

## Bölüm 22

# Testiküler Tümörler ve Paraneoplastik Sendromlar

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### GİRİŞ

Testis kanserleri, tüm erkeklerde görülen kanserlerin yalnızca %1'ini temsil etmekle beraber, 15-35 yaş arasındaki erkeklerin en sık görülen kanser türrüdür.<sup>1</sup> Amerika Birleşik Devletlerinde yılda 9000'den fazla vaka görülmekte ve 460 bireyin ölümüne neden olmaktadır. Testis tümörlerinin iki ana kategorisi, vakaların yüzde 95'ini oluşturan germ hücreli tümörler (GHT) ve seks kord-stromal tümörler(SKST)'dır.<sup>2</sup> (**Tablo 1**)

Saf seminomlar, tüm testis GHT'lerin yaklaşık %50 sinı oluşturur ve miks GHT'lerin yaklaşık %20'sinde seminom bileşeni bulunur.<sup>3,4</sup> Testis kanserine özgü serum tümör belirteçleri seminomlarda genellikle normaldir, ancak insan koryonik gonadotropin beta subünniti (Beta-HCG) dağınık sinsityotrofoblastik dev hücreler içeren tümörlerde hafif (<100 mIU/mL) yükseltebilir. Saf seminomlu hastalar arasından metastatik hastalığı bulunanlarda yüzde 15 ila 20'sinde yükselmiş serum beta-hCG saptanmıştır.<sup>5</sup> Serum beta-hCG'deki artış öncelikle daha yüksek tümör yükü ile koloredir, ancak metastatik bir hastalığı predikte etmez.<sup>6</sup> Bu nedenle erken evre seminomlu bir hastada orsiekktomi sonrası normale dönen serum beta-hCG yüksekliği ilerlemiş hastalığı ekarte ettirebilir.

Anaplastik seminom terimi Dünya Sağlık Örgütü (WHO) tarafından artık kullanılmamaktadır. Sınıflandırmadaki bu değişikliğin altında, daha önce "anaplastik seminomlar" olarak adlandırılan tümörlerin, modern tedavi ile birlikte klasik seminomlarla benzer tedavi sonuçlarına sahip olması yatkın-

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kadarı, klinik olarak palpe edilebilen bir tümör olsun veya olmasın, başvuru anında jinekomasti bulunabilmektedir.<sup>59</sup> Palpe edilebilen leydig hücreli tümörlerin %15-16'sı da jinekomasti görülmektedir.<sup>60</sup>

## DİĞER SENDROMLAR

Mutlak eritrositoz, kan hematokrit düzeyi ile birlikte eritrosit kitlesindeki artması olarak tanımlanır. Polistemia Vera'ya bağlı olanlar primer ve Eritropoetin üreten faktörlere bağlı (GHT, hipoksi) gelişenler sekonder olarak tanımlanmaktadır.<sup>61,62</sup> Testis kanserine bağlı membranöz glomeronefrit ve ürtikelyalı vaskülit vakaları literatürde bulunmaktadır.<sup>63,64</sup>

