



BÖLÜM 2

NORMAL TİROİD DOKUSU VE TİROİD PATOLOJİSİNE GİRİŞ

Yazgı KÖY¹

1. NORMAL TİROİD

Normal yetişkin tiroid bezi kelebek şeklinde, ince bir isthmus ile birbirine bağlı iki lateral lobdan oluşur(Resim 1). Her bir lateral lob 2-2.5 cm genişliğinde, 5-6 cm uzunluğunda ve 2 cm derinliğindedir. Piramidal lob tiroglossal kanalın kalınlığı olarak yaklaşık %40 oranında görülür.



Resim 1. Normal tiroid bezinin makroskopik görünümü (Dr.Yazgı Köy arşivi)

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Medüller karsinom, tek nodül ya da tiroidin her iki lobunda mutipl nodüller şeklinde görülebilir. Multisentrik lezyonlar ailesel olgularda daha sık görülür. Mikroskopik olarak; yuvalar, trabeküller oluşturan, poligonal ya da iğsi morfolojide hücrelerden oluşur. Olguların çoğunda amiloid birikimi görülür. Tümör hücrelerinin sitoplazmasında ve stromasında Kalsitonin varlığı immunhistokimya ile gösterilebilir. Ailesel olgularda sporadik olanların aksine komşu dokuda C hücre hiperplazisi odakları bulunur.

Klinik olarak sıklıkla boyunda kitle, nadiren de ses kısıklığı veya yutma güçlüğü ile bulgu verir. Bazen salgılanan peptidlere bağlı bulgular (vazoaktif intestinal peptide bağlı diyare) görülebilir.

Ailesel olgularda kalsitonin düzeylerinin veya RET mutasyonunun taranması erken tanı alınmasını sağlar. Ayrıca MEN 2 sendromlu ailelerde RET mutasyonu taşıyan bireylere profilaktik tiroidektomi de önerilmektedir(3).

KAYNAKLAR

1. Hegedus L, Perrild H, Poulsen LR, et al. The determination of thyroid volume by ultrasound and its relationship to body weight, age, and sex in normal subjects. *The Journal of Clinical Endocrinology and Metabolism*. 1983;56:260–263.
2. Hegedus L, Karstrup S, Rasmussen N. Evidence of cyclic alterations of thyroid size during the menstrual cycle in healthy women. *The American Journal of Obstetrics and Gynecology*. 1986;155:142–145.
3. Kumar, V., Abbas, A. K., & Aster, J. C. Robbins Temel Patoloji (Sıtkı Tuzlalı, Mine Güllüoğlu, Çev. ed.). Ankara. Güneş Kitabevi; 2017.
4. Feind C. The head and neck. In: Haagensen CD, Feind C, Herter FP, Slanetz CA Jr, Weinberg JA, eds. *The Lymphatics in Cancer*. Philadelphia, PA: WB Saunders; 1972:59– 222.
5. Boerner SL, Asa SL. Tiroid Biyopsilerinin Yorumu. (Filiz Özyılmaz, Çev. Ed.). İstanbul: Nobel Kitabevi; 2015.
6. Bell CD, Kovacs K, Horvath E, et al. Histologic, immunohistochemical, and ultrastructural findings in a case of minocycline-associated “black thyroid”. *Endocrine Pathology*. 2001; 12:443–451.
7. Wolfe HJ, Voelkel EF, Tashjian AH Jr. Distribution of calcitonin-containing cells in the normal adult human thyroid gland: a correlation of morphology with peptide content. *The Journal of Clinical Endocrinology and Metabolism*. 1974 Apr;38(4):688-94. doi: 10.1210/jcem-38-4-688.
8. de Lellis RA, Wolfe HJ. The pathobiology of the human calcitonin (C)-cell: a review. *Pathology Annual*. 1981;16(Pt 2):25-52.
9. Harach HR. Histological markers of solid cell nests of the thyroid. With some emphasis on their expression in thyroid ultimobranchial-related tumors. *Acta Anatomica*. 1985;124(1-2):111-6.
10. Beckner ME, Shultz JJ, Richardson T. Solid and cystic ultimobranchial body remnants in the thyroid. *Archives of Pathology & Laboratory Medicine*. 1990 Oct;114(10):1049-52.
11. McNicol AM, Lewis PD (1996) The endocrine system. In: Lewis PD (ed) *Systemic pathology*. Churchill Livingstone, Edinburgh, pp 131–185.
12. Organ GM, Organ CH Jr Thyroid gland and surgery of the thyroglossal duct: exercise in applied embryology. *World Journal of Surgery*. 2000; 24(8):886–890.

