

MALIGN EPİTELYAL TÜMÖRLER -II

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GİRİŞ

Meme kanseri kadınlarında en sık görülen kanser türüdür, kadın kanserlerinin % 23'ünü oluşturur ve kadınlarında kansere bağlı ölümlerin ikinci onde gelen nedenidir. Gelişmekte olan ülkelerde değişen yaşam tarzı nedeniyle meme kanseri görme sıklığı artmıştır. Geçen yüzyılın başında, hastanın meme kanseri olduğunu bilmek yeterliydi ve tüm meme kanseri hastalarına aynı tür tedavi uygulanıyordu. Ancak zaman içerisinde, aynı kanser tipine sahip hastaların farklı prognozlarının gözlemlenmesi ve son 50 yılda patologlar tarafından farklı morfolojik varyantlarının tanımlanması, meme kanseri sınıflandırmasının önemini ön plana çıkarmıştır (1).

INVAZİV MİKROPAPİLLER KARSİNOM

Invasiv Mikropapiller karsinom (IMPK), ilk olarak 1980 yılında Fisher ve ark.(2) tarafından tanımlanmış ve 1993 yılında Petersen ve ark.(3) tarafından invaziv meme kanserinin bir alt tipi olarak kabul edilmiştir. IMPK, tüm invaziv meme kanseri vakalarının yaklaşık %2-8'ini oluşturan, invaziv duktal karsinomun (IDK) agresif bir var-

yantı olarak kabul edilmektedir (1). IMPK, meme kanserinin nadir görülen bir patolojik alt tipidir ve IMPK'un saf varyantı daha da nadirdir. Önceki çalışmalar çoğu hastanın (% 80-86) mikst tipte tümörler içinde IMPK'a sahip olduğunu göstermiştir (4). IMPK, yüksek lenfovasküler invazyon (LVI), lenf nodu (LN) metastazı eğilimi gösterir, dolayısıyla IDK'den daha agresif bir davranış sergiler (1,4,5).

Mikroskopik olarak, invaziv papiller karsinom ile karşılaştırıldığında, IMPK genellikle fibroasküler kor içermeyen, daha küçük epitel yuvaları ve bunların etrafında boşluklardan oluşur (*Resim 1*). Her boşlukta genellikle bir veya seyrek olarak daha fazla mikropapiller yapı bulunur (6). IMPK'nın morfolojisi farklıdır ve immünohistokimyasal olarak epitel membran antijeni (EMA), psödopapiller neoplazm veya glandüler yapının periferinde immünekspresyon gösterir. Çoğu IMPK vakası, en yaygın olarak invaziv duktal karsinomda olmak üzere, diğer invaziv meme karsinom tipleri ile birlikte görülmektedir. % 25'lik nodal metastaz insidansı, hastalarda sık nüks ve kötü прогноз göstergesidir. 5 yıllık genel sağkalım oranı % 87,5'tir. Mikropapiller yapıların oranı <%

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Küçük hücreli karsinomlar, vakaların % 30-60'ında ER ekspresyonu gösterir ve tipik olarak HER2-negatiftir. Memeye metastatik küçük hücreli karsinom, klinik olarak veya belirsiz durumlarda görüntüleme yoluyla dışlanmalıdır (64).

SONUÇ

Yeni WHO 2019 mavi kitaba göre tümör sınıflamasında bazı değişiklikler olmuştur. Nöroendokrin özellik gösteren meme tümörleri, nöroendokrin tümör ve nöroendokrin karsinom olarak primer nöroendokrin tümörler olarak sınıflandırılmıştır. Müsinöz kistadenokarsinom ve ters polariteli tall cell karsinom yeni başlıklar altında sınıflamaya eklenmiştir. Meme kanserli hastalarda, tümör tipi, hormon reseptör durumu (ER, PR), Her 2 skorlaması, tümör boyutu, nodal tutulum ve lenfovasküler invazyon gibi parametreler hastanın прогнозunu belirlemeye önemlidir. Meme kanserinde doğru tanı konulması, hangi aşamada olduğu ve alacağı tedaviye bağlı olarak günlük hayatı birçok yönden etkileyebilir. Bu nedenle bu yazımızda meme tümörlerine ait tanılar güncel bilgiler ışığında anlatılmıştır.

