BÖLÜM 3

ADENOVİRAL KERATOKONJONKTİVİT

Ahmet ELBEYLİ[1]

Tüm akut konjunktivit vakalarının yaklaşık %80'i virüslere bağlı olarak ortaya çıkar (Fitch et al., 1989; Uchio et al., 2000). İnsan adenovirüsleri (HAdV), viral konjonktivit vakalarının yaklaşık % 65-90'ından sorumludur (O'Brien, Jeng, McDonald, & Raizman, 2009) Adenovirüsler (HAdV'ler), üst ve alt solunum yolunu, gastrointestinal (GI) sistemi veya konjonktivayı enfekte eden ve sıklıkla hafif klinik bulgulara neden olan DNA virüsleridir. HAdV nadiren hemorajik sistit, hepatit, pankreatit, hemorajik kolit, ensefalit veya nefrite neden olur (Lynch, Fishbein, & Echavarria, 2011).

Son yıllarda, hematopoietik kök hücre ve solid organ nakli olan hasta sayısının artması ve daha uzun hayatta kalma süreleri nedeniyle edinilmiş immün yetmezliği olan hasta sayısı artmıştır. Yeni üretilmiş ve daha güçlü immünsüpresif ajanların kullanılması, şiddetli adenovirüs enfeksiyonlarının sıklığını artırmıştır. (Echavarría, 2008). İnsan adenovirüsleri (HAdV'ler), bağışıklığı zayıf veya bağışıklığı baskılanmış kişilerde önemli bir bulaşıcı ajandır ve bu durum tanı ve tedavide klinik zorluklara neden olmaktadır. (Aslan, 2014).

Farklı enfeksiyonlara neden olan birçok adenovirüs serotipi vardır. Adenovirüsün oküler manifestasyonları arasında faringokonjunktival ateş, epidemik keratokonjunktivit (EKC) ve spesifik olmayan konjunktivit bulunur.

Adenoviral konjunktivit, Amerika Birleşik Devletleri'ndeki doktor ziyaretlerinin önemli bir bölümünü oluşturduğu için sağlık hizmetleri üzerinde büyük bir mali yüke neden olmaktadır. ABD'deki adenovirüs enfeksiyonlarının sayısının yılda 20 milyona kadar olduğu tahmin edilmektedir (Garcia-Zalisnak, Rapuano, Sheppard, & Davis, 2018).

TANI:

Adenoviral konjonktivit tanısı genellikle klinik olarak konulmaktadır, ancak gerekirse laboratuvar tarafından doğrulanabilir(Pihos, 2013) (Azari & Barney, 2013) Günümüzde maalesef HAdV'nin mükemmel bir klinik ve etiyolojik tanı yöntemine sahip değiliz. Mevcut yöntemler, immünofloresans veya immünokro-

[1] Dr. Öğr. Üyesi, Hatay Mustafa Kemal Üniversitesi, ahmetelbeyli@yahoo.com

de tekrarlama olmaksızın SEI'yi ortadan kaldırmada veya azaltmada etkili olduğu görülmüştür. (Reinhard, Godehardt, Pfahl, & Sundmacher, 2000). % 0.05 ve% 2 siklosporin ve takrolimus% 0.03 formları gibi ajanlar, steroidlerin potansiyel olarak zararlı etkileri olmadan SEI'lerin temizlenmesinde faydalı olabilir (Levinger, Trivizki, Shachar, Levinger, & Verssano, 2014); (Clement et al., 2011; Hillenkamp et al., 2002).

Gansiklovir ve sidofovir gibi antiviral ilaçlar, in vitro çalışmalarla çeşitli HAdV tiplerinin tedavisinde vaat etmektedir(Toth et al., 2015; Ying et al., 2014). Cidofovir% 1 ümit verici olsa da hastalığın seyrini değiştirmediği (Y. Jerold Gordon et al., 1996; Y. J. Gordon, Romanowski, & Araullo-Cruz, 1994) ve düşük dozlarda bile önemli oküler toksisiteye neden olduğu gösterilmiştir (Clement et al., 2011; Hillenkamp et al., 2002).