13. Murray D (1998) The thyroid gland. In: Kalman K, Asa SL (eds) Functional endocrine pathology, 2nd edn. Blackwell, Oxford, UK, pp 295–380.
14. Lloyd RV, Douglas BR, Young WF. (2002) Thyroid gland. In: Atlas of non-tumor pathology: endocrine diseases (First series Fascicle 1). Armed Forces Institute of Pathology, Washington DC, pp 91–169.
15. Yoon JS, Won KC, Cho IH, Lee JT, Lee HW Clinical characteristics of ectopic thyroid in Korea. *Thyroid*. 2007; 17(11):1117–1121.
16. Zieren J, Paul M, Scharfenberg M, Menenakos C. Submandibular ectopic thyroid gland. *Journal of Craniofacial Surgery*. 2006; 17(6): 1194–1198.
17. Jamshidi M, Kasirye O, Smith DJ Ectopic thyroid nodular goiter presenting as a porta hepatis mass. *American Surgeon*. 1998; 64(4):305–306.
18. Pistono M, Occhetta E, Sarasso G et al Intracardiac ectopic thyroid: a report of a clinical case with a long-term follow-up. *Cardiologia*. 1999;44(1):83–88.
19. Pollice L, Caruso G. Struma cordis. Ectopic thyroid goiter in the right ventricle. *Archives of Pathology & Laboratory Medicine*. 1986; 110(5):452–453.
20. Curtis LE, Sheahan DG. Heterotopic tissues in the gallbladder. *Archives of Pathology*. 1969; 88(6):677–683.
21. Kurman RJ, Prabha AC. Thyroid and parathyroid glands in the vaginal wall: report of a case. *American Journal of Clinical Pathology*; 59(4):503–507.
22. Ruchti C, Balli-Antunes M, Gerber HA. Follicular tumor in the sellar region without primary cancer of the thyroid. Heterotopic carcinoma?. *American Journal of Clinical Pathology*. 1987; 87(6):776–780
23. Baloch ZW, Livolsi V (2002) Pathology of thyroid gland. In: Livolsi V, Asa SL (eds) Endocrine pathology. Churchill Livingstone, Philadelphia, pp 61–88.
24. Gerard-Marchant R. Thyroid follicle inclusions in cervical lymph nodes. *Archives of Pathology*. 1964 77:633–637.
25. Roth LM. Inclusions of non-neoplastic thyroid tissue within cervical lymph nodes. *Cancer*. 1965; 18:105–111
26. Arabi A, Zayour D, Salti I. Papillary carcinoma arising in a thyroglossal duct cyst; two case reports and review of the literature. *International Surgery*. 2007; 92(6):327–330.
27. Hilger AW, Thompson SD, Smallman LA, Watkinson JC. Papillary carcinoma arising in a thyroglossal duct cyst: a case report and literature review. *The Journal of Laryngology & Otology*. 1995;109(11):1124–1127.
28. Martin-Perez E, Larranaga E, Marron C et al. Primary papillary carcinoma arising in a thyroglossal duct cyst. *European Journal of Surgery*. 1997; 163(2):143–145.
29. McNicoll MP, Hawkins DB, England K et al. Papillary carcinoma arising in a thyroglossal duct cyst. *Otolaryngology- Head & Neck Surgery*. 1988;99(1):50–54.
30. Patel SG, Escrig M, Shaha AR et al. Management of well-differentiated thyroid carcinoma presenting within a thyroglossal duct cyst. *Journal of Surgical Oncology*. 2002; 79(3):134–139 discussion 40–41.
31. Patti G, Ragni G, Calisti APapillary thyroid carcinoma in a thyroglossal duct cyst in a child. *Medical and Pediatric Oncology*. 2000; 34(1):67–69
32. Plaza CP, Lopez ME, Carrasco CE et al. Management of well-differentiated thyroglossal remnant thyroid carcinoma: time to close the debate? Report of five new cases and proposal of a definitive algorithm for treatment. *Annals of Surgical Oncology*. 2006; 13(5):745–752.
33. Samara C, Bechrakis I, Kavadias S et al. Thyroglossal duct cyst carcinoma: case report and review of the literature, with emphasis on CT findings. *Neuroradiology*. 2001;43(8):647–649.
34. Berni Canani F, Dall’Olio D, Chiarini V et al. Papillary carcinoma of a thyroglossal duct cyst in a patient with thyroid hemiagenesis: effectiveness of conservative surgical treatment. *Endocrine Practice*. 2008;14(4):465–469.