KAYNAKÇA

1. Kaya C, Uçak R, Bozkurt E, et al. The Impact of Micropapillary Component Ratio on the Prognosis of Patients With Invasive Micropapillary Breast Carcinoma. *J Invest Surg.* 2020 Jan;33(1):31-39. doi: 10.1080/08941939.2018.1474302. Epub 2018 May 29.
2. Fisher ER, Palekar AS, Redmond C, et al.. Pathologic findings from the national surgical adjuvant breast project (protocol no. 4). vi. invasive papillary cancer. *Am J Clin Pathol.* 1980;73:313-22. doi:10.1093/ajcp/73.3.313..
3. Petersen JL. Breast carcinomas with an unexpected insideout growth pattern: rotation of polarization associated with angioinvasion. *Pathol Res Pract.* 1993;189:A780.
4. Li G, Yang S, Yao J, et al. Invasive micropapillary carcinoma of the breast had poor clinical characteristics but showed no difference in prognosis compared with invasive ductal carcinoma. *World J Surg Oncol.* 2016 Aug 5;14(1):207. doi: 10.1186/s12957-016-0960-z
- 5.Ye F, Yu P, Li N, et al. Prognosis of invasive micro-papillary carcinoma compared with invasive ductal carcinoma in breast: A meta-analysis of PSM studies. *Breast.* 2020 Jun;51:11-20. doi: 10.1016/j.breast.2020.01.041. Epub 2020 Jan 29.
- 6.Gokce H, Durak MG, Akin MM, et al. Invasive micropapillary carcinoma of the breast: a clinicopathologic study of 103 cases of an unusual and highly aggressive variant of breast carcinoma. *Breast J.* 2013 Jul-Aug;19(4):374-81. doi: 10.1111/tbj.12128. Epub 2013 May 29.
- 7.Han CH, Yao WG, He J et al. MRI and the pathology of breast invasive micropapillary carcinoma. *Oncol Lett.* 2020 Sep;20(3):2811-2819. doi: 10.3892/ol.2020.11848. Epub 2020 Jul 9.
- 8.Coyle EA, Taj H, Comba I, et al. Invasive Micropapillary Carcinoma: A Rare Case of Male Breast Cancer. *Cureus.* 2020 Sep 21;12(9):e10571. doi: 10.7759/cureus.10571.
- 9.Zekioglu O, Erhan Y, Ciris M, et al. Invasive micropapillary carcinoma of the breast: high incidence of lymph node metastasis with extranodal extension and its immunohistochemical profile compared with invasive ductal carcinoma. *Histopathology* 2004;44:18-23.
10. Soo MS, Williford ME, Walsh R, et al. Papillary carcinoma of the breast: imaging findings. *AJR* 1995;164: 321-6.
11. Arciero CA, Diehl AH 3rd, Liu Y, et al. Triple-negative apocrine carcinoma: A rare pathologic subtype with a better prognosis than other triple-negative breast cancers. *J Surg Oncol.* 2020 Jul 15. doi: 10.1002/jso.26129. Epub ahead of print.
12. Cserni G. Histological type and typing of breast carcinomas and the WHO classification changes over time. *Pathologica.* 2020 Mar;112(1):25-41. doi: 10.32074/1591-951X-1-20. PMID: 32202537.
13. Wu W, Wu M, Peng G, et al. Prognosis in triple-negative apocrine carcinomas of the breast: A population-based study. *Cancer Med.* 2019 Dec;8(18):7523-7531. doi: 10.1002/cam4.2634. Epub 2019 Oct 23.
- 14.McMullen ER, Zoumberos NA, Kleer CG. Metaplastic Breast Carcinoma: Update on Histopathology and Molecular Alterations. *Arch Pathol Lab Med.* 2019 Dec;143(12):1492-1496. doi: 10.5858/arpa.2019-0396-RA.
- 15.Djomehri SI, Gonzalez ME, da Veiga Leprevost F, et al. Quantitative proteomic landscape of metaplastic breast carcinoma pathological subtypes and their relationship to triple-negative tumors. *Nat Commun.* 2020 Apr 7;11(1):1723. doi: 10.1038/s41467-020-15283-z.
- 16.Abouharb S, Moulder S. Metaplastic breast cancer: clinical overview and molecular aberrations for potential targeted therapy. *Curr Oncol Rep.* 2015;17(3): 431.

