves' disease is mediated through the insulin-like growth factor I receptor pathway. *J Immunol.* 2003;170(12):6348-54. DOI: 10.4049/jimmunol.170.12.6348
5. Bartley GB. The epidemiologic characteristics and clinical course of ophthalmopathy associated with autoimmune thyroid disease in Olmsted County, Minnesota. *Trans Am Ophthalmol Soc.* 1994;92:477.
6. Dolman PJ. Evaluating Graves' orbitopathy. *Best Pract Res Clin Endocrinol Metab.* 2012;26(3):229-48. DOI: 10.1016/j.beem.2011.11.007
7. Frueh BR, Grill R, Musch DC. Lid Protractor Force Generation in Graves' Eye Disease. *Ophthalmology.* 1986;93(1):8-13. DOI: 10.1016/s0161-6420(86)33786-2
8. Kendler DL, Lippa J, Rootman J. The initial clinical characteristics of Graves' orbitopathy vary with age and sex. *Arch Ophthalmol.* 1993;111(2):197-201. DOI: 10.1001/archophth.1993.01090020051022
9. Regensburg NI, Wiersinga WM, Berendschot TTJM, Saeed P, Mourits MP. Densities of orbital fat and extraocular muscles in graves orbitopathy patients and controls. *Ophthalmic Plast Reconstr Surg.* 2011;27(4):236-40. DOI: 10.1097/IOP.0b013e31820365d5
10. Polito E, Leccisotti A. MRI in Graves orbitopathy: recognition of enlarged muscles and prediction of steroid response. *Ophthalmologica.* 1995;209(4):182-6. DOI: 10.1159/000310609
11. Kazim M, Trokel SL, Acaroglu G, Elliott A. Reversal of dysthyroid optic neuropathy following orbital fat decompression. *Br J Ophthalmol.* 2000;84(6):600. DOI: 10.1136/bjo.84.6.600
12. Vestergaard P. Smoking and thyroid disorders--a meta-analysis. *Eur J Endocrinol.* 2002;146(2):153-61. DOI: 10.1530/eje.0.1460153
13. Bartalena L, Tanda ML, Piantanida E, Lai A. Oxidative stress and Graves' ophthalmopathy: in vitro studies and therapeutic implications. *Biofactors.* 2003;19(3-4):155-63. DOI: 10.1002/biof.5520190308
14. Bartalena L, Pinchera A, Marcocci C. Management of Graves' ophthalmopathy: reality and perspectives. *Endocr Rev.* 2000;21(2):168-99. DOI: 10.1210/edrv.21.2.0393
15. Drutel A, Archambeaud F, Caron P. Selenium and the thyroid gland: more good news for clinicians. *Clin Endocrinol (Oxf).* 2013;78(2):155-64. DOI: 10.1111/cen.12066
16. Rayman MP. Selenium and human health. *Lancet.* 2012;379(9822):1256-68. DOI: 10.1016/S0140-6736(11)61452-9
17. Rayman MP. The importance of selenium to human health. *Lancet.* 2000;356(9225):233-41. DOI: 10.1016/S0140-6736(00)02490-9
18. Hoffmann PR, Berry MJ. The influence of selenium on immune responses. *Mol Nutr Food Res.*

- 2008;52(11):1273. DOI: 10.1002/mnfr.200700330
19. Maciej Serda, Becker FG, Cleary M, et al. Enhanced induction of a 72 kDa heat shock protein in cultured retroocular fibroblasts. G. Balint, Antala B, Carty C, Mabieme JMA, Amar IB, Kaplanova A, editors. *Invest Ophthalmol Vis Sci*. 1992;33(2):466-70.