## KAYNAKLAR

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021;71(3):209-249.
2. Moch H, Cubilla AL, Humphrey PA, Reuter VE, Ulbright TM. The 2016 WHO classification of tumours of the urinary system and male genital organs—part A: renal, penile, and testicular tumours. *Eur Urol.* 2016;70(1):93-105.
3. Jacobsen GK, Barlebo H, Olsen J, et al. Testicular germ cell tumours in Denmark 1976–1980 pathology of 1058 consecutive cases. *Acta Radiol Oncol.* 1984;23(4):239-247.
4. Ulbright TM. Tumors of the testis, adnexa, spermatic cord and scrotum. *Armed Forces Inst Pathol.* Published online 1999:59-85.
5. Gilligan TD, Seidenfeld J, Basch EM, et al. American Society of Clinical Oncology Clinical Practice Guideline on uses of serum tumor markers in adult males with germ cell tumors. *J Clin Oncol.* 2010;28(20):3388-3404.
6. Hori K, Uematsu K, Yasoshima H, Yamada A, Sakurai K, Ohya M. Testicular seminoma with human chorionic gonadotropin production. *Pathol Int.* 1997;47(9):592-599.
7. Reddy EK, Burke M, Giri S, et al. Testicular neoplasms: seminoma. *J Natl Med Assoc.* 1990;82(9):651.
8. Stein M, Dale J, Kuten A, Moshkowitz B. Anaplastic seminoma and spermatocytic seminoma—a retrospective analysis. *S Afr J Surg.* 1993;31(4):144-146.
9. Mostofi FK, Sesterhenn IA, Davis Jr CJ. Developments in histopathology of testicular germ cell tumors. In: *Seminars in Urology.* Vol 6. ; 1988:171-188.
10. Talerman A, Haije WG, Baggerman L. Serum alphafetoprotein (AFP) in patients with germ cell tumors of the gonads and extragonadal sites: correlation between endodermal sinus (yolk sac) tumor and raised serum AFP. *Cancer.* 1980;46(2):380-385.
11. Pohl HG, Shukla AR, Metcalf PD, et al. Prepubertal testis tumors: actual prevalence rate of histological types. *J Urol.* 2004;172(6 Part 1):2370-2372.
12. Brown NJ. Yolk-sac tumor (“teratoma”) and other testicular tumours of childhood. *Pathol Testis.* Published online 1976:356-366.
13. Westhoff C, Pike M, Vessey M. Benign ovarian teratomas: a population-based case-control study. *Br J Cancer.* 1988;58(1):93-98.

14. Comerci Jr JT, Licciardi F, Bergh PA, Gregori C, Breen JL. Mature cystic teratoma: a clinicopathologic evaluation of 517 cases and review of the literature. *Obstet Gynecol.* 1994;84(1):22-28.
15. Cheville JC, Sebo TJ, Lager DJ, Bostwick DG, Farrow GM. Leydig cell tumor of the testis: a clinicopathologic, DNA content, and MIB-1 comparison of nonmetastasizing and metastasizing tumors. *Am J Surg Pathol.* 1998;22(11):1361-1367.
16. Dilworth JP, Farrow GM, Oesterling JE. Non-germ cell tumors of testis. *Urology.* 1991;37(5):399-417.
17. Ulbright TM. The most common, clinically significant misdiagnoses in testicular tumor pathology, and how to avoid them. *Adv Anat Pathol.* 2008;15(1):18-27.
18. Jimenez-Quintero LP, Ro JY, Zavala-Pompa A, et al. Granulosa cell tumor of the adult testis: a clinicopathologic study of seven cases and a review of the literature. *Hum Pathol.* 1993;24(10):1120-1126.
19. GARRETT JE, CARTWRIGHT PC, SNOW BW, COFFIN CM. Cystic testicular lesions in the pediatric population. *J Urol.* 2000;163(3):928-936.
20. Young RH. WHO classification of tumours of female reproductive organs. Published online 2014.
21. Ulbright TM, Young RH. *Tumors of the Testis and Adjacent Structures.* Amer Registry of Pathology; 2013.
22. Scully RE. Gonadoblastoma. A review of 74 cases. *Cancer.* 1970;25(6):1340-1356.
23. Wang Q, Zheng D, Chai D, et al. Primary testicular diffuse large B-cell lymphoma: Case series. *Medicine (Baltimore).* 2020;99(12).
24. Vähämrö P. Aggressive B-cell lymphomas of sinonasal tract and testis: clinical manifestations and treatment outcome. *Diss Sch Dr ad Sanit Investig Univ Hels.* Published online 2020.
25. Gaynon PS, Qu RP, Chappell RJ, et al. Survival after relapse in childhood acute lymphoblastic leukemia: Impact of site and time to first relapse the Children's Cancer Group experience. *Cancer Interdiscip Int J Am Cancer Soc.* 1998;82(7):1387-1395.
26. Bennett JL, Galetta SL, Frohman LP, et al. Neuro-ophthalmologic manifestations of a paraneoplastic syndrome and testicular carcinoma. *Neurology.* 1999;52(4):864.
27. Hoffmann LA, Jarius S, Pellkofer HL, et al. Anti-Ma and anti-Ta associated paraneoplastic neurological syndromes: 22 newly diagnosed patients and review of previous cases. *J Neurol Neurosurg Psychiatry.* 2008;79(7):767-773.
28. Mathew RM, Vandenberghe R, Garcia-Merino A, et al. Orchiectomy for suspected microscopic tumor in patients with anti-Ma2-associated encephalitis. *Neurology.* 2007;68(12):900-905.
29. Mandel-Brehm C, Dubey D, Kryzer TJ, et al. Kelch-like protein 11 antibodies in seminoma-associated paraneoplastic encephalitis. *N Engl J Med.* 2019;381(1):47-54.
30. Maudes E, Landa J, Muñoz-Lopetegi A, et al. Clinical significance of Kelch-like protein 11 antibodies. *Neurol Neuroinflammation.* 2020;7(3).
31. Kayser MS, Titulaer MJ, Gresa-Arribas N, Dalmau J. Frequency and characteristics of isolated psychiatric episodes in anti-N-methyl-d-aspartate receptor encephalitis. *JAMA Neurol.* 2013;70(9):1133-1139.
32. Guasp M, Giné-Servén E, Maudes E, et al. Clinical, neuroimmunologic, and CSF investigations in first episode psychosis. *Neurology.* 2021;97(1):e61-e75.
33. Lancaster E, Martinez-Hernandez E, Dalmau J. Encephalitis and antibodies to synaptic and neuronal cell surface proteins. *Neurology.* 2011;77(2):179-189.
34. Clayton AJ, Mead GM. Germ cell cancer and dermatomyositis. *Clin Oncol.* 1998;10(1):56-58.

