

35. BÖLÜM

DİFERANSİYE TİROİD KANSERİNE YAKLAŞIM VE TAKİP

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GİRİŞ

Tiroid foliküler epitelinden kaynaklanan karsinomlar temelde, diferansiye ve non-diferansiye tiroid karsinomu olarak ikiye ayrılır. Diferansiye tiroid karsinomu (DTK), papiller tiroid karsinomu (PTK) ve foliküler tiroid karsinomu (FTK) alt ana başlıkları altında sınıflandırılır. Bu bölümde DTK tanılı hastaya yaklaşım, hastanın tedavi yönetimi ve takibi derlenmiştir.

Amerikan Tiroid Derneği (ATA) (1), Avrupa Tiroid Derneği (ETA), National Comprehensive Cancer Network (NCCN) (2) ve Türkiye Endokrinoloji ve Metabolizma Hastalıkları Derneği (TEMĐ) (3) konuyla ilgili kılavuzlar hazırlamışlardır. Bu bölümün yazımında yaygın kabul gören bu kılavuzlardan yararlanılmıştır.

PTK ve FTK'nin farklı histolojik özellikleri olmasına rağmen bu iki tümör için benzer tedavi stratejileri uygulanır. Prognozları benzerdir, ancak bazı alt histolojik tipleri kötü prognozlu olarak bilinmektedir (4,5).

DTK'nin primer tedavisi cerrahidir. Cerrahi sonrası TSH supresyon tedavisi ve endikasyonu varsa radyoaktifiyot (RAI) tedavisi uygulanır.

Cerrahi sonrası hastaların takibinin, tiroid kanseri konusunda uzmanlaşmış endokrinologlar tarafından yapılması önerilir.

CERRAHİ TEDAVİ

DTK için temel tedavi cerrahidir. Cerrahi ile hedeflenen, tiroid dokusunun veya bazı durumlarda cerrahi sınırı tümörsüz bırakacak şekilde tümör dokusunun tamamını ve varsa metastatik tüm lenf bezlerini çıkarmaktır.

Ancak son yıllarda seçilmiş bazı papiller mikrokanserlerin, opere edilmeksizin “aktif izlem stratejisi” ile takip edilebileceği tartışılmaktadır. Bu, sessiz seyredeceği düşünülen bir patolojiyi, tedaviye yönelik bir girişim yapılmaksızın düzenli aralıklarla izlem yöntemidir. Düşük riskli papiller mikrokarsinomların 5-10 yıllık takiplerinde genellikle sessiz ve sabit boyutta kaldığı ya da çok yavaş büyüdükleri gösterilmiştir, üstelik az sayıda hastada zaman içerisinde tümör boyutunda küçülme görülebilmektedir. Çalışmalarında hastaların takibinde %0,8-3,8 oranında lenf nodu metastazı saptanabilmektedir. Şu ana kadar bu gruptaki hastaların hiçbirisinde uzak metas-

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yüksek tümör nüksü riski ve kansere bağlı ölüm oranı ile ilişkili bir dizi risk faktör tanımlanmıştır. En önemli prognostik faktörler tanı yaşı, primer tümörün boyutu ve yumuşak doku invazyonunun veya uzak metastazların varlığıdır. PTK ile karşılaştırıldığında, FTK tipik olarak daha yaşlı hastalarda ortaya çıkar. Ek olarak, PTK'den daha agresif klinik seyir, uzak metastazlar ve daha yüksek mortalite ile ilişkilidir.