  20. Burch HB, Lahiri S, Bahn RS, Barnes S. Superoxide radical production stimulates retroocular fibroblast proliferation in Graves' ophthalmopathy. *Exp Eye Res*. 1997;65(2):311-6. DOI: 10.1006/exer.1997.0353
  21. Marcocci C, Kahaly GJ, Krassas GE, et al. Selenium and the course of mild Graves' orbitopathy. *N Engl J Med*. 2011;364(20):1920-31. DOI: 10.1056/NEJMc1107080
  22. Uddin JM, Davies PD. Treatment of upper eyelid retraction associated with thyroid eye disease with subconjunctival botulinum toxin injection. *Ophthalmology*. 2002;109(6):1183-7. DOI: 10.1016/s0161-6420(02)01041-2
  23. Wiersinga WM, Bartalena L. Epidemiology and prevention of Graves' ophthalmopathy. *Thyroid*. 2002;12(10):855-60. DOI: 10.1089/105072502761016476
  24. Zang S, Ponto KA, Kahaly GJ. Clinical review: Intravenous glucocorticoids for Graves' orbitopathy: efficacy and morbidity. *J Clin Endocrinol Metab*. 2011;96(2):320-32. DOI: 10.1210/jc.2010-1962
  25. Bartalena L, Krassas GE, Wiersinga W, et al. Efficacy and safety of three different cumulative doses of intravenous methylprednisolone for moderate to severe and active Graves' orbitopathy. *J Clin Endocrinol Metab*. 2012;97(12):4454-63. DOI: 10.1210/jc.2012-2389
  26. Stiebel-Kalish H, Robenshtok E, Hasanreisoglu M, Ezrachi D, Shimon I, Leibovici L. Treatment modalities for Graves' ophthalmopathy: systematic review and metaanalysis. *J Clin Endocrinol Metab*. 2009;94(8):2708-16. DOI: 10.1210/jc.2009-0376
  27. Bartalena L, Marcocci C, Chiovato L, et al. Orbital cobalt irradiation combined with systemic corticosteroids for Graves' ophthalmopathy: comparison with systemic corticosteroids alone. *J Clin Endocrinol Metab*. 1983;56(6):1139-44. DOI: 10.1210/jcem-56-6-1139
  28. Trott KR, Kamprad F. Radiobiological mechanisms of anti-inflammatory radiotherapy. *Radiother Oncol*. 1999;51(3):197-203. DOI: 10.1016/s0167-8140(99)00066-3
  29. Dolman PJ, Rath S. Orbital radiotherapy for thyroid eye disease. *Curr Opin Ophthalmol*. 2012;23(5):427-32. DOI: 10.1097/ICU.0b013e3283560b2b
  30. Wiersinga WM. Graves orbitopathy: Management of difficult cases. *Indian J Endocrinol Metab*. 2012;16(Suppl 2):S150. DOI: 10.4103/2230-8210.104026
  31. Bhatt R, Nelson CC, Douglas RS. Thyroid-associated orbitopathy: Current insights into the pathophysiology, immunology and management. *Saudi Journal of Ophthalmology*. 2011;25(1):15. DOI: 10.1016/j.sjopt.2010.11.002
  32. Bartalena L, Baldeschi L, Dickinson A, et al. Consensus statement of the European Group on Graves' orbitopathy (EUGOGO) on management of GO. *Eur J Endocrinol*. 2008;158(3):273-85. DOI: 10.1530/EJE-07-0666
  33. Kumar S, Iyer S, Bauer H, Coenen M, Bahn RS. A Stimulatory Thyrotropin Receptor Antibody Enhances Hyaluronic Acid Synthesis in Graves' Orbital Fibroblasts: Inhibition by an IGF-I Receptor Blocking Antibody. *J Clin Endocrinol Metab*. 2012;97(5):1681-7. DOI: 10.1210/jc.2011-2890
  34. Bartley GB, Fatourehchi V, Kadrmas EF, et al. Clinical features of Graves' ophthalmopathy in an incidence cohort. *Am J Ophthalmol*. 1996;121(3):284-90. DOI: 10.1016/s0002-9394(14)70276-4
