

Bölüm 38

MEME KANSERİNDE GEBELİK TAKİBİ

Eda Adeviye ŞAHİN¹
Hasan Berkan SAYAL²

GİRİŞ

Gebelik veya hamilelikle ilişkili meme kanseri, hamilelik sırasında, doğum sonrası ilk yılda veya emzirme döneminde herhangi bir zamanda teşhis edilen meme kanseri olarak tanımlanır. Gebelik sırasında tespit edilen meme kanserinde hem annenin hem de fetüsün iyilik hali, herhangi bir tedavi planlaması aşamasında dikkate alınması gerektiğinden zorlu bir klinik durum olarak ortaya çıkmaktadır. Gebelik ve meme kanseri ile ilgili prospektif çalışmalar sayıca çok azdır ve klinik kanıtların çoğu retrospektif vaka serileri ve vaka raporları ile sınırlıdır.

EPİDEMİYOLOJİ

Meme kanseri gebe olmayan ve hamile kadınlarda en sık görülen kanserlerden biridir [1]. Servikal karsinomadan sonra gebelikte en sık görülen ikinci malignitedir. 30 yaşın altındaki kadınlardaki tüm meme kanserlerinin yüzde 20'si kadar gebelikle ilişkilidir; ancak 50 yaşın altındaki kadınlarda teşhis edilen meme kanserlerinin yüzde 5'inden azı gebelik sırasında veya doğum sonrası dönemde tespit edilir [2,3].

Gebelikle birlikte olan ya da ilk olarak gebelik sırasında tespit edilen meme kanseri nispeten nadir bir olaydır. Gebelik ve meme kanseri insidansı (doğum öncesi ve doğum sonrası emzirme dönemi dahil) 100.000 doğum başına yaklaşık 15 ila 35'tir [4-7]. Gebeliğe bağlı meme kanseri insidansı, çocuk doğurma yaşları yaşlara geciktirildiği için artmaktadır [6,8].

¹ Op.Dr., Malatya Eğitim ve Araştırma Hastanesi Obstetri ve Jinekoloji Kliniği

² Op. Dr., Malatya Eğitim ve Araştırma Hastanesi Perinatoloji Kliniği

masyon riskini arttırmıyor gibi görünmektedir [107]. Yine de teratojenite riskleri nedeniyle, hamilelik girişimine başlamadan önce hormon reseptörü pozitif meme kanseri olup tamoksifen kullanan kadınların bu tedaviyi üç ay öncesinden kesmeleri önerilmektedir. Ek olarak, bir insan epidermal büyüme faktörü reseptörü 2 (HER2) pozitif meme kanseri için trastuzumab ile tedavi edilen kadınların, fetüste trastuzumab ile ilgili oligohidramnios olası riski nedeniyle gebelikten önce, en az yedi ay boyunca etkili kontrasepsiyon kullanmaları gerekir.

Genç yaştaki meme kanserli kadınlar, kemoterapiye bağlı gonadotoksisite ve beş yıllık hormonal tedaviyi alırken çocuk doğurmada gecikme nedeniyle tedavi sonrası infertilite yaşayabilirler [106].