35. Curiel R V, Brindle KA, Kressel BR, Katz JD. Clinical images: Dysphagia after testicular cancer. *Arthritis Rheum.* 2005;52(12):3712.
36. Fujiwara Y, Fukuda N, Ohmoto A, et al. An extragonadal germ cell tumor with dermatomyositis: A case report and literature review. *Mol Clin Oncol.* 2020;13(5):1.
37. Venalis P, Selickaja S, Lundberg K, Rugiene R, Lundberg IE. Association of Anti–Transcription Intermediary Factor 1 Antibodies With Paraneoplastic Rheumatic Syndromes Other Than Dermatomyositis. *Arthritis Care Res (Hoboken).* 2018;70(4):648-651.
38. Darnell RB, Posner JB. Paraneoplastic syndromes involving the nervous system. *N Engl J Med.* 2003;349(16):1543-1554.
39. Bataller L, Dalmau JO. Paraneoplastic disorders of the central nervous system: update on diagnostic criteria and treatment. In: *Seminars in Neurology.* Vol 24. Copyright© 2004 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New ...; 2004:461-471.
40. Evans CC, Kaufman HD. Unusual presentation of seminoma of the testis. *Br J Surg.* 1971;58(9):703-704.
41. Littler WA. Peripheral sensorimotor neuropathy in association with a seminoma of an undescended testicle. *Postgrad Med J.* 1970;46(533):166.
42. Doll DC, Yarbro JW. Vascular toxicity associated with antineoplastic agents. In: *Seminars in Oncology.* Vol 19. ; 1992:580-596.
43. Guillot B, Bessis D, Dereure O. Mucocutaneous side effects of antineoplastic chemotherapy. *Expert Opin Drug Saf.* 2004;3(6):579-587.
44. Taillan B, Castanet J, Garnier G, et al. Paraneoplastic Raynaud's phenomenon. *Clin Rheumatol.* 1993;12(2):281-282.
45. Shurbaji MS, Epstein JI. Testicular vasculitis: implications for systemic disease. *Hum Pathol.* 1988;19(2):186-189.
46. Fleischmann A, Studer UE. Isolated polyarteritis nodosa of the male reproductive system associated with a germ cell tumor of the testis: a case report. *Cardiovasc Pathol.* 2007;16(6):354-356.
47. Grem JL, Robins HI, Wilson KS, Gilchrist K, Trump DL. Metastatic leydig cell tumor of the testis report of three cases and review of the literature. *Cancer.* 1986;58(9):2116-2119.
48. Papadimitris C, Alevizaki M, Pantazopoulos D, Nakopoulou L, Athanassiades P, Dimopoulos MA. Cushing syndrome as the presenting feature of metastatic Leydig cell tumor of the testis. *Urology.* 2000;56(1):153.
49. Jain SH, Sadow PM, Nosé V, Dluhy RG. A patient with ectopic cortisol production derived from malignant testicular masses. *Nat Clin Pract Endocrinol Metab.* 2008;4(12):695-700.
50. Zapf J. Role of insulin-like growth factor II and IGF binding proteins in extrapancreatic tumor hypoglycemia. *Horm Res Paediatr.* 1994;42(1-2):20-26.
51. Teale JD, Marks V. Inappropriately elevated plasma insulin like growth factor II in relation to suppressed insulin like growth factor I in the diagnosis of non islet cell tumour hypoglycaemia. *Clin Endocrinol (Oxf).* 1990;33(1):87-98.
52. Mukherjee S, Diver M, Weston PJ. Non islet cell tumor hypoglycaemia in a metastatic Leydig cell tumor. *Acta Oncol (Madr).* 2005;44(7):761-763.
53. Giralt SA, Dexeu F, Amato R, Sella A, Logothetis C. Hyperthyroidism in men with germ cell tumors and high levels of beta human chorionic gonadotropin. *Cancer.* 1992;69(5):1286-1290.
54. GOLTZMAN D, STEWART AF, BROADUS AE. Malignancy-associated hypercalcemia: evaluation with a cytochemical bioassay for parathyroid hormone. *J Clin Endocrinol Metab.* 1981;93(5):899-904.
55. Stewart AF. Hypercalcemia associated with cancer. *N Engl J Med.* 2005;352(4):373-379.

