

Breast Cancer Advisor

BY DR. SILVANA MARTINO

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Best regards,

Dr. Silvana Martino

BIOGRAPHY

Dr. Silvana Martino

is the Director of Breast Cancer Research and Education at The Angeles Clinic Foundation in Santa Monica, California. She is board certified in internal medicine and medical oncology. Dr. Martino has specialized in the treatment and research of breast cancer for over three decades. She is a nationally recognized leader in the field of breast cancer. Her body of work has included research in breast cancer prevention, treatments for early breast cancer and metastatic disease. Dr. Martino has conducted and coordinated large national and international studies which have resulted in changing the standard of care worldwide.

DR. MARTINO'S
CURRICULUM VITAE

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BIOLOGY BASICS

In the last several issues, I have discussed the metastatic patterns of breast cancer and the most common organs of involvement. In this and the next few issues, I will discuss metastatic complications that are somewhat less common but nevertheless must be recognized. Because they are less common, less experienced physicians may have limited experience with these clinical presentations and may not consider the process of metastasis in evaluating patients with certain symptoms.

In this issue I will discuss two abdominal patterns of metastases from breast cancer. The first of these is that of involvement of the gastrointestinal system. The second is that of obstruction of the urinary system. Both of these are somewhat more likely to occur with invasive lobular carcinoma rather than with invasive ductal carcinoma.

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BIOLOGY BASICS continued

The metastatic process may involve any portion of the gastrointestinal system. Tumor may be found within the wall of the esophagus or the stomach. Symptoms may vary widely and may include pain, difficulty swallowing, heartburn, indigestion, a feeling of fullness and nausea. Symptoms may not be localized; rather, the patient may present with generalized systemic symptoms such as anemia from blood loss, weight loss or simply not feeling well.

A more common manifestation is that of bowel obstruction, particularly of the small bowel. Nausea, vomiting, abdominal pain, distension, constipation and fever may be experienced. This can occur over a few days or may be acute. The patient may look relatively well or may look quite ill. The diagnosis is confirmed with abdominal X-rays or a CT scan. At times all that is needed to resolve the problem is to place the intestines at rest by restricting food intake and also drain gastrointestinal fluids with a small tube. Most of the time, however, there are several areas of obstruction, and simple measures do not suffice, making surgery necessary. Because there are often several areas of obstruction and not all of them can be released when metastatic breast cancer is the underlying cause, it is prudent to have a surgeon who is experienced with this obstructive cancer process and not proceed to surgery too quickly. I have seen many times when surgery is undertaken only to be faced with extensive tumor involvement such that the obstructive process cannot be relieved. The patient's condition has not been improved but is subsequently more debilitated because surgery has been added to their already weakened state. As with all decisions made in medicine, judgment is key.

Another manifestation of metastatic disease to the abdomen

is that of obstruction of the ureters, resulting in interference of urine flow from the kidneys. X-rays and scans of the abdomen and urinary system almost always fail to show a discrete tumor mass. The tumor is interspersed within the abdominal cavity and is often confused with scarring. Endoscopic examination of the bladder and the inside of the two ureters fails to demonstrate obvious tumor. All that is apparent is the area of obstruction to the flow of urine. Attempted biopsies of the "retroperitoneum," the part of the abdomen where the ureters are positioned, in my experience, rarely demonstrate tumor. The obstruction is caused from tumor cells that line the outside of the ureter but do not tend to form a tumor mass. Again, these are patterns more typical of the infiltrative nature of lobular carcinoma but will be seen with invasive ductal carcinoma as well. Often, placement of a small tube within the ureter will relieve the obstruction.

It is important to recognize that the obstructive patterns described above can occur from causes other than cancer. However, in a patient with an underlying diagnosis of cancer, the principles described above should be kept in mind.

WHAT'S NEW**BREAST CANCER STATISTICS UPDATE**

Each year the American Cancer Society provides updated statistics that are published in CA, A Cancer Journal for Clinicians. The source of the data is the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute. This program has been collecting clinical, pathological, and demographic cancer information on a large segment of the United States population since 1973. Originally, data were grouped as whites, African Americans, and all races combined. In 1992, data were further subdivided into American Indians/Alaska Natives,

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WHAT'S NEW continued

Asian Americans/Pacific Islanders, and Hispanics/Latinas. Information on estrogen receptor (ER) status of breast cancer was first collected in 1990. As of 2010, ER status is available on 96% of patients. The year 2013 is the last year from which data have been collected. Statistics for the year 2014 are estimates based on existing trends.