Bir çalışmada, gansiklovirin bir ön ilacı olan valgansiklovirin, Suriye hamsterlerinde Adenovirüsün DNA replikasyonunu inhibe ettiği öne sürülmüştür (Toth et al., 2015; Ying et al., 2014). Başka bir in vitro temelli çalışmada, gansiklovir, oküler adenoviral keratokonjunktivit ile ilişkili HAdV3, 4, 8, 19 ve 37 türlerinde doza bağlı bir anti-adenoviral etki göstermiştir. Ayrıca gansiklovir oftalmik jelin% 0.15'inin terapötik olarak faydalı olabileceği de öne sürülmüştür. (Huang, Kadonosono, & Uchio, 2014).

KAYNAKLAR

Alai, N. (2016). Enhancing best practices in ophthalmology for prevention of nosocomial epidemic keratoconjunctivitis infections. *Current Medical Research and Opinion*, 32(10), 1757–1758.

Aoki, K., Kaneko, H., Kitaichi, N., Ohguchi, T., Tagawa, Y., & Ohno, S. (2011). Clinical features of adenoviral conjunctivitis at the early stage of infection. *Japanese Journal of Ophthalmology*, 55(1), 11–15.

Aydin Kurna, S., Altun, A., Oflaz, A., & Karatay Arsan, A. (2015). Evaluation of the impact of persistent subepithelial corneal infiltrations on the visual performance and corneal optical quality after epidemic keratoconjunctivitis. *Acta Ophthalmologica*, 93(4), 377–382.

Azari, A. A., & Barney, N. P. (2013). Conjunctivitis: a systematic review of diagnosis and treatment. *JAMA: The Journal of the American Medical Association*, 310(16), 1721–1729.

Bennett MD, J., Dolin, R., & Blaser, M. J. (2014). *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases: 2-Volume Set*. Elsevier Health Sciences.

bialasiewicz, a., brehler, r., draeger, j., & schmitz, h. (2008). mathematıcal modellıng of epıdemıs under specıfıc regard of adenovıral keratoconjunctıvıtıs. *European Journal of Medical Research*, 13(8), 355–365.

Butt, A. L., & Chodosh, J. (2006). Adenoviral keratoconjunctivitis in a tertiary care eye clinic. *Cornea*, 25(2), 199–202.

Chigbu, D. I., & Labib, B. A. (2018). Pathogenesis and management of adenoviral keratoconjunctivitis. *Infection and Drug Resistance*, 11, 981–993.

Clement, C., Capriotti, J. A., Kumar, M., Hobden, J. A., Foster, T. P., Bhattacharjee, P. S., … Hill, J. M. (2011). Clinical and antiviral efficacy of an ophthalmic formulation of dexamethasone povidone-iodine in a rabbit model of adenoviral keratoconjunctivitis. *Investigative Ophthalmology & Visual Science*, 52(1), 339–344.

D'angelo, L. J., Heerholzer, J. C., Holman, R. C., & Smith, J. D. (1981). epıdemıc keratoconjunctıvıtıs caused by adenovırus type 8: epıdemıologıc and laboratory aspects of a large outbreak. *American Journal of Epidemiology*, 113(1), 44–49. Retrieved 27 May 2020 from

Darougar, S., Grey, R. H., Thaker, U., & McSwiggan, D. A. (1983). Clinical and epidemiological features of adenovirus keratoconjunctivitis in London. *The British Journal of Ophthalmology*, 67(1), 1–7.

Echavarría, M. (2008). Adenoviruses in immunocompromised hosts. *Clinical Microbiology Reviews*, 21(4), 704–715.

Fitch, C. P., Rapoza, P. A., Owens, S., Murillo-Lopez, F., Johnson, R. A., Quinn, T. C., … Taylor, H. R. (1989). Epidemiology and diagnosis of acute conjunctivitis at an inner-city hospital. *Ophthalmology*, 96(8), 1215–1220.

Fujimoto, T., Okafuji, T., Okafuji, T., Ito, M., Nukuzuma, S., Chikahira, M., & Nishio, O. (2004). Evaluation of a bedside immunochromatographic test for detection of adenovirus in respiratory samples, by comparison to virus isolation, PCR, and real-time PCR. *Journal of Clinical Microbiology*, 42(12), 5489–5492.

Garcia-Zalisnak, D., Rapuano, C., Sheppard, J. D., & Davis, A. R. (2018). Adenovirus Ocular Infections: Prevalence, Pathology, Pitfalls, and Practical Pointers. *Eye & Contact Lens*, 44 Suppl 1, S1–S7.

Gonzalez, G., Yawata, N., Aoki, K., & Kitaichi, N. (2019). Challenges in management of epidemic keratoconjunctivitis with emerging recombinant human adenoviruses. *Journal of Clinical Virology: The Official Publication of the Pan American Society for Clinical Virology*, 112, 1–9.