KAYNAKLAR

1. Antonelli NM, Dotters DJ, Katz VL, Kuller JA. Cancer in pregnancy: a review of the literature. Part I. *Obstet Gynecol Surv* 1996; 51:125.
2. Wallack MK, Wolf JA Jr, Bedwinek J, et al. Gestational carcinoma of the female breast. *Curr Probl Cancer* 1983; 7:1.
3. Anderson BO, Petrek JA, Byrd DR, et al. Pregnancy influences breast cancer stage at diagnosis in women 30 years of age and younger. *Ann Surg Oncol* 1996; 3:204.
4. Smith LH, Danielsen B, Allen ME, Cress R. Cancer associated with obstetric delivery: results of linkage with the California cancer registry. *Am J Obstet Gynecol* 2003; 189:1128.
5. Woo JC, Yu T, Hurd TC. Breast cancer in pregnancy: a literature review. *Arch Surg* 2003; 138:91.
6. Stensheim H, Møller B, van Dijk T, Fosså SD. Cause-specific survival for women diagnosed with cancer during pregnancy or lactation: a registry-based cohort study. *J Clin Oncol* 2009; 27:45.
7. Andersson TM, Johansson AL, Hsieh CC, et al. Increasing incidence of pregnancy-associated breast cancer in Sweden. *Obstet Gynecol* 2009; 114:568.
8. Ventura SJ. First births to older mothers, 1970-86. *Am J Public Health* 1989; 79:1675.
9. Ishida T, Yokoe T, Kasumi F, et al. Clinicopathologic characteristics and prognosis of breast cancer patients associated with pregnancy and lactation: analysis of case-control study in Japan. *Jpn J Cancer Res* 1992; 83:1143.
10. Shen T, Vortmeyer AO, Zhuang Z, Tavassoli FA. High frequency of allelic loss of BRCA2 gene in pregnancy-associated breast carcinoma. *J Natl Cancer Inst* 1999; 91:1686.
11. Johansson O, Loman N, Borg A, Olsson H. Pregnancy-associated breast cancer in BRCA1 and BRCA2 germline mutation carriers. *Lancet* 1998; 352:1359.
12. Cullinane CA, Lubinski J, Neuhausen SL, et al. Effect of pregnancy as a risk factor for breast cancer in BRCA1/BRCA2 mutation carriers. *Int J Cancer* 2005; 117:988.
13. Albrechtsen G, Heuch I, Kvåle G. The short-term and long-term effect of a pregnancy on breast cancer risk: a prospective study of 802,457 parous Norwegian women. *Br J Cancer* 1995; 72:480.
14. Lambe M, Hsieh C, Trichopoulos D, et al. Transient increase in the risk of breast cancer after giving birth. *N Engl J Med* 1994; 331:5.
15. Wohlfahrt J, Andersen PK, Mouridsen HT, Melbye M. Risk of late-stage breast cancer after a childbirth. *Am J Epidemiol* 2001; 153:1079.
16. Middleton LP, Amin M, Gwyn K, et al. Breast carcinoma in pregnant women: assessment of clinicopathologic and immunohistochemical features. *Cancer* 2003; 98:1055.
17. Reed W, Hannisdal E, Skovlund E, et al. Pregnancy and breast cancer: a population-based study. *Virchows Arch* 2003; 443:44.