35. Tovi F, Fliss DM, Inabar-Yanai I. Hurthle cell adenoma of the thyroglossal duct. *Otolaryngology- Head & Neck Surgery*. 1988; 10:346–349.
36. Nussbaum M, Buchwald RP, Ribner A et al. Anaplastic carcinoma arising from median ectopic thyroid (thyroglossal duct remnant). *Cancer*. 1981; 48(12):2724–2728.
37. Sawin C. The heritage of the thyroid. In: Braverman LE, Utiger RD (eds) Werner and Ingbar's the thyroid: a fundamental and clinical text. Lippincott Williams & Wilkins, Philadelphia, 2000. pp 3–6.
38. Brent GA. Clinical practice. Graves' disease. *The New England Journal of Medicine*. 2008; 358(24):2594–2605 .
39. Davies T. The pathogenesis of Graves' disease. In: Braverman LE, Utiger RD (eds) Werner and Ingbar's the thyroid: a fundamental and clinical text. Lippincott-Raven, Philadelphia, 1996 pp 525–536.
40. Dai G, Levy O, Carrasco N. Cloning and characterization of the thyroid iodide transporter. *Nature*. 1996; 379(6564):458.
41. Zakarija M. Transient neonatal hypothyroidism: characterization of maternal antibodies to the thyrotropin receptor. *The Journal of Clinical Endocrinology & Metabolism*. 1990; 70(5):1239–1246.
42. Martin A. Successful production of intrathyroidal human T cell hybridomas: evidence for intact helper T cell function in Graves' disease. *The Journal of Clinical Endocrinology & Metabolism*. 1989; 69(6):1104–1108.
43. Watson PF. Analysis of cytokine gene expression in Graves' disease and multinodular goiter. *The Journal of Clinical Endocrinology & Metabolism*. 1994; 79(2):355–360.
44. Burch HB, Nagy EV, Lukes YG et al. Nucleotide and amino acid homology between the human thyrotropin receptor and the HIV-1 Nef protein: identification and functional analysis. *Biochemical and Biophysical Research Communications*. 1991; 181(1):498–505.
45. Londei M, Lamb JR, Bottazzo GF et al. Epithelial cells expressing aberrant MHC class II determinants can present antigen to cloned human T cells. *Nature*. 1984; 312(5995):639–641.
46. Muixi L, Alvarez I, Jaraquemada D. Peptides presented in vivo by HLA-DR in thyroid autoimmunity. *Advances in Immunology*. 2008 99:165–209.
47. Burman KD, Baker JR Jr. Immune mechanisms in Graves' disease. *Endocrine Reviews*. 1985; 6(2):183–232.
48. Paschke R, Schuppert F, Taton M et al. Intrathyroidal cytokine gene expression profiles in autoimmune thyroiditis. *Journal of Endocrinology*. 1994; 141(2):309–315.
49. Belfiore A, Garofalo MR, Giuffrida D et al. Increased aggressiveness of thyroid cancer in patients with Graves' disease. *The Journal of Clinical Endocrinology & Metabolism*. 1990; 70(4):830–835.
50. Vander JB, Gaston EA, Dawber TR. The significance of nontoxic thyroid nodules. Final report of a 15-year study of the incidence of thyroid malignancy. *Annals of Internal Medicine*. 1968; 69(3):537–540.
51. Dobyns BM, Sheline GE, Workman JB et al. Malignant and benign neoplasms of the thyroid in patients treated for hyperthyroidism: a report of the cooperative thyrotoxicosis therapy follow-up study. *The Journal of Clinical Endocrinology & Metabolism*. 1974; 38(6):976–998.
52. Belfiore A, Russo D, Vigneri R et al. Graves'disease, thyroid nodules and thyroid cancer. *Clinical Endocrinology*. 2001; 55(6): 711–718.
53. Giles Senyurek Y, Fatih T, Harika B. The risk factors for malignancy in surgically treated patients for Graves' disease, toxic multinodular goiter, and toxic adenoma. *Surgery*. 2008; 144(6):1028–1036 discussion 36–37.
54. Farwell AP. Infectious thyroiditis. In: Braverman LE, Utiger RD (eds) Werner and Ingbar's the thyroid: a fundamental and clinical text, 8th edn. Lippincott Williams & Wilkins, Philadelphia, 2000 pp 1044–1050.