17. Rakha EA, Coimbra ND, Hodi Z, et al. Immunoprofile of metaplastic carcinomas of the breast. *Histopathology*. 2017; 70(6):975–985.
18. Salah F, Gerges AD, Heba EE, et al. Metaplastic breast carcinoma: Analysis of 31 cases from a single institute. *J Egypt Natl Canc Inst*. 2017;29:141-5.
19. Aydiner A, Sen F, Tambos M, et al. Metaplastic breast carcinoma versus triple-negative breast cancer: Survival and response to treatment. *Medicine*. 2015; 94:e2341.
20. Ng CKY, Piscuoglio S, Geyer FC, et al. the landscape of somatic genetic alterations in metaplastic breast carcinomas. *Clin Cancer Res*. 2017;23(14):3859–3870.
21. Tan PH, Ellis I, Allison K, et al. WHO Classification of Tumours Editorial Board. The 2019 World Health Organization classification of tumours of the breast. *Histopathology*. 2020 Aug;77(2):181-185. doi: 10.1111/his.14091. Epub 2020 Jul 29.
22. Langlands F, Cornford E, Rakha E, et al. Imaging overview of metaplastic carcinomas of the breast: A large study of 71 cases. *Br J Radiol*. 2016;89:20140644.
23. Hasbay B, Bolat FA, Aytaç Hö, et al. Metaplastic Carcinoma of the Breast: Analysis of 38 Cases from a Single Institute. *Turk Patoloji Derg*. 2020;36(1):23-30. English. doi: 10.5146/tjpath.2019.01472.
24. Zhu H, Li K, Dong DD, et al. Spindle cell metaplastic carcinoma of breast: a clinicopathological and immunohistochemical analysis. *Asia Pac J Clin Oncol*. 2017;13(2):e72–e78.
25. Cheah AL, Billings SD, Rowe JJ. Mesenchymal tumours of the breast and their mimics: a review with approach to diagnosis. *Pathology*. 2016;48(5):406–424.
26. Leibl S, Gogg-Kammerer M, Sommersacher A, et al. Metaplastic breast carcinomas: are they of myoepithelial differentiation: immunohistochemical profile of the sarcomatoid subtype using novel myoepithelial markers. *Am J Surg Pathol*. 2005;29(3):347–353.
27. Tekin L, Elibol FD, Bacaksızlar Sarı F, et al. Spindle cell metaplastic carcinoma of the breast. *Breast J*. 2020 Jul;26(7):1421-1422. doi: 10.1111/tbj.13753. Epub 2020 Jan 7.
28. Cha N, Wang S, Lv M, et al. Breast metaplastic squamous cell carcinoma diagnosed with fine needle and core biopsy: a case study. *Am J Case Rep*. 2018; 19:203–206.
29. Salemis NS. Metaplastic carcinoma of the breast with mesenchymal differentiation (carcinosarcoma): a unique presentation of an aggressive malignancy and literature review. *Breast Dis*. 2018;37(3):169–175.
30. González-Martínez S, Pérez-Mies B, Carretero-Barrio I, et al. Molecular Features of Metaplastic Breast Carcinoma: An Infrequent Subtype of Triple Negative Breast Carcinoma. *Cancers (Basel)*. 2020 Jul 8;12(7):1832. doi: 10.3390/cancers12071832.
31. Tan PH, Ellis I, Allison K, et al. WHO Classification of Tumours Editorial Board. *Breast tumours*. Lyon (France): International Agency for Research on Cancer; 2019. (WHO classification of tumours series, 5th ed.; vol. 2)
32. Hammond ME, Hayes DF, Dowsett M, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. *Arch Pathol Lab Med*. 2010;134:907-22.
33. Beca F, Sebastiao APM, Pareja F, et al. Whole-exome analysis of metaplastic breast carcinomas with extensive osseous differentiation. *Histopathology*. 2020 Aug;77(2):321-326. doi: 10.1111/his.14088.
34. Limite G, Di Micco R, Esposito E, et al. Acinic cell carcinoma of the breast: review of the literature. *Int J Surg*. 2014;12 Suppl 1:S35-9. doi: 10.1016/j.ijssu.2014.05.004. Epub 2014 May 22.
35. Beca F, Lee SSK, Pareja F, et al. Whole-exome sequencing and RNA sequencing analyses of acinic cell carcinomas of the breast. *Histopathology*. 2019 Dec;75(6):931-937. doi: 10.1111/his.13962. Epub 2019 Oct 13.
36. Damiani S, Pasquinelli G, Lamovec J, et al. Acinic cell carcinoma of the breast: an immunohistochemical and ultrastructural study. *Virchows Arch* 2000;437:74-81
37. Elster EA, Markusic J, Ball R et al. Primary acinic cell carcinoma of the breast. *Am Surg* 2002;68:993-5.
38. Chang ED, Lee EJ, Lee AW, et al. Primary acinic cell carcinoma of the breast: a case report with an immunohistochemical and ultrastructural studies. *J Breast Cancer*. 2011 Jun;14(2):160-4. doi: 10.4048/jbc.2011.14.2.160. Epub 2011 Jun 18.
- 39.. Bhutani N, Kajal P, Singla S. Adenoid cystic carcinoma of the breast: Experience at a tertiary care centre of Northern India. *Int J Surg Case Rep*. 2018;51:204-209. doi: 10.1016/j.ijscr.2018.08.035. Epub 2018 Aug 31.
40. Y. Zhao, W. Li, R. Lang, et al., Primary acinic cell carcinoma of the breast: a case report and review of the literature, *Int. J. Surg. Pathol.* 22 (2) (2014 Apr) 177e181.
41. Limite G, Di Micco R, Esposito E, Sollazzo V, Cervotti M, Pettinato G, Varone V, Benassai G, Amato B, Pi-