Gordon, Y. J., Jerold Gordon, Y., Naesens, L., DeClercq, E., Maudgal, P. C., & Veckeneer, M. (1996). Treatment of Adenoviral Conjunctivitis with Topical Cidofovir. *Cornea*. Retrieved from https://doi.org/10.1097/00003226-199609000-00018

Gordon, Y. J., Romanowski, E. G., & Araullo-Cruz, T. (1994). Topical HPMPC inhibits adenovirus type 5 in the New Zealand rabbit ocular replication model. *Investigative Ophthalmology & Visual Science*, 35(12), 4135–4143.

Harley, D., Harrower, B., Lyon, M., & Dick, A. (2001). A primary school outbreak of pharyngoconjunctival fever caused by adenovirus type 3. *Communicable Diseases Intelligence*, 25(1), 9–12.

Hillenkamp, J., Reinhard, T., Ross, R. S., Böhringer, D., Cartsburg, O., Roggendorf, M., … Sundmacher, R. (2002). The effects of cidofovir 1% with and without cyclosporin a 1% as a topical treatment of acute adenoviral keratoconjunctivitis: a controlled clinical pilot study. *Ophthalmology*, 109(5), 845–850.

Horton, J. C., & Miller, S. (2015). Magnetic Resonance Imaging in Epidemic Adenoviral Keratoconjunctivitis. *JAMA Ophthalmology*, 133(8), 960–961.

Huang, J., Kadonosono, K., & Uchio, E. (2014). Antiadenoviral effects of ganciclovir in types inducing keratoconjunctivitis by quantitative polymerase chain reaction methods. *Clinical Ophthalmology* , 8, 315–320.

Jhanji, V., Chan, T. C. Y., Li, E. Y. M., Agarwal, K., & Vajpayee, R. B. (2015). Adenoviral keratoconjunctivitis. *Survey of Ophthalmology*. Retrieved from https://doi.org/10.1016/j.survophthal.2015.04.001

Kaneko, H., Maruko, I., Iida, T., Ohguchi, T., Aoki, K., Ohno, S., & Suzutani, T. (2008). The possibility of human adenovirus detection from the conjunctiva in asymptomatic cases during nosocomial infection. *Cornea*, 27(5), 527–530.

Kimura, R., Migita, H., Kadonosono, K., & Uchio, E. (2009). Is it possible to detect the presence of adenovirus in conjunctiva before the onset of conjunctivitis? *Acta Ophthalmologica*. Retrieved from https://doi.org/10.1111/j.1755-3768.2007.01148.x

Levinger, E., Trivizki, O., Shachar, Y., Levinger, S., & Verssano, D. (2014). Topical 0.03% tacrolimus for subepithelial infiltrates secondary to adenoviral keratoconjunctivitis. *Graefe's Archive for Clinical and Experimental Ophthalmology = Albrecht von Graefes Archiv Fur Klinische Und Experimentelle Ophthalmologie*, 252(5), 811–816.

Lion, T. (2014). Adenovirus infections in immunocompetent and immunocompromised patients. *Clinical Microbiology Reviews*, 27(3), 441–462.

Lynch, J. P., 3rd, Fishbein, M., & Echavarria, M. (2011). Adenovirus. *Seminars in Respiratory and Critical Care Medicine*, 32(4), 494–511.

Meyer-Rüsenberg, B., Loderstädt, U., Richard, G., Kaulfers, P.-M., & Gesser, C. (2011). Epidemic keratoconjunctivitis: the current situation and recommendations for prevention and treatment. *Deutsches Ärzteblatt International*, 108(27), 475.

Muller, M. P., Siddiqui, N., Ivancic, R., & Wong, D. (2018). Adenovirus-related epidemic keratoconjunctivitis outbreak at a hospital-affiliated ophthalmology clinic. *American Journal of Infection Control*, 46(5), 581–583.

O'Brien, T. P., Jeng, B. H., McDonald, M., & Raizman, M. B. (2009). Acute conjunctivitis: truth and misconceptions. *Current Medical Research and Opinion*, 25(8), 1953–1961.

Pelletier, J. S., Stewart, K., Trattler, W., Ritterband, D. C., Braverman, S., Samson, C. M., Capriotti, J. A. (2009). A combination povidone-iodine 0.4%/dexamethasone 0.1% ophthalmic suspension in the treatment of adenoviral conjunctivitis. *Advances in Therapy*, 26(8), 776–783.