Approximately 235,030 new cases of invasive breast cancer are expected to be diagnosed in the U.S. in 2014. A total of 2,360 will be in men and 232,670 are expected to occur in women. Additionally, over 64,000 cases of in situ breast cancer are anticipated. The expected death rate from breast cancer during 2014 is 40,000 women and 430 men.

Over time, the incidence of breast cancer for women living in the United States has continued to rise. Women living in the U.S. presently have a 1-in-8 or 12.3% risk of being diagnosed with breast cancer during their lifetime. Causes for the increase are speculated to be a longer life expectancy of our population, changes in child bearing patterns, use of hormone replacement therapy, increasing rates of obesity, diet, alcohol consumption, minimal level of exercise, and other unknown factors. It is believed that the practice of screening mammography has also resulted in increasing the number of cancers that are diagnosed yearly with the greatest influence being seen in early breast cancer including the number of cases of ductal carcinoma in situ.

Age is a key component of breast cancer risk. A clear rise in risk is evident as a woman becomes older. Women in their 20's have a risk of 1-in-1,732, rising to a risk of 1-in-69 once they are age 40, and to 1-in 29 by age 60. Women with a strong family history of breast or ovarian cancer and women who carry the breast cancer genes (BRCA 1 or 2) have a higher risk at all age groups.

Incidence rates vary considerably among the 5 ethnic groups

with non-Hispanic white women continuing to have the highest risk of breast cancer (127.3 cases per 100,000 women) and Asian American/Pacific Islander having the lowest rate (84.7 cases per 100,000 women). Though African American women generally have a lower rate of breast cancer compared to non-Hispanic white women, they have a higher incidence in the age group less than 40 years old.

Hormone receptor status also varies by ethnic group with non-Hispanic white women having the highest rate of estrogen receptor positive breast cancer and African American women having the highest rate of estrogen receptor negative breast cancer. In the total population, however, more estrogen receptor positive breast cancers are being observed over time with a general decrease in estrogen receptor negative breast cancers. Though this may in part be a function of how testing is done, it appears that this represents a true change in pattern. Trends in other markers such as progesterone receptor status and HER2 status are not reported in this publication.

Overall, breast cancer death rates have decreased by 34% for the 20-year period between 1990 and 2010. The largest decline has been noted in women less than age 50. The decline in death rate is attributed to both improvement in early detection as a result of screening mammography and improvements in treatment. Breast cancer related survival rates differ among the ethnic groups with African American women having the lowest 5-year survival rate of 78.9% and Asian American/Pacific Islander women having the highest 5-year breast cancer survival rate of 91.1%. Factors such as lower income, less education and lack of health insurance coverage are associated with a lower survival rate from breast cancer.

This article concludes by describing data gathered from the 2010 National Health Interview Survey that suggests that the adoption of agents such as tamoxifen and raloxifene as chemoprevention

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PREVIOUS ISSUES

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WHAT'S NEW continued

for breast cancer has been singularly unsuccessful with an adoption rate of less than 1%. This is a very different scenario than what is seen with agents that are used to reduce death from cardiovascular causes. The reluctance in adopting hormonal agents for breast cancer prevention is likely multifactorial but I believe is due in great part to (1) the fact that these agents are viewed by clinicians as cancer drugs with which non-oncologists lack experience, and (2) the fact that breast cancer prevention has not been accepted as a responsibility of primary care physicians. This task has been relegated to oncologists who, by the very nature of their practice, do not see the appropriate population.

As a medical oncologist dedicated to the treatment of patients with breast cancer, I look forward to the yearly update of statistics provided by the American Cancer Society. It is a clear and detailed presentation. These data highlight our points of strength and our weakness. Though breast cancer remains a very common disease in our country, our therapies have resulted in a marked improvement in survival rates. Not all share equally in this improvement and not all are cured from their diagnosis of breast cancer. There is still much to be done. I believe that early detection and prevention strategies are still key features of our future success.

Reference: DeSantis C, MA J, Bryan L, Jemal A, Breast Cancer Statistics, 2013, CA, A Cancer Journal for Clinicians, Volume 64, Number 1, Jan/Feb 2014, pg52-62.