55. Carnell NE, Valente WA. Thyroid nodules in Graves' disease: classification, characterization, and response to treatment. *Thyroid*. 1998; 8(8):647–652.
56. Chang DC, Wheeler MH, Woodcock JP et al. The effect of preoperative Lugol's iodine on thyroid blood flow in patients with Graves' hyperthyroidism. *Surgery*. 1987; 102(6):1055–1061.
57. Farwell AP, Braverman LE. Inflammatory thyroid disorders. *Otolaryngologic Clinics of North America*. 1996; 29(4):541–556.
58. Weetman A. Chronic autoimmune thyroiditis. In: Braverman LE, Utiger RD (eds) Werner and Ingbar's the thyroid: a fundamental and clinical text, 8th edn. Lippincott Williams & Wilkins, Philadelphia, 2000. pp 721–732
59. del Prete GF. Cytolytic T lymphocytes with natural killer activity in thyroid infiltrate of patients with Hashimoto's thyroiditis: analysis at clonal level. *The Journal of Clinical Endocrinology & Metabolism*. 1986; 62(1):52–57.
60. Burman P. Thyroid autoimmunity in patients on long term therapy with leukocyte-derived interferon. *The Journal of Clinical Endocrinology & Metabolism*. 1986; 63(5):1086–1090.
61. Chopra IJ, Solomon DH, Chopra U et al. Abnormalities in thyroid function in relatives of patients with Graves' disease and Hashimoto's thyroiditis: lack of correlation with inheritance of HLA-B8. *The Journal of Clinical Endocrinology & Metabolism*. 1977;45(1):45–54.
62. Doniach D, Bottazzo GF, Russell RC.) Goitrous autoimmune thyroiditis (Hashimoto's disease). *The Journal of Clinical Endocrinology & Metabolism*. 1979; 8(1):63–80.
63. Ewins DL, Rossor MN, Butler J et al. Association between autoimmune thyroid disease and Familial Alzheimers disease. *Clinical Endocrinology*. 1991; 35(1):93–96.
64. Kennedy RL, Jones TH, Cuckle HS. Down's syndrome and the thyroid. *Clinical Endocrinology*. 1992; 37(6):471–476.
65. Roitt IM, Doniach D. A reassessment of studies on the aggregation of thyroid autoimmunity in families of thyroiditis patients. *Clinical & Experimental Immunology*. 1967; 2(Suppl):727.
66. Shalitin S, Phillip M. Autoimmune thyroiditis in infants with Down's syndrome. *Journal of Pediatric Endocrinology and Metabolism*. 2002; 15(5):649–652.
67. Emerson CH, Farwell AP. Sporadic silent thyroiditis, post- partum thyroiditis, and subacute thyroiditis. In: Braverman LE, Utiger RD (eds) Werner and Ingbar's the thyroid: a fundamental and clinical text. Lippincott, Williams & Wilkins, Philadelphia, 2000. pp 578–589
68. Daniels GH. Atypical subacute thyroiditis: preliminary observations. *Thyroid*. 2001; 11(7):691–695.
69. Volta C, Carano N, Street ME et al. Atypical subacute thyroiditis caused by Epstein–Barr virus infection in a three- year-old girl. *Thyroid*. 2005; 15(10):1189–1191.
70. Obuobie K, Al-Sabah A, Lazarus JH. Subacute thyroiditis in an immunosuppressed patient. *The Journal of Endocrinological Investigation*. 2002; 25(2): 169–171.
71. Sherman SI, Ladenson PW. Subacute thyroiditis causing thyroid storm. *Thyroid*. 2007; 17(3):283.
72. Benker G, Olbricht T, Windeck R et al. The sonographical and functional sequelae of de Quervain's subacute thyroiditis: long-term follow-up. *Acta Endocrinologica (Copenh)*. 1988: 117(4):435–441.
73. De Pauw BE, de Rooy HA. De Quervain's subacute thyroiditis. A report on 14 cases and a review of the literature. *The Netherlands Journal of Medicine*. 1975; 18(2):70–78.
74. Hay ID. Thyroiditis: a clinical update. *Mayo Clinic Proceedings*. 1985; 60(12):836–843.
75. Singer P. Primary hypothyroidism due to other causes. In: Braverman LE, Utiger RD (eds) Werner and Ingbar's the thyroid: a fundamental and clinical text, 8th edn. Lippincott Williams & Wilkins, Philadelphia, 2000. pp 755–761
76. De Lange WE, Freling NJM, Molenaar WM et al. Invasive fibrous thyroiditis (Riedel's struma): a manifestation of multifocal fibrosclerosis? a case report with review of the literature. *The Quarterly Journal of Medicine*. 1989; 72(2):709–717.