Pepose, J. S., Ahuja, A., Liu, W., Narvekar, A., & Haque, R. (2018). Randomized, Controlled, Phase 2 Trial of Povidone-Iodine/Dexamethasone Ophthalmic Suspension for Treatment of Adenoviral Conjunctivitis. *American Journal of Ophthalmology*. Retrieved from https://doi.org/10.1016/j.ajo.2018.05.012

Pihos, A. M. (2013). Epidemic keratoconjunctivitis: A review of current concepts in management. *Journal of Optometry*, 6(2), 69–74.

Ramakrishnan, S., Vempati, J., & Baskaran, P. (2019). Randomized, Controlled, Phase 2 Trial of Povidone-Iodine/Dexamethasone Ophthalmic Suspension for the Treatment of Adenoviral Conjunctivitis. *American Journal of Ophthalmology*. Retrieved from https://doi.org/10.1016/j.ajo.2019.03.003

Reinhard, T., Godehardt, E., Pfahl, H.-G., & Sundmacher, R. (2000). Lokales Cyclosporin A bei Nummuli nach Keratoconjunctivitis epidemica Eine Pilotstudie. *Der Ophthalmologe: Zeitschrift der Deutschen Ophthalmologischen Gesellschaft*, 97(11), 764–768. Retrieved 28 May 2020 from

Rönnerstam, R., Persson, K., Hansson, H., & Renmarker, K. (1985). Prevalence of chlamydial eye infection in patients attending an eye clinic, a VD clinic, and in healthy persons. *The British Journal of Ophthalmology*, 69(5), 385–388.

Sambursky, R., Tauber, S., Schirra, F., Kozich, K., Davidson, R., & Cohen, E. J. (2006). The RPS adeno detector for diagnosing adenoviral conjunctivitis. *Ophthalmology*, 113(10), 1758–1764.

Smith, J. G., Wiethoff, C. M., Stewart, P. L., & Nemerow, G. R. (2010). Adenovirus. *Current Topics in Microbiology and Immunology*. Retrieved from https://doi.org/10.1007/82_2010_16

Tabbara, K. F., Omar, N., Hammouda, E., Akanuma, M., Ohguchi, T., Ariga, T., … Ohno, S. (2010). Molecular epidemiology of adenoviral keratoconjunctivitis in Saudi Arabia. *Molecular Vision*, 16, 2132–2136.

Tezcan Ülger, S., Bekçi, A., Yılmaz, A., & Aslan, G. (2019). [Detection and Molecular Characterization of Human Adenoviruses from Acute Conjunctivitis Cases]. *Mikrobiyoloji bulteni*, 53(3), 297–307.

Toth, K., Ying, B., Tollefson, A. E., Spencer, J. F., Balakrishnan, L., Sagartz, J. E., … Wold, W. S. M. (2015). Valganciclovir inhibits human adenovirus replication and pathology in permissive immunosuppressed female and male Syrian hamsters. *Viruses*, 7(3), 1409–1428.

Trinavarat, A., & Atchaneeyasakul, L.-O. (2012). Treatment of Epidemic Keratoconjunctivitis with 2% Povidone–Iodine: A Pilot Study. *Journal of Ocular Pharmacology and Therapeutics: The Official Journal of the Association for Ocular Pharmacology and Therapeutics*, 28(1), 53–58.

Uchio, E., Takeuchi, S., Itoh, N., Matsuura, N., Ohno, S., & Aoki, K. (2000). Clinical and epidemiological features of acute follicular conjunctivitis with special reference to that caused by herpes simplex virus type 1. *The British Journal of Ophthalmology*, 84(9), 968–972.

Ying, B., Tollefson, A. E., Spencer, J. F., Balakrishnan, L., Dewhurst, S., Capella, C., … Wold, W. S. M. (2014). Ganciclovir inhibits human adenovirus replication and pathogenicity in permissive immunosuppressed Syrian hamsters. *Antimicrobial Agents and Chemotherapy*, 58(12), 7171–7181.

Yousuf, M. A., Zhou, X., Mukherjee, S., Chintakuntlawar, A. V., Lee, J. Y., Ramke, M., … Rajaiya, J. (2013). Caveolin-1 associated adenovirus entry into human corneal cells. *PloS One*, 8(10), e77462.