THE HUMAN MICROBIOME

Though each of us is viewed as an individual, the reality is that each of us is a community. We carry with us our own vast supply of microbes. They are positioned on and in our skin, on mucosal surfaces (such as the mouth, nose, eyes and vaginal area), and in our gastrointestinal system. It has been calculated that the average human has 100 trillion microbes in the gastrointestinal system alone, which is 10 times more than all the cells in the human body. As you can see, we could argue whether we contain them or they contain us since they vastly outnumber us.

Our collection of microbes is composed of bacteria, fungi and primitive single-celled organisms called archaea. Collectively they are referred to as the human microbiome. In the past it was generally believed that these microorganisms were primarily passengers in our bodies that occasionally caused disease. It is now evident that they play a crucial role in our health. The human microbiome has evolved with us over thousands of years. It expresses a symbiotic and mutually dependent role in our lives.

Different parts of our body are populated with different members of our microbiome. Various members function best in certain locations, giving some predictability of where they are found. However, since their number and location are influenced at least, in part, by our environment, our diet, our level of hygiene and our genetics, there is variability from person to person.

The functions of this complex system are numerous and I suspect most have yet to be recognized. We know that our microbiome interacts with the immune system, it produces vitamins, it aids in digestion and appears to have an influence on hormone levels. The various members of the microbiome exist in a balance with each other. Disruption in the system and its balance are a hazard to our health. Several diseases are now believed to have links to our microbiome. These include clostridium difficile infections, irritable bowel syndrome, inflammatory bowel disease, obesity, allergic disorders, stomach ulcers and certain neuropsychiatric illnesses. It is postulated that heart disease and some cancers may also be related to disruption to the normal balance of the microbiome.

As with the Human Genome Project, the National Institutes of Health have provided support for the Human Microbiome Project, which seeks to understand the details of the human microbiome and its function in human health and disease.

Reference: Khanna S, Tosh PK, A Clinician's Primer on the Role of Microbiome in Human Health and Disease, Mayo Clinic Proceedings, volume 89, number 1, January 2014, pg107-114.

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DISCLOSURE

The information contained in this newsletter is for educational purposes only. It is not designed to diagnose or provide treatment recommendations. Please consult your own physicians for all decisions about your care.

WHAT'S NEW continued**AVOIDING RADIATION THERAPY IN DCIS**

Screening mammography has greatly increased the number of women diagnosed with ductal carcinoma in situ (DCIS). Currently, DCIS makes up 20% to 30% of all mammographically detected breast cancers in the U.S. Standard therapy for DCIS is either a mastectomy or lumpectomy with radiation therapy. It has been noted for decades that when patients with DCIS experience a local recurrence, about half of the time they will again have DCIS, but half of the time the recurrence will be invasive breast cancer. It has also been demonstrated by many studies that the addition of radiation therapy after lumpectomy reduced both types of recurrences by approximately 50%.

There continues to be a debate about whether radiation therapy is really necessary following lumpectomy for DCIS, or whether it can be avoided at least in some patients who either by tumor characteristics or older age are considered to be at lower risk of recurrence.

The most recent published study that deals with the question of radiation in the treatment of DCIS is an update of study EORTC 10853. This trial was conducted from 1986 to 1996. It enrolled 1,010 patients with DCIS that measured less than 5 cm, who were randomized to treatment with either lumpectomy or a lumpectomy followed by radiation therapy. The present analysis was conducted based on a median follow-up of 15.8 years. No data are provided on whether patients also received any additional therapy such as tamoxifen for their DCIS. During this period, 23% of patients developed a local recurrence. Of these local recurrences, 48% were again DCIS and 52% were invasive cancer. A total of 30% of those treated only with surgery versus 17% of those treated with both surgery and radiation developed a local recurrence. For all patients, the risk of local recurrence was highest during the first five years. Certain factors predicted for a greater probability of

local recurrence: age less than 40, DCIS detected clinically rather than by screening mammography, surgical margins that were not free of tumor and a solid or cribriform growth pattern of DCIS. The study concluded that even long-term, radiation therapy reduces local recurrence from DCIS by about one-half. They did not identify a subgroup of patients that did not benefit from radiation.