77. Best TB, Munro RE, Burwell S, Volpe R () Riedel's thyroiditis associated with Hashimoto's thyroiditis, hypoparathyroidism, and retroperitoneal fibrosis. *The Journal of Endocrinological Investigation*. 1991; 14(9):767-772.
78. Ozgen A, Cila A. Riedel's thyroiditis in multifocal fibrosclerosis: CT and MR imaging findings. *American Journal of Neuroradiology*. 2000; 21(2):320-321.
79. Roti E, Uberti E. Post-partum thyroiditis – a clinical update. *European Journal of Endocrinology*. 2002; 146(3):275-279.
80. Lucas A, Pizarro E, Granada ML et al. Postpartum thyroiditis: long-term follow-up. *Thyroid*. 2005; 15(10):1177-1181.
81. Volpe R. Is silent thyroiditis an autoimmune disease? *Archives of Internal Medicine*. 1988; 148(9):1907-1908.
82. Mittra ES, McDougall IR. Recurrent silent thyroiditis: a report of four patients and review of the literature. *Thyroid*. 2007; 17(7):671-675.
83. Chung DH, Kang GH, Kim WH et al. Clonal analysis of a solitary follicular nodule of the thyroid with the polymerase chain reaction method. *Modern Pathology*. 1999; 12(3):265-271.
84. Stassi G, Todaro M, Bucchieri F et al. Fas/Fas ligand-driven T cell apoptosis as a consequence of ineffective thyroid immuno- privilege in Hashimoto's thyroiditis. *The Journal of Immunology*. 1999; 162(1):263-267.
85. Perez-Montiel MD, Suster S. The spectrum of histologic changes in thyroid hyperplasia: a clinicopathologic study of 300 cases. *Human Pathology*. 2008; 39(7):1080-1087.
86. Abu-Eshy SA, Khan AR, Khan GM et al. Thyroid malignancy in multinodular goitre and solitary nodule. *Journal of the Royal College of Surgeons of Edinburgh*. 1995; 40(5):310-312.
87. Belfiore A, La Rosa GL, La Porta GA et al. Cancer risk in patients with cold thyroid nodules: relevance of iodine intake, sex, age, and multinodularity. *The American Journal of Medicine*. 1992; 93(4):363-369.
88. McCall A, Jarosz H, Lawrence AM et al. The incidence of thyroid carcinoma in solitary cold nodules and in multinodular goiters. *Surgery*. 1986; 100(6):1128-1132.
89. Mishra A, Agarwal A, Agarwal G, et al. Total thyroidectomy for benign thyroid disorders in an endemic region. *World Journal of Surgery*. 2001; 25(3):307-310.
90. Sachmechi I, Miller E, Varatharajah R et al. Thyroid carcinoma in single cold nodules and in cold nodules of multinodular goiters. *Endocrine Practice*. 2000; 6(1):5-7.
91. Adeniran AJ, Zhu Z, Gandhi M et al. Correlation between genetic alterations and microscopic features, clinical manifestations, and prognostic characteristics of thyroid papillary carcinomas. *American Journal of Surgical Pathology*. 2006; 30(2):216-222.
92. Small PK, Smith D. Sporadic medullary thyroid carcinoma associated with toxic multinodular goitre. *Journal of the Royal College of Surgeons of Edinburgh*. 1997; 42(3):199-200.
93. Hundahl SA, Cady B, Cunningham MP et al. Initial results from a prospective cohort study of 5583 cases of thyroid carcinoma treated in the United States during 1996. U.S. and German Thyroid Cancer Study Group. An American College of Surgeons Commission on Cancer Patient Care Evaluation study. *Cancer*. 2000; 89(1):202-217.
94. Boelaert K, Horacek J, Holder RL et al. Serum thyrotropin concentration as a novel predictor of malignancy in thyroid nodules investigated by fine- needle aspiration. *The Journal of Clinical Endocrinology & Metabolism*. 2006; 91(11):4295-4301.
95. Grodski S, Brown T, Sidhu S et al. Increasing incidence of thyroid cancer is due to increased pathologic detection. *Surgery*. 2008; 144(6):1038-1043 discussion 43.
96. Leenhardt L, Bernier MO, Boin-Pineau MH et al. Advances in diagnostic practices affect thyroid cancer incidence in France. *European Journal of Endocrinology*. 2004; 150(2):133-139.
97. Leenhardt L, Grosclaude P, Cherie-Challine L. Increased incidence of thyroid carcinoma in France: a true epidemic or thyroid nodule management effects? Report from the French Thyroid Cancer Committee. *Thyroid*. 2004; 14(12):1056-1060.