18. Bonnier P, Romain S, Dilhuydy JM, et al. Influence of pregnancy on the outcome of breast cancer: a case-control study. Societe Francaise de Senologie et de Pathologie Mammaire Study Group. *Int J Cancer* 1997; 72:720.
19. Berry DL, Theriault RL, Holmes FA, et al. Management of breast cancer during pregnancy using a standardized protocol. *J Clin Oncol* 1999; 17:855.
20. Elledge RM, Ciocca DR, Langone G, McGuire WL. Estrogen receptor, progesterone receptor, and HER-2/neu protein in breast cancers from pregnant patients. *Cancer* 1993; 71:2499.
21. King RM, Welch JS, Martin JK Jr, Coulam CB. Carcinoma of the breast associated with pregnancy. *Surg Gynecol Obstet* 1985; 160:228.
22. Lethaby AE, O'Neill MA, Mason BH, et al. Overall survival from breast cancer in women pregnant or lactating at or after diagnosis. Auckland Breast Cancer Study Group. *Int J Cancer* 1996; 67:751.
23. BUNKER ML, PETERS MV. Breast cancer associated with pregnancy or lactation. *Am J Obstet Gynecol* 1963; 85:312.
24. Saber A, Dardik H, Ibrahim IM, Wolodiger F. The milk rejection sign: a natural tumor marker. *Am Surg* 1996; 62:998.
25. Goldsmith HS. Milk-rejection sign of breast cancer. *Am J Surg* 1974; 127:280.
26. Liberman L, Giess CS, Dershaw DD, et al. Imaging of pregnancy-associated breast cancer. *Radiology* 1994; 191:245.
27. Samuels TH, Liu FF, Yaffe M, Haider M. Gestational breast cancer. *Can Assoc Radiol J* 1998; 49:172.
28. Yang WT, Dryden MJ, Gwyn K, et al. Imaging of breast cancer diagnosed and treated with chemotherapy during pregnancy. *Radiology* 2006; 239:52.
29. Ahn BY, Kim HH, Moon WK, et al. Pregnancy- and lactation-associated breast cancer: mammographic and sonographic findings. *J Ultrasound Med* 2003; 22:491.
30. Ray JG, Vermeulen MJ, Bharatha A, et al. Association Between MRI Exposure During Pregnancy and Fetal and Childhood Outcomes. *JAMA* 2016; 316:952.
31. Talele AC, Slanetz PJ, Edmister WB, et al. The lactating breast: MRI findings and literature review. *Breast J* 2003; 9:237.
32. Collins JC, Liao S, Wile AG. Surgical management of breast masses in pregnant women. *J Reprod Med* 1995; 40:785.
33. Dominici L, Kuerer H, Babiera G, et al. Wound complications from surgery in pregnancy-associated breast cancer. American Society of Breast Surgeons Annual Meeting 2009.
34. Sherlock FG, Crues JV. MR procedures: biologic effects, safety, and patient care. *Radiology* 2004; 232:635.
35. Baker J, Ali A, Groch MW, et al. Bone scanning in pregnant patients with breast carcinoma. *Clin Nucl Med* 1987; 12:519.
36. Rosenthal DI. Radiologic diagnosis of bone metastases. *Cancer* 1997; 80:1595.
- Topic 786 Version 20.0.
37. Amant F, Deckers S, Van Calsteren K, et al. Breast cancer in pregnancy: recommendations of an international consensus meeting. *Eur J Cancer* 2010; 46:3158.
38. Hahn KM, Johnson PH, Gordon N, et al. Treatment of pregnant breast cancer patients and outcomes of children exposed to chemotherapy in utero. *Cancer* 2006; 107:1219.
39. Woo JC, Yu T, Hurd TC. Breast cancer in pregnancy: a literature review. *Arch Surg* 2003; 138:91.
40. BYRD BF Jr, BAYER DS, ROBERTSON JC, STEPHENSON SE Jr. Treatment of breast tumors associated with pregnancy and lactation. *Ann Surg* 1962; 155:940.
41. Mazze RI, Källén B. Reproductive outcome after anesthesia and operation during pregnancy: a registry study of 5405 cases. *Am J Obstet Gynecol* 1989; 161:1178.
42. Gianopoulos JG. Establishing the criteria for anesthesia and other precautions for surgery during pregnancy. *Surg Clin North Am* 1995; 75:33.
43. Duncan PG, Pope WD, Cohen MM, Greer N. Fetal risk of anesthesia and surgery during pregnancy. *Anesthesiology* 1986; 64:790.