- lone V, Luglio G, Vitiello A, Hasani A, Liccardo F, Forestieri P. Acinic cell carcinoma of the breast: review of the literature. *Int J Surg.* 2014;12 Suppl 1:S35-9. doi: 10.1016/j.ijsu.2014.05.004. Epub 2014 May 22.
42. Slodkowska E, Xu B, Kos Z, et al. Predictors of Outcome in Mammary Adenoid Cystic Carcinoma: A Multi-Institutional Study. *Am J Surg Pathol.* 2020 Feb;44(2):214-223. doi: 10.1097/PAS.00000000000001378.
43. Shukla A, Arshad F, Naseem I. Secretory carcinoma of breast: A diagnostic dilemma. *Indian J Pathol Microbiol.* 2020 Feb;63(Supplement):S143-S145. doi: 10.4103/IJPM.IJPM_367_18.
44. Hoda RS, Brogi E, Pareja F, et al. Secretory carcinoma of the breast: clinicopathologic profile of 14 cases emphasizing distant metastatic potential. *Histopathology.* 2019;75:213–224.
45. Li D, Xiao X, Yang W, et al. Secretory breast carcinoma: a clinicopathological and immunophenotypic study of 15 cases with a review of the literature. *Mod Pathol.* 2012;25:567–575.
46. Harrison BT, Fowler E, Krings G, et al. Pan-TRK Immunohistochemistry: A Useful Diagnostic Adjunct For Secretory Carcinoma of the Breast. *Am J Surg Pathol.* 2019 Dec;43(12):1693-1700. doi: 10.1097/PAS.0000000000001366.
47. Altundag K. Secretory carcinoma of the breast in postmenopausal women. *J BUON.* 2020 Mar-Apr;25(2):1266.
48. Yan M, Gilmore H, Harbhajana A. Mucoepidermoid Carcinoma of the Breast With MAML2 Rearrangement: A Case Report and Literature Review. *Int J Surg Pathol.* 2020 Oct;28(7):787-792. doi: 10.1177/1066896920916779. Epub 2020 May 4.
49. García JJ, Hunt JL, Weinreb I, et al. Fluorescence in situ hybridization for detection of MAML2 rearrangements in oncocytic mucoepidermoid carcinomas: utility as a diagnostic test. *Hum Pathol.* 2011 Dec;42(12):2001-9. doi: 10.1016/j.humpath.2011.02.028. Epub 2011 Jul 20.
50. Cheng M, Geng C, Tang T, et al. Mucoepidermoid carcinoma of the breast: Four case reports and review of the literature. *Medicine (Baltimore).* 2017 Dec;96(51):e9385. doi: 10.1097/MD.0000000000009385.
51. Trihia HJ, Valavanis C, Novkovic N, et al. Polymorphous adenocarcinoma of the breast—an exceptionally rare entity: Clinicopathological description of a case and brief review. *Breast J.* 2020 Feb;26(2):261-264. doi: 10.1111/tbj.13623. Epub 2019 Sep 20.
52. Foschini MP, Morandi L, Asioli S, et al. The morphological spectrum of salivary gland type tumours of the breast. *Pathology.* 2017 Feb;49(2):215-227. doi: 10.1016/j.pathol.2016.10.011. Epub 2016 Dec 30.
