Advances in Cancer Research & Therapy

www.advancejournals.org
Open Access Scientific Publisher

Case Study

LI-FRAUMENI SYNDROME IN A PATIENT WITH FAMILIAL *HYPERLIPIDEMIA* FROM WESTERN IRAN, A CASE REPORT

Masoud Sadeghi[1,*], Mehrdad Payandeh[2], Reza Khodarahmi[1], Edris Sadeghi[1]
[1]Medical Biology Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran
[2]Department of Hematology and Medical Oncology, Kermanshah University of Medical Sciences, Kermanshah, Iran

Correspondence should be addressed to **Masoud Sadeghi**

Received 1 December 2014; Accepted 18 January 2015; Published 20 January 2015

ABSTRACTS

Mutations of germ-cell line *TP53* gene are mainly reported in Li–Fraumeni syndrome(LFS). LFS-associated breast cancers are both hormone receptor and human epidermal growth factor receptor 2 positive. The purpose of this study is presentation of one case of LFS, associated with familial hyperlipidemias. A 52-year-old woman referred to clinic of oncology with a pain in the left breast. Her pathology report showed that she had breast cancer and computed tomography scan showed no evidence of metastasis. Markers of estrogen receptor, progesterone receptor and p53 were positive, IHC3^{+} and Ki67 in 20% of cells. We report the first case of a LFS patient with breast cancer and familial hyperlipidemias in Iran who ER, PR, P53 and HER-2 markers for her are positive. Also it is probably that LFS-associated cancer and atherosclerosis diseases are related to each other.

KEYWORDS: Germ-Line Mutation, *Hyperlipidemias*, Li-Fraumeni Syndrome

INTRODUCTION

Li-Fraumeni syndrome (LFS;OMIM #151623) is a rare autosomal-dominant, inherited tumor predisposition syndrome associated with an increased risk of a variety of malignancies[1] that caused by heterozygous germline mutations in the *TP53* gene and almost one third (15-35%) of cancer survivors with LFS will develop multiple primary cancers over their lifetimes.[2] Breast cancers in *TP53* mutation carriers, recently, have more often been reported to be hormone receptor and HER-2 positive by immunohistochemistry, and most invasive ductal carcinomas in LFS are also hormone receptor positive and/or HER-2 positive.[3] Additionally, a study in 1999[4] and the other study in 2006[5] reported that P53 deficiency developed severe hyperlipidemias and atherosclerosis in vivo.

CASE REPORT

Here, we report the first case of a LFS patient with breast cancer and familial hyperlipidemias in Iran who estrogen receptor(ER), progesterone receptor (PR), P53 and HER-2 markers for her are positive.

In December 2010, a 52-year-old woman referred to Clinic of Oncology, Kermanshah University of Medical Sciences, Kermanshah, Iran, with a pain in the left breast. She had no history of other breast complaints or surgeries. Her mother had breast cancer. Her father, brother, two sisters and Mother's brother died due to hyperlipidemia complications (cardiovascular events). One of her other sisters had anti-phospholipid antibody syndrome (APLAS).Her blood group was AB^{+}. Pathology report showed that she had breast cancer (medullary carcinoma) and computed tomography (CT) scan showed no evidence of metastasis. Results of immunohistochemistry (IHC) for markers showed: ER, PR and p53 were positive, Her2 was 3 positive and Ki67 in 20% of cells. She did 4 courses of chemotherapy with doxorubicin plus cyclophosphamide (endoxan) and paclitaxel (300mg per day). Due to financial

constraints, she couldn't prepare trastuzumab (herceptin). She was then treated with radiotherapy (5000 CGY) for 25 courses.

In October 2013, three years after first cancer diagnosis, her pathology report showed colon cancer (invasive adenocarcinoma). A tumoral lesion in distal part of rectum was evidenced by rectosigmoidoscopy and also CT that was identified a tumor with 10cmof anal verge in rectum. After sphincter sparing surgery, she was treated with six courses of chemotherapy with xeloda (capecitabine) + oxaliplatin. At now (May 2014), she is treating with hormone therapy for breast cancer with25 mg per day of aromasin (exemestane, an aromatase inhibitor).

DISCUSSION

Breast cancer is the most common tumor in women with LFS, an inherited cancer syndrome.[3]In our report, we describe a 52-year-old, woman patient with two tumors (breast + colon) with no metastasis based on clinical criteria. The markers of case presented herein (ER, PR, p53, Ki67 and HER-2 markers) were positive. In agreement with current study, recent reports [6],[8] suggest that LFS-associated breast cancers is both hormone receptor and HER-2 positive. Also, the other studies[9],[10] showed that breast cancer, in germline TP53 mutation carriers, is commonly HER-2^{+} (63-83%).Moreover, results of Abrahams et al.[11]indicate that the ER response can possibly be employed as a prognostic marker to identify carriers in various hereditary cancer-prone syndromes (such as Li-Fraumeni Syndrome) at an early age. A number of studies,[1],[3],[12],[13] and our knowledge of other study showd case reports of Li-Fraumeni Syndrome in patients with breast cancer that the onset age for the first tumor (age of first cancer diagnosis) is between 10 to 52 years but focuses on 20-40 years interval.