  35. Rajendram R, Bunce C, Adams GGW, Dayan CM, Rose GE. Smoking and strabismus surgery in patients with thyroid eye disease. *Ophthalmology*. 2011;118(12):2493-7. DOI: 10.1016/j.ophttha.2011.06.003
  36. Tamhankar MA, Ying GS, Volpe NJ. Prisms are effective in resolving diplopia from incomitant, large, and combined strabismus. *Eur J Ophthalmol*. 2012;22(6):890-7. DOI: 10.5301/

- ejo.5000144
37. Dawson E, Ali N, Lee JP. Botulinum toxin injection into the superior rectus for treatment of strabismus. *Strabismus*. 2012;20(1):24-5. DOI: 10.3109/09273972.2011.650814
  38. Borumandi F, Hammer B, Kamer L, von Arx G. How predictable is exophthalmos reduction in Graves' orbitopathy? A review of the literature. *Br J Ophthalmol*. 2011;95(12):1625-30. DOI: 10.1136/bjo.2010.181313
  39. Dagi LR, Elliott AT, Roper-Hall G, Cruz OA. Thyroid eye disease: honing your skills to improve outcomes. *J AAPOS*. 2010;14(5):425-31. DOI: 10.1016/j.jaapos.2010.07.005
  40. Yoo SH, Pineles SL, Goldberg RA, Velez FG. Rectus muscle resection in Graves' ophthalmopathy. *J AAPOS*. 2013;17(1):9. DOI: 10.1016/j.jaapos.2013.03.025
  41. Bartley GB, Fatourechi V, Kadrmas EF, et al. The incidence of Graves' ophthalmopathy in Olmsted County, Minnesota. *Am J Ophthalmol*. 1995;120(4):511-7. DOI: 10.1016/s0002-9394(14)72666-2
  42. Regensburg NI, Wiersinga WM, Berendschot TTJM, Potgieser P, Mourits MP. Do subtypes of graves' orbitopathy exist? *Ophthalmology*. 2011;118(1):191-6. DOI: 10.1016/j.ophtaha.2010.04.004
  43. Victores AJ, Takashima M. Thyroid eye disease: Optic neuropathy and orbital decompression. *Int Ophthalmol Clin*. 2016;56(1):69-79. DOI: 10.1097/IIO.000000000000101
  44. Boboridis KG, Uddin J, Mikropoulos DG, et al. Critical Appraisal on Orbital Decompression for Thyroid Eye Disease: A Systematic Review and Literature Search. *Adv Ther*. 2015;32(7):595-611. DOI: 10.1007/s12325-015-0228-y
  45. Boboridis KG, Bunce C. Surgical orbital decompression for thyroid eye disease. *Cochrane Database Syst Rev*. 2011;(12). DOI: 10.1002/14651858.CD007630.pub2
  46. Wu CH, Chang TC, Liao SL. Results and predictability of fat-removal orbital decompression for disfiguring graves exophthalmos in an Asian patient population. *Am J Ophthalmol*. 2008;145(4):755-9. DOI: 10.1016/j.ajo.2007.11.020
  47. Rao R, Macintosh PW, Yoon MK, Lefebvre DR. Current trends in the management of thyroid eye disease. *Curr Opin Ophthalmol*. 2015;26(6):484-90. DOI: 10.1097/ICU.0000000000000203
  48. Ünal M, Ileri F, Konuk O, Hasanreisolu B. Balanced orbital decompression combined with fat removal in Graves ophthalmopathy: do we really need to remove the third wall? *Ophthalmic Plast Reconstr Surg*. 2003;19(2):112-8. DOI: 10.1097/01.IOP.0000056145.71641.F5
  49. Zoumalan CI, Kazim M, Lisman RD. Endoscopic orbital decompression. *Oper Tech Otolaryngol Head Neck Surg*. 2011;22(3):223-8.
  50. Braun TL, Bhadkamkar MA, Jubbal KT, Weber AC, Marx DP. Oculofacial Plastic and Reconstructive Surgery: Orbital Decompression for Thyroid Eye Disease. *Semin Plast Surg*. 2017;31(1):40.