KAYNAKLAR

- Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, Schuff KG, Sherman SI, Sosa JA, Steward DL, Tuttle RM, Wartofsky L. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid*. 2016;26(1):1.
- https://www.nccn.org/professionals/physician_gls/default.aspx.
- https://temd.org.tr/admin/uploads/tbl_kilavuz/20200929134733-2020tbl_kilavuzf527c34496.pdf
- Asioli S, Erickson LA, Sebo TJ, Zhang J, Jin L, Thompson GB, Lloyd RV. Papillary thyroid carcinoma with prominent hobnail features: a new aggressive variant of moderately differentiated papillary carcinoma. A clinicopathologic, immunohistochemical, and molecular study of eight cases. *Am J Surg Pathol*. 2010 Jan;34(1):44-52.
- Ghossein RA, Leboeuf R, Patel KN, Rivera M, Katabi N, Carlson DL, Tallini G, Shaha A, Singh B, Tuttle RM. Tall cell variant of papillary thyroid carcinoma without extrathyroid extension: biologic behavior and clinical implications. *Thyroid*. 2007;17(7):655.
- Saravana-Bawan B, Bajwa A, Paterson J, McMullen T. Active surveillance of low-risk papillary thyroid cancer: a meta-analysis. *Surgery*. 2020;167(1):46-55. PMID: 31526581.
- Adam MA, Thomas S, Youngwirth L, Hyslop T, Reed SD, Scheri RP, Roman SA, Sosa JA. Is There a Minimum Number of Thyroidectomies a Surgeon Should Perform to Optimize Patient Outcomes? *Ann Surg*. 2017 Feb;265(2):402-407
- Lee DY, Seok J, Jeong WJ, Ahn SH. Prediction of thyroid hormone supplementation after thyroid lobectomy. *J Surg Res*. 2015 Jan;193(1):273-8. Epub 2014 Jul 5.
- Pujol P, Daures JP, Nsakala N, Baldet L, Bringer J, Jaffiol C. Degree of thyrotropin suppression as a prognostic determinant in differentiated thyroid cancer. *J Clin Endocrinol Metab*. 1996;81(12):4318.
- DS, Specker B, Ho M, Sperling M, Ladenson PW, Ross DS, Ain KB, Bigos ST, Brierley JD, Haugen BR, Klein I, Robbins J, Sherman SI, Taylor T, Maxon HR. Thyrotropin suppression and disease progression in patients with differentiated thyroid cancer: results from the National Thyroid Cancer Treatment Cooperative Registry. *Thyroid*. 1998;8(9):737.
- Jonklaas J, Sarlis NJ, Litofsky D, Ain KB, Bigos ST, Brierley JD, Cooper DS, Haugen BR, Ladenson PW, Magner J, Robbins J, Ross DS, Skarulis M, Maxon HR, Sherman SI. Outcomes of patients with differentiated thyroid carcinoma following initial therapy. *Thyroid*. 2006;16(12):1229
- Stall GM, Harris S, Sokoll LJ, Dawson-Hughes B. Accelerated bone loss in hypothyroid patients overtreated with L-thyroxine. *Ann Intern Med*. 1990;113(4):265.
- Sawin CT, Geller A, Wolf PA, Belanger AJ, Baker E, Bacharach P, Wilson PW, Benjamin EJ, D'Agostino RB. Low serum thyrotropin concentrations as a risk factor for atrial fibrillation in older persons. *N Engl J Med*. 1994;331(19):1249.
- Fazio S, Biondi B, Carella C, Sabatini D, Cittadini A, Panza N, Lombardi G, Saccà L. Diastolic dysfunction in patients on thyroid-stimulating hormone suppressive therapy with levothyroxine: beneficial effect of beta-blockade. *J Clin Endocrinol Metab*. 1995;80(7):2222.
- Tuttle RM, Leboeuf R. Follow up approaches in thyroid cancer: a risk adapted paradigm. *Endocrinol Metab Clin North Am*. 2008 Jun;37(2):419-35, ix-x.
- Tuttle RM, Tala H, Shah J, Leboeuf R, Ghossein R, Gonen M, Brokhin M, Omry G, Fagin JA, Shaha A. Estimating risk of recurrence in differentiated thyroid cancer after total thyroidectomy and radioactive iodine remnant ablation: using response to therapy variables to modify the in-