44. Barron WM. The pregnant surgical patient: medical evaluation and management. *Ann Intern Med* 1984; 101:683.
45. Berry DL, Theriault RL, Holmes FA, et al. Management of breast cancer during pregnancy using a standardized protocol. *J Clin Oncol* 1999; 17:855.
46. Kuerer HM, Gwyn K, Ames FC, Theriault RL. Conservative surgery and chemotherapy for breast carcinoma during pregnancy. *Surgery* 2002; 131:108.
47. Kuerer HM, Cunningham JD, Bleiweiss IJ, et al. Conservative surgery for breast carcinoma associated with pregnancy. *Breast J* 1998; 4:171.
48. Annane K, Bellocq JP, Brettes JP, Mathelin C. Infiltrative breast cancer during pregnancy and conservative surgery. *Fetal Diagn Ther* 2005; 20:442.
49. Dominici LS, Kuerer HM, Babiera G, et al. Wound complications from surgery in pregnancy-associated breast cancer (PABC). *Breast Dis* 2010; 31:1.
50. Kal HB, Struikmans H. Radiotherapy during pregnancy: fact and fiction. *Lancet Oncol* 2005; 6:328.
51. Greskovich JF Jr, Macklis RM. Radiation therapy in pregnancy: risk calculation and risk minimization. *Semin Oncol* 2000; 27:633.
52. Petrek JA. Breast cancer during pregnancy. *Cancer* 1994; 74:518.
53. Antypas C, Sandilos P, Kouvaris J, et al. Fetal dose evaluation during breast cancer radiotherapy. *Int J Radiat Oncol Biol Phys* 1998; 40:995.
54. Gemignani ML, Petrek JA, Borgen PI. Breast cancer and pregnancy. *Surg Clin North Am* 1999; 79:1157.
55. www.bt.cdc.gov/radiation/prenatalphysician.asp (Accessed on July 09, 2012).
56. Schwartz GF, Giuliano AE, Veronesi U, Consensus Conference Committee. Proceedings of the consensus conference on the role of sentinel lymph node biopsy in carcinoma of the breast, April 19-22, 2001, Philadelphia, Pennsylvania. *Cancer* 2002; 94:2542.
57. Lyman GH, Giuliano AE, Somerfield MR, et al. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. *J Clin Oncol* 2005; 23:7703.
58. Filippakis GM, Zografos G. Contraindications of sentinel lymph node biopsy: are there any really? *World J Surg Oncol* 2007; 5:10.
59. Gropper AB, Calvillo KZ, Dominici L, et al. Sentinel lymph node biopsy in pregnant women with breast cancer. *Ann Surg Oncol* 2014; 21:2506.
60. Nicklas AH, Baker ME. Imaging strategies in the pregnant cancer patient. *Semin Oncol* 2000; 27:623.
61. Morita ET, Chang J, Leong SP. Principles and controversies in lymphoscintigraphy with emphasis on breast cancer. *Surg Clin North Am* 2000; 80:1721.
62. Keleher A, Wendt R 3rd, Delpassand E, et al. The safety of lymphatic mapping in pregnant breast cancer patients using Tc-99m sulfur colloid. *Breast J* 2004; 10:492.
63. Gentilini O, Cremonesi M, Trifirò G, et al. Safety of sentinel node biopsy in pregnant patients with breast cancer. *Ann Oncol* 2004; 15:1348.
64. Mondini MM, Cuenca RE, Ollila DW, et al. Sentinel lymph node biopsy during pregnancy: initial clinical experience. *Ann Surg Oncol* 2007; 14:218.
65. Khera SY, Kiluk JV, Hasson DM, et al. Pregnancy-associated breast cancer patients can safely undergo lymphatic mapping. *Breast J* 2008; 14:250.
66. Amant F, Vandenbroucke T, Verheecke M, et al. Pediatric Outcome after Maternal Cancer Diagnosed during Pregnancy. *N Engl J Med* 2015; 373:1824.
67. Ring AE, Smith IE, Jones A, et al. Chemotherapy for breast cancer during pregnancy: an 18-year experience from five London teaching hospitals. *J Clin Oncol* 2005; 23:4192.
68. Giacalone PL, Laffargue F, Bénos P. Chemotherapy for breast carcinoma during pregnancy: A French national survey. *Cancer* 1999; 86:2266.
69. Cardonick E, Gilmandyar D, Somer RA. Maternal and neonatal outcomes of dose-dense chemotherapy for breast cancer in pregnancy. *Obstet Gynecol* 2012; 120:1267.