  51. Boboridis KG, Bunce C. Surgical orbital decompression for thyroid eye disease. *Cochrane Database Syst Rev*. 2011;(12). DOI: 10.1002/14651858.CD007630.pub2
  52. Leong SC, Karkos PD, MacEwen CJ, White PS. A systematic review of outcomes following surgical decompression for dysthyroid orbitopathy. *Laryngoscope*. 2009;119(6):1106-15. DOI: 10.1002/lary.20213
  53. Jernfors M, Välimäki MJ, Setälä K, Malmberg H, Laitinen K, Pitkäranta A. Efficacy and safety of orbital decompression in treatment of thyroid-associated ophthalmopathy: long-term follow-up of 78 patients. *Clin Endocrinol (Oxf)*. 2007;67(1):101-7. DOI: 10.1111/j.1365-2265.2007.02845.x
  54. Osaki T, Monteiro L, Osaki M. Management of eyelid retraction related to thyroid eye disease. *Taiwan J Ophthalmol*. 2022;12(1):12. DOI: 10.4103/tjo.tjo\_57\_21
  55. Cockerham KP, Hidayat AA, Brown HG, Cockerham GC, Graner SR. Clinicopathologic evaluation of the Mueller muscle in thyroid-associated orbitopathy. *Ophthalmic Plast Reconstr Surg*. 2002;18(1):11-7. DOI: 10.1097/00002341-200201000-00003

56. Ohnishi T, Noguchi S, Murakami N, et al. Levator palpebrae superioris muscle: MR evaluation of enlargement as a cause of upper eyelid retraction in Graves disease. *Radiology*. 1993;188(1):115-8. DOI: 10.1148/radiology.188.1.8511284
57. Harrison AR, McLoon LK. Effect of hyperthyroidism on the orbicularis oculi muscle in rabbits. *Ophthalmic Plast Reconstr Surg*. 2002;18(4):289-94. DOI: 10.1097/00002341-200207000-00011
58. Hintschich C, Haritoglou C. Full thickness eyelid transection (blepharotomy) for upper eyelid lengthening in lid retraction associated with Graves' disease. *Br J Ophthalmol*. 2005;89(4):413-6. DOI: 10.1136/bjo.2004.052852
59. ben Simon GJ, Mansury AM, Schwarcz RM, Modjtahedi S, McCann JD, Goldberg RA. Transconjunctival Müller muscle recession with levator disinsertion for correction of eyelid retraction associated with thyroid-related orbitopathy. *Am J Ophthalmol*. 2005;140(1):94.e1-94.e7. DOI: 10.1016/j.ajo.2005.02.034
60. Watanabe A, Shams PN, Katori N, Kinoshita S, Selva D. Turn-over orbital septal flap and levator recession for upper-eyelid retraction secondary to thyroid eye disease. *Eye (Lond)*. 2013;27(10):1174-9. DOI: 10.1038/eye.2013.160
61. Lee NG, Habib L, Hall J, Freitag SK. Simultaneous ipsilateral transconjunctival repair of upper and lower eyelid retraction in thyroid-associated ophthalmopathy. *Orbit*. 2019;38(2):124-9. DOI: 10.1080/01676830.2018.1474237
62. Wiersinga WM. Quality of life in Graves' ophthalmopathy. *Best Pract Res Clin Endocrinol Metab*. 2012;26(3):359-70. DOI: 10.1016/j.beem.2011.11.001
63. Morgenstern KE, Evanchan J, Foster JA, et al. Botulinum toxin type a for dysthyroid upper eyelid retraction. *Ophthalmic Plast Reconstr Surg*. 2004;20(3):181-5. DOI: 10.1097/00002341-200405000-00001
64. Kohn JC, Rootman DB, Liu W, Goh AS, Hwang CJ, Goldberg RA. Hyaluronic acid gel injection for upper eyelid retraction in thyroid eye disease: functional and dynamic high-resolution ultrasound evaluation. *Ophthalmic Plast Reconstr Surg*. 2014;30(5):400-4. DOI: 10.1097/IOP.0000000000000130
65. Chee E, Chee SP. Subconjunctival injection of triamcinolone in the treatment of lid retraction of patients with thyroid eye disease: a case series. *Eye (Lond)*. 2008;22(2):311-5. DOI: 10.1038/sj.eye.6702933
66. Young SM, Kim YD, Lang SS, Woo KI. Transconjunctival Triamcinolone Injection for Upper Lid Retraction in Thyroid Eye Disease-A New Injection Method. *Ophthalmic Plast Reconstr Surg*. 2018;34(6):587-93. DOI: 10.1097/IOP.00000000000001120