- itial risk estimates predicted by the new American Thyroid Association staging system. *Thyroid*. 2010;20(12):1341. Epub 2010 Oct 29.
17. Robenshtok E, Grewal RK, Fish S, Sabra M, Tuttle RM. A low postoperative nonstimulated serum thyroglobulin level does not exclude the presence of radioactive iodine avid metastatic foci in intermediate-risk differentiated thyroid cancer patients. *Thyroid*. 2013 Apr;23(4):436-42. Epub 2013 Mar 18.
 18. Ritter A, Mizrahi A, Bachar G, Vainer I, Shimon I, Hirsch D, Diker-Cohen T, Duskin-Bitan H, Robenshtok E. Detecting Recurrence Following Lobectomy for Thyroid Cancer: Role of Thyroglobulin and Thyroglobulin Antibodies. *J Clin Endocrinol Metab*. 2020;105(6)
 19. Leboulleux S, Girard E, Rose M, Travagli JP, Sabbah N, Caillou B, Hartl DM, Lassau N, Baudin E, Schlumberger M. Ultrasound criteria of malignancy for cervical lymph nodes in patients followed up for differentiated thyroid cancer. *J Clin Endocrinol Metab*. 2007;92(9):3590. Epub 2007 Jul 3.
 20. Robbins RJ, Wan Q, Grewal RK, Reibke R, Gonen M, Strauss HW, Tuttle RM, Drucker W, Larson SM. Real-time prognosis for metastatic thyroid carcinoma based on 2-[18F] fluoro-2-deoxy-D-glucose-positron emission tomography scanning. *J Clin Endocrinol Metab*. 2006;91(2):498. Epub 2005 Nov 22.
 21. van Tol KM, Jager PL, Piers DA, Pruim J, de Vries EG, Dullaart RP, Links TP. Better yield of (18) fluorodeoxyglucose-positron emission tomography in patients with metastatic differentiated thyroid carcinoma during thyrotropin stimulation. *Thyroid*. 2002;12(5):381.
 22. Wang H, Fu HL, Li JN, Zhou RJ, Hui Gu Z, Wu JC, Huang G. Comparison of whole-body 18F-FDG SPECT and posttherapeutic 131I scintigraphy in the detection of metastatic thyroid cancer. *Clin Imaging*. 2008;32(1):32.
 23. Peiling Yang S, Bach AM, Tuttle RM, Fish SA. Frequent screening with serial neck ultrasound is more likely to identify false-positive abnormalities than clinically significant disease in the surveillance of intermediate risk papillary thyroid cancer patients without suspicious findings on follow-up ultrasound evaluation. *J Clin Endocrinol Metab*. 2015;100(4):1561. Epub 2015 Jan 29.
 24. Torlontano M, Crocetti U, Augello G, D'Aloiso L, Bonfitto N, Varraso A, Dicembrino F, Modoni S, Frusciante V, Di Giorgio A, Bruno R, Filetti S, Trischitta V. Comparative evaluation of recombinant human thyrotropin-stimulated thyroglobulin levels, 131I whole-body scintigraphy, and neck ultrasonography in the follow-up of patients with papillary thyroid microcarcinoma who have not undergone radioiodine therapy. *J Clin Endocrinol Metab*. 2006;91(1):60. Epub 2005 Oct 11.
 25. Wang W, Larson SM, Tuttle RM, Kalaigian H, Kolbert K, Sonenberg M, Robbins RJ. Resistance of [18f]-fluorodeoxyglucose-avid metastatic thyroid cancer lesions to treatment with high-dose radioactive iodine. *Thyroid*. 2001;11(12):1169.
 26. Vassilopoulou-Sellin R, Schultz PN, Haynie TP. Clinical outcome of patients with papillary thyroid carcinoma who have recurrence after initial radioactive iodine therapy. *Cancer*. 1996;78(3):493.
 27. Hay ID, Charboneau JW. The coming of age of ultrasound-guided percutaneous ethanol ablation of selected neck nodal metastases in well-differentiated thyroid carcinoma. *J Clin Endocrinol Metab*. 2011 Sep;96(9):2717-20.
 28. Monchik JM, Donatini G, Iannuccilli J, Dupuy DE. Radiofrequency ablation and percutaneous ethanol injection treatment for recurrent local and distant well-differentiated thyroid carcinoma. *Ann Surg*. 2006;244(2):296.
 29. Eustatia-Rutten CF, Romijn JA, Guijt MJ, Vielvoye GJ, van den Berg R, Corssmit EP, Pereira AM, Smit JW. Outcome of palliative embolization of bone metastases in differentiated thyroid carcinoma. *J Clin Endocrinol Metab*. 2003;88(7):3184.
 30. Bernier MO, Leenhardt L, Hoang C, Aurengo A, Mary JY, Menegaux F, Enkaoua E, Turpin G, Chiras J, Saillant G, Hejblum G. Survival and therapeutic modalities in patients with bone metastases of differentiated thyroid carcinomas. *J Clin Endocrinol Metab*. 2001;86(4):1568.
 31. Chiu AC, Delpassand ES, Sherman SI. Prognosis and treatment of brain metastases in thyroid carcinoma. *J Clin Endocrinol Metab*. 1997;82(11):3637.
 32. Porterfield JR, Cassivi SD, Wigle DA, Shen KR, Nichols FC, Grant CS, Allen MS, Deschamps C. Thoracic metastasectomy for thyroid malignancies. *Eur J Cardiothorac Surg*. 2009;36(1):155.
 33. Muresan MM, Olivier P, Leclère J, Sirveaux F, Brunaud L, Klein M, Zarnegar R, Weryha G. Bone metastases from differentiated thyroid carcinoma. *Endocr Relat Cancer*. 2008;15(1):37.
 34. National Comprehensive Cancer Network (NCCN) guidelines. Available at: <http://www.nccn.org>

nccn.org/professionals/physician_gls/f_guidelines.asp (Accessed on September 14, 2011).

35. Ma C, Kuang A, Xie J. Radioiodine therapy for differentiated thyroid carcinoma with thyroglobulin positive and radioactive iodine negative metastases. *Cochrane Database Syst Rev*. 2009.
36. Pachucki J, Burmeister LA. Evaluation and treatment of persistent thyroglobulinemia in patients with well-differentiated thyroid cancer. *Eur J Endocrinol*. 1997;137(3):254.
37. Toubert ME, Cyna-Gorse F, Zagdanski AM, Noel-Wekstein S, Cattani P, Billotey C, Sarfati E, Rain JD. Cervicomedial magnetic resonance imaging in persistent or recurrent papillary thyroid carcinoma: clinical use and limits. *Thyroid*. 1999;9(6):591.
38. Baudin E, Schlumberger M, Lombroso J, Travagli JP, Caillou B, Parmentier C. Octreotide scintigraphy in patients with differentiated thyroid carcinoma: contribution for patients with negative radioiodine scan. *J Clin Endocrinol Metab*. 1996;81(7):2541.
39. Khan N, Oriuchi N, Higuchi T, Zhang H, Endo K. PET in the follow-up of differentiated thyroid cancer. *Br J Radiol*. 2003;76(910):690.
40. Denise P, Momesso R, Michael Tuttle. Update on differentiated thyroid cancer staging. *Endocrinol Metab Clin North Am*. 2014 Jun;43(2):401-21.