70. Cardonick E, Iacobucci A. Use of chemotherapy during human pregnancy. *Lancet Oncol* 2004; 5:283.
71. Wiebe VJ, Sipila PE. Pharmacology of antineoplastic agents in pregnancy. *Crit Rev Oncol Hematol* 1994; 16:75.
72. Stevenson J, Giantonio B, Boyd RL, Bruner JA. Adjuvant chemotherapy for breast cancer in pregnancy: can recommendations be made with confidence. *Semin Oncol* 1997; 24:xxv.
73. van Kalken CK, Giaccone G, van der Valk P, et al. Multidrug resistance gene (P-glycoprotein) expression in the human fetus. *Am J Pathol* 1992; 141:1063.
74. Doll DC, Ringenberg QS, Yarbrow JW. Antineoplastic agents and pregnancy. *Semin Oncol* 1989; 16:337.
75. Germann N, Goffinet F, Goldwasser F. Anthracyclines during pregnancy: embryo-fetal outcome in 160 patients. *Ann Oncol* 2004; 15:146.
76. Ebert U, Löffler H, Kirch W. Cytotoxic therapy and pregnancy. *Pharmacol Ther* 1997; 74:207.
77. Briggs GG, Freeman RK, Yaffe SJ. *Drugs in Pregnancy and Lactation*, 8th ed, Lippincott Williams & Wilkins, Philadelphia, PA 2008.
78. Mulvihill JJ, McKeen EA, Rosner F, Zarrabi MH. Pregnancy outcome in cancer patients. Experience in a large cooperative group. *Cancer* 1987; 60:1143.
79. Garcia V, Miguel JS, Borrascas AL. Doxorubicin in the first trimester of pregnancy. *Ann Intern Med* 1981; 94:547.
80. Stephens JD, Golbus MS, Miller TR, et al. Multiple congenital anomalies in a fetus exposed to 5-fluorouracil during the first trimester. *Am J Obstet Gynecol* 1980; 137:747.
81. Zemlickis D, Lishner M, Degendorfer P, et al. Maternal and fetal outcome after breast cancer in pregnancy. *Am J Obstet Gynecol* 1992; 166:781.
82. Buzdar AU, Smith TL, Powell KC, et al. Effect of timing of initiation of adjuvant chemotherapy on disease-free survival in breast cancer. *Breast Cancer Res Treat* 1982; 2:163.
83. Durodola JI. Administration of cyclophosphamide during late pregnancy and early lactation: a case report. *J Natl Med Assoc* 1979; 71:165.
84. Cullins SL, Pridjian G, Sutherland CM. Goldenhar's syndrome associated with tamoxifen given to the mother during gestation. *JAMA* 1994; 271:1905.
85. Tewari K, Bonebrake RG, Asrat T, Shanberg AM. Ambiguous genitalia in infant exposed to tamoxifen in utero. *Lancet* 1997; 350:183.
86. Isaacs RJ, Hunter W, Clark K. Tamoxifen as systemic treatment of advanced breast cancer during pregnancy--case report and literature review. *Gynecol Oncol* 2001; 80:405.
87. Nugent P, O'Connell TX. Breast cancer and pregnancy. *Arch Surg* 1985; 120:1221.
88. Clark RM, Chua T. Breast cancer and pregnancy: the ultimate challenge. *Clin Oncol (R Coll Radiol)* 1989; 1:11.
89. Litton JK, Warneke CL, Hahn KM, et al. Case control study of women treated with chemotherapy for breast cancer during pregnancy as compared with nonpregnant patients with breast cancer. *Oncologist* 2013; 18:369.
90. Amant F, von Minckwitz G, Han SN, et al. Prognosis of women with primary breast cancer diagnosed during pregnancy: results from an international collaborative study. *J Clin Oncol* 2013; 31:2532.
91. Murthy RK, Theriault RL, Barnett CM, et al. Outcomes of children exposed in utero to chemotherapy for breast cancer. *Breast Cancer Res* 2014; 16:500.
92. Dessolle L, Dalmon C, Roche B, Darai E. [Placental metastases from maternal malignancies: review of the literature]. *J Gynecol Obstet Biol Reprod (Paris)* 2007; 36:344.
93. Al-Adnani M, Kiho L, Scheimberg I. Maternal pancreatic carcinoma metastatic to the placenta: a case report and literature review. *Pediatr Dev Pathol* 2007; 10:61.
94. Azim HA, Bellettini G, Liptrott SJ, et al. Breastfeeding in breast cancer survivors: pattern, behavior and effect on breast cancer outcome. *Ann Oncol* 2010; 21 (suppl 8):viii89 (abstr 251P).
95. Higgins S, Haffty BG. Pregnancy and lactation after breast-conserving therapy for early stage breast cancer. *Cancer* 1994; 73:2175.