98. Kuma K, Matsuzuka F, Kobayashi A et al. Outcome of long standing solitary thyroid nodules. *World Journal of Surgery*. 1992; 16(4):583–587 discussion 7–8.
99. Logani S, Gupta PK, LiVolsi VA et al. Thyroid nodules with FNA cytology suspicious for follicular variant of papillary thyroid carcinoma: follow-up and management. *Diagnostic Cytopathology*. 2000; 23(6):380–385.
100. Tonacchera M, Chiovato L, Pinchera A et al. Hyperfunctioning thyroid nodules in toxic multinodular goiter share activating thyrotropin receptor mutations with solitary toxic adenoma. *The Journal of Clinical Endocrinology & Metabolism*. 1998; 83(2):492–498.
101. Parma J, Duprez L, Van Sande J et al. Somatic mutations in the thyrotropin receptor gene cause hyperfunctioning thyroid adenomas. *Nature* 1993; 365(6447):649–651.
102. Livolsi V. Surgical pathology of the thyroid. Saunders, Philadelphia.1990.
103. Lloyd RV, Osamura RY, Kloppel G et al. WHO classification of tumours of endocrine organs. 4th ed. Lyon: International Agency for Research on Cancer (IARC); 2017. pp. 65–143.
104. Ruben Harach H. Familial nonmedullary thyroid neoplasia. *Endocrine Pathology*. 2001; 12(2):97–112.
105. Hay ID. Papillary thyroid carcinoma. *Endocrinology and Metabolism Clinics of North America*. 19(3):545–576.