- 53..Jassim M, Premalata CS, Okaly G, et al. Tall Cell Carcinoma with Reverse Polarity of Breast: Report of a Case with Unique Morphologic and Molecular Features. *Turk Patoloji Derg.* 2020 Oct 6. English. doi: 10.5146/tjpath.2020.01511.
54. Haefliger S., Muenst S., Went P. et al. Tall cell carcinoma of the breast with reversed polarity (TCC-RP) with mutations in the IDH2 and PIK3CA genes: a case report. *Mol Biol Rep* 47, 4917–4921 (2020).
55. Chiang S, Weigelt B, Wen H, et al. IDH2 mutations define a unique subtype of breast cancer with altered nuclear polarity. *Cancer Research.* 2016;76:7118-29.
56. Trevisi E, La Salvia A, Daniele L, et al. Neuroendocrine breast carcinoma: a rare but challenging entity. *Med Oncol.* 2020 Jul 25;37(8):70. doi: 10.1007/s12032-020-01396-4.
57. Pareja F, D'Alfonso TM. Neuroendocrine neoplasms of the breast: A review focused on the updated World Health Organization (WHO) 5th Edition morphologic classification. *Breast J.* 2020 Jun;26(6):1160-1167. doi: 10.1111/tbj.13863. Epub 2020 May 7.
58. Kelten Talu C, Leblebici C, Kilicaslan Ozturk T, et al. Primary breast carcinomas with neuroendocrine features: clinicopathological features and analysis of tumor growth patterns in 36 cases. *Ann Diagn Pathol.* 2018;34:122-130.
59. Sapino A, Righi L, Cassoni P, et al. Expression of apocrine differentiation markers in neuroendocrine breast carcinomas of aged women. *Mod Pathol.* 2001;14:768-776
60. Roininen N, Takala S, Haapasaari KM, et al. Primary neuroendocrine breast carcinomas are associated with poor local control despite favourable biological profile: a retrospective clinical study. *BMC Cancer.* 2017;17:72.
61. Mohanty SK, Kim SA, DeLair DF, et al. Comparison of metastatic neuroendocrine neoplasms to the breast and primary invasive mammary carcinomas with neuroendocrine differentiation. *Mod Pathol.* 2016;29:788-798.
62. Bogina G, Munari E, Brunelli M, et al. Neuroendocrine differentiation in breast carcinoma: clinicopathological features and outcome. *Histopathology.* 2016;68:422-432.
63. Bean G, Shin SJ, Hosfield E, et al. Molecular characterization of small cell/neuroendocrine carcinomas of the breast. *Modern Pathol.* 2018;31:49-50.
64. Pareja F, D'Alfonso TM. Neuroendocrine neoplasms of the breast: A review focused on the updated World Health Organization (WHO) 5th Edition morphologic classification. *Breast J.* 2020 Jun;26(6):1160-1167. doi: 10.1111/tbj.13863. Epub 2020