56. Rodríguez-Gutiérrez R, Zapata-Rivera MA, Quintanilla-Flores DL, et al. 1, 25-dihydroxy-vitamin D and PTHrP mediated malignant hypercalcemia in a seminoma. *BMC Endocr Disord.* 2014;14(1):1-5.
57. Daniels IR, Layer GT. Testicular tumours presenting as gynaecomastia. *Eur J Surg Oncol.* 2003;29(5):437-439.
58. Hernes EH, Harstad K, Fosså SD. Changing incidence and delay of testicular cancer in southern Norway (1981-1992). *Eur Urol.* 1996;30:349-357.
59. Hands LJ, Greenall MJ. Gynaecomastia. *J Br Surg.* 1991;78(8):907-911.
60. Carmignani L, Salvioni R, Gadda F, et al. Long-term followup and clinical characteristics of testicular Leydig cell tumor: experience with 24 cases. *J Urol.* 2006;176(5):2040-2043.
61. Ascensao JL, Gaylis F, Bronson D, Fraley EE, Zanjani ED. Erythropoietin production by a human testicular germ cell line. Published online 1983.
62. Kaito K, Otsubo H, Usui N, Kobayashi M. Secondary polycythaemia as a paraneoplastic syndrome of testicular seminoma. *Ann Hematol.* 2004;83(1):55-57.
63. Schneider BF, Glass WF, Brooks CH, Koenig KG. Membranous glomerulonephritis associated with testicular seminoma. *J Intern Med.* 1995;237(6):599-602.
64. Sprossmann A, Müller RP. Urticaria-vasculitis syndrome in metastatic malignant testicular teratoma. *Hautarzt.* 1994;45(12):871-874.