We pointed out that father, brother, two sisters and Mother's brother of the case died due to hyperlipidemia complications. It has been previously demonstrated that there are several common molecular pathways of disease pathogenesis in atherosclerosis and cancer [14]. Cell proliferation regulatory pathways including genes involved in the G1 to S checkpoint have been associated with plaque progression (atherosclerosis), stenosis and restenosis after angioplasty as well as in cancer progression[15] so that absence of p53 accelerates atherosclerosis by increasing cell proliferation in vivo.[4] The case presented herein shows an evident association between both hyperlipidemia complications and common diagnosed (breast) cancer and the patient's family history. Our observations emphasize on previous reports that the role of p53 in atherosclerotic lesion development might be associated with its function in cell replication control.

Conclusions

Although modern treatments, such as those mentioned in this article, may result in improved outcomes for women with LFS-associated breast cancer, future emerging therapeutic strategies such as the new cell cycle and angiogenesis regulators may be simultaneously successful in blocking the development and progression of both LFS-associated cancer and atherosclerosis diseases.

REFERENCES

[1] Kast K, Krause M, Schuler M, Friedrich K, Thamm B, Bier A, et al. Lateonset Li-Fraumeni Syndrome with bilateral breast cancer and other malignancies: case report andreview of the literature. BMC Cancer 2012;12:217

[2] Sorrell AD, Espenschied CR, Culver JO, Weitzel JN. Tumor protein p53 (TP53) testing and Li-Fraumenisyndrome : current status of clinical applications and future directions. MolDiagnTher 2013;17(1):31-47.

[3] Masciari S, Dillon DA, Rath M, Robson M, Weitzel JN, Balmana J, et al. Breast cancer phenotype in women with TP53 germline mutations: a Li-Fraumeni syndrome consortium effort. Breast Cancer Res Treat2013;133(3):1125-30.

[4] Guevara NV, Kim HS, Antonova EI, Chan L. The absence of p53 accelerates atherosclerosis by increasing cell proliferation in vivo. Nat Med 1999; 5(3):335-9.

[5] Wu Y, Zhou H, Wu K, Lee S, Li R, Liu X. PTEN phosphorylation and nuclear export mediate free fatty acid-induced oxidative stress. Antioxid Redox Signal 2014; 20(9):1382-95.

[6] Melhem-Bertrandt A, Bojadzieva J, Ready KJ, Obeid E, Liu DD, Gutierrez-Barrera AM, et al. Early onset HER2-positive breastcancer is associated with germline TP53 mutations. Cancer 2012;118(4):908-13.

[7] Wilson JR, Bateman AC, Hanson H, An Q, Evans G, Rahman N, et al. Anovel HER2-positive breast cancer phenotype arising from germline TP53 mutations.J MedGenet 2010;47(11):771-4.

[8] Masciari SKM, Digianni L, Dillon D, Li F, Garber G. Histopathological features of breastcancers in women with germline TP53 mutations. Journal of Clinical Oncology, 2006 ASCOAnnual Meeting Proceedings(Post-Meeting Edition), 24(18Supp):10031.2006. Available from: http://meeting.ascopubs.org/cgi/content/short/24/18_suppl/10031.Accessed in 2014(Jun 4).

[9] Rath MG, Masciari S, Gelman R, Miron A, Miron P, Foley K, et al. Prevalence of germline TP53 mutations in HER2+ breastcancer patients. Breast Cancer Res Treat 2013;139(1):193-8.

[10] Wilson JR, Bateman AC, Hanson H, An Q, Evans G, Rahman N, et al. A novel HER2-positive breast cancer phenotype arising from germline TP53 mutations.J MedGenet 2010;47(11):771-4.

[11] Abrahams PJ, Houweling A, Cornelissen-Steijger DM, Arwert F, Menko FH, Pinedo HM, et al. Inheritance of abnormal expression of SOS-like response in xerodermapigmentosum and hereditary cancer-prone syndromes. Cancer Res 1996;56(11):2621-5.

[12] Ariffin H, Martel-Planche G, Daud SS, Ibrahim K, Hainaut P. Li-Fraumeni syndrome in aMalaysian kindred. Cancer Genet Cytogenet 2008;186(1):49-53.

[13] Bang YJ1, Kang SH, Kim TY, Jung CW, Oh SM, Choe KJ, et al. The first documentationof Li-Fraumeni syndrome in Korea. J Korean Med Sci 1995;10(3):205-10.

[14] Ross JS, Stagliano NE, Donovan MJ, Breitbart RE, Ginsburg GS. Atherosclerosis a cancer of the blood vessels?Am J ClinPathol 2001;116 (Suppl):S97-107.

[15] Ross JS, Stagliano NE, Donovan MJ, Breitbart RE, Ginsburg GS. Atherosclerosis and cancer: commonmolecularpathways of diseasedevelopment and progression. Ann N Y Acad Sci 2001; 947:271-92. discussion 292-3.