As has been the case in such studies in general, no difference was reported in overall survival (death from any cause) between the two groups. The authors make it clear that this study did not include enough patients to be able to identify a difference in overall survival. They were able to make observations about breast cancer specific survival (breast cancer as the cause of death) in patients who recurred versus those who did not. Those who recurred with a DCIS, had a breast cancer specific survival rate equal to those who did not recur. However, those who at recurrence had an invasive breast cancer, had a 5 times higher risk of death than those who did not recur.

So, what does this study tell us that we did not know before? Its main value is in providing data on a group of patients followed for a relatively long time of nearly 16 years. It confirms that these patients generally do well. It confirms that radiation reduces local recurrence. It tells us that those who at recurrence again have DCIS continue to do well. In contrast, those who recur with an invasive cancer are more likely to die from breast cancer. Reducing invasive breast cancer is the most significant effect of radiation. This study fails to answer the question of whether radiation alters overall survival.

I believe that radiation post lumpectomy remains standard therapy for patients with DCIS. I do think that for selected women who are older and who have a small, non-aggressive DCIS, that radiation can be avoided, if it is the patient's preference.

Reference: Donker M, Litiere S, Werutsky G, et al. Breast-Conserving Treatment With or Without Radiotherapy in Ductal Carcinoma In Situ: 15-Year Recurrence Rates and

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WHAT'S NEW continued

Outcome After a Recurrence, From the EORTC 10853 Randomized Phase III Trial.
Journal of Clinical Oncology, Volume 31, Number 32, November 10, 2013, pg4054-4066.

QUESTIONS & ANSWERS

(Q) Dr. Martino, is it OK for me to get my teeth cleaned during chemotherapy? My oncologist has told me that I should wait until my chemo is finished. My dentist wants me to stay on schedule. Isn't it important to have regular dental checkups?

(A) As I hope your oncology care team has informed you, chemotherapy drugs, in general, lower your blood counts. As your counts decrease, you are more vulnerable to developing infections. The longer your counts stay down, the more susceptible you are to infections. It is wise to reduce the risk of this problem as much as possible.

As you probably know, the mouth is a part of the body that is filled with bacteria. Dental cleaning and dental work can be a source of infection. If one has the option, it is best to do dental cleaning and dental repair before chemotherapy is started. In a similar manner, if you are about to complete your chemotherapy in the near future, you might postpone dental cleaning or any dental work that is optional and is not an emergency until your chemotherapy is completed and your counts have returned to normal. If you are dealing with an emergency situation, then you may not have the option of waiting. In that case, your oncologist and dentist need to coordinate your care. You may need to delay the next dose of chemotherapy or perhaps neupogen can be administered to help return your counts to normal. It is best to time dental work to when your white count is normal and avoid periods when it is low or is anticipated to drop.

(Q) Dr. Martino, the oncology nurse has told me that I should avoid using a hot tub. Why? I find the hot tub very soothing and calming. I would think that it would be good for me.

(A) Please see the answer to the question above as some of the same principles apply to your question. A hot tub is also a place where bacteria grows easily. The increase in temperature assists in its growth. In my own practice, I have discouraged patients from using hot tubs particularly in public places such as in a health club or hotel. I am more lenient on this issue if it is a hot tub within your own home where use by others is limited.

COMMENTARY

Among the statistics published each January by the American Cancer Society is a list of the ten leading causes of death in the United States. My eyes go quickly to details related to the updated statistics on cancer. I also routinely give a passing glance to the statistics on cardiovascular disease, which still dominates the list as the number one cause of death for both males and females when all age groups are combined. For reasons unknown to me, this year my attention was arrested by the causes of death in children and young adults which are divided and grouped by ages and gender. As I did this, I was startled by the causes of death listed for young males in the U. S. For the age groups 1-19 and 20-39, the top three causes of death in males was not a disease at all. It was (1) accidents/unintentional injuries, (2) assaults/homicides and (3) intentional self-harm/suicides. I confess that it took me several days to get over this list. So much loss of our youth from trauma and crime. I am certain that I have seen this list before since it is published every year, but these facts had escaped my notice. I was focused on cancer and heart disease and I have ignored the rest.

Perhaps I should not have been so surprised having lived in both Detroit and the Los Angeles area, but I was shocked. I was shocked at the reality and equally as disturbed by my own blindness. I don't know what to do about it other than to continue to be disturbed.

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