96. Moran MS, Colasanto JM, Haffty BG, et al. Effects of breast-conserving therapy on lactation after pregnancy. *Cancer J* 2005; 11:399.
97. Wobbles T. Effect of a breast saving procedure on lactation. *Eur J Surg* 1996; 162:419.
98. Findlay PA, Gorrell CR, d'Angelo T, Glatstein E. Lactation after breast radiation. *Int J Radiat Oncol Biol Phys* 1988; 15:511.
99. Hassey KM. Pregnancy and parenthood after treatment for breast cancer. *Oncol Nurs Forum* 1988; 15:439.
100. Mueller BA, Simon MS, Deapen D, et al. Childbearing and survival after breast carcinoma in young women. *Cancer* 2003; 98:1131.
101. Blakely LJ, Buzdar AU, Lozada JA, et al. Effects of pregnancy after treatment for breast carcinoma on survival and risk of recurrence. *Cancer* 2004; 100:465.
102. Rosenberg L, Thalib L, Adami HO, Hall P. Childbirth and breast cancer prognosis. *Int J Cancer* 2004; 111:772.
103. Kroman N, Jensen MB, Wohlfahrt J, et al. Pregnancy after treatment of breast cancer--a population-based study on behalf of Danish Breast Cancer Cooperative Group. *Acta Oncol* 2008; 47:545.
104. de Bree E, Makrigiannakis A, Askoxylakis J, et al. Pregnancy after breast cancer. A comprehensive review. *J Surg Oncol* 2010; 101:534.
105. Azim HA Jr, Santoro L, Pavlidis N, et al. Safety of pregnancy following breast cancer diagnosis: a meta-analysis of 14 studies. *Eur J Cancer* 2011; 47:74.
106. Largillier R, Savignoni A, Gligorov J, et al. Prognostic role of pregnancy occurring before or after treatment of early breast cancer patients aged <35 years: a GET(N)A Working Group analysis. *Cancer* 2009; 115:5155.
107. Helewa M, Lévesque P, Provencher D, et al. Breast cancer, pregnancy, and breastfeeding. *J Obstet Gynaecol Can* 2002; 24:164.
108. Gziri MM, Hui W, Amant F, et al. Myocardial function in children after fetal chemotherapy exposure. A tissue Doppler and myocardial deformation imaging study. *Eur J Pediatr* 2013; 172:163.
109. Gziri MM, Debiève F, DE Catte L, et al. Chemotherapy during pregnancy: effect of anthracyclines on fetal and maternal cardiac function. *Acta Obstet Gynecol Scand* 2012; 91:1465.
110. Mir O, Berveiller P, Goffinet F, et al. Taxanes for breast cancer during pregnancy: a systematic review. *Ann Oncol* 2010; 21:425.
111. HERCEPTIN® (trastuzumab) Prescribing Information http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/103792s5256lbl.pdf.
112. Zagouri F, Sergentanis TN, Chrysikos D, et al. Trastuzumab administration during pregnancy: a systematic review and meta-analysis. *Breast Cancer Res Treat* 2013; 137:349.
113. Kelly H, Graham M, Humes E, et al. Delivery of a healthy baby after first-trimester maternal exposure to lapatinib. *Clin Breast Cancer* 2006; 7:339.
114. Zemlickis D, Klein J, Moselhy G, Koren G. Cisplatin protein binding in pregnancy and the neonatal period. *Med Pediatr Oncol* 1994; 23:476.
115. National Library of Medicine drug and lactation database, LactMed. <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT> (Accessed on July 09, 2012).