Triple-negative breast cancer (TNBC) is considered a rare diagnosis. This malignancy targets a specific population of women and has risk factors differing from those of other breast cancers. TNBC exhibits distinct pathologic features that result in aggressive metastasis and poor prognosis. Pathologically, TNBC cancer cells are characterized by negative receptors for progesterone and estrogen and by the lack of over-expression of human epidermal growth factor receptor 2, which limits chemotherapeutic treatment options for women with TNBC. Nurses can assist in early detection by offering patient education about the little known risk factors for TNBC. Psychosocial issues can overwhelm patients diagnosed with breast cancer. This article provides suggestions for nurses as they guide women who are experiencing an atypical breast cancer diagnosis with an uncertain prognosis and limited treatment options.

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Medical History

R.D. has hypertension treated with atenolol 50 mg by mouth daily, overactive bladder managed with oxybutynin 10 mg by mouth daily, and rosacea controlled with minocycline 100 mg by mouth daily. Her allergies include codeine and clemastine. R.D. was aged 11 years at menarche, and at ages 21 and 25, she vaginally delivered two children without complications. She breastfed both of her infants for seven days and had a 30-day course of bromocriptine after she stopped breastfeeding the first time. R.D. had an uncomplicated tonsillectomy as a child. In 2000, she had a hysterectomy with a unilateral salpingo-oophorectomy (for menometrorrhagia unresponsive to pharmacotherapy) and a bladder suspension (for history of urinary incontinence since childhood). No history of malignancies exist in any first-degree relatives. R.D.’s maternal great-grandfather died from lung cancer, one maternal uncle passed from pancreatic cancer, and another maternal uncle died from angiosarcoma. Review of systems revealed no complaints or chronic medical problems.

Pathophysiology

Breast cancer is divided into subgroups and distinguished by tumor appearance based on a histologic classification system (de Ruijter, Veeck, J. de Hoon, van Engeland, & Tjian-Heijnen, 2011). The histology of breast cancer includes subtypes and grading based on tumor size, lymph node involvement, and distant metastasis occurrence (de Ruijter et al., 2011; Edge et al., 2010). Important characteristics, such as stage, histopathology, grade, and receptor status, help identify the type of breast cancer among women. These characteristics are used by clinicians to determine what treatment would be most effective (Francescutti et al., 2011).

TNBC is defined pathologically by the lack of expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) (Masuda et al., 2011). According to Telli and Ford (2010), the majority of TNBCs have similarity in their basal-like pattern of gene expression, characterized by a high appearance of multiplying genes and basal cytokeratins. Subsequently, TNBC is typically more aggressive biologically when compared to other types of breast cancer, making it unresponsive to endocrine and monoclonal antibody therapies (Colfry, Humphries, & Fuhrman, 2011; Reeder-Hayes, Carey, & Sikov, 2010).

The aggressive nature of TNBC exhibits large tumors of elevated nuclear and histologic grades, with a high proliferative rate leading to poorer prognosis and increased recurrence rates (Reeder-Hayes et al., 2010). TNBC also displays rapid metastasis, spreading to distant sites, particularly the lungs and brain (Colfry et al., 2011). Breast cancers that are metastatic hormone receptor-positive usually cause late bone metastases, whereas TNBC is more likely to cause early visceral metastases (Hudis & Gianni, 2011).

Treatment

Therapeutic options available for TNBC range from primary surgery to adjuvant chemotherapy, radiotherapy, hormonal therapy, or targeted therapy (de Ruijter et al., 2011). Prior to beginning systemic therapy, a central venous access device is surgically implanted to safely deliver chemotherapy. The standard chemotherapeutic treatment for women with early-stage TNBC currently involves an anthracycline and taxane-based combination chemotherapy regimen (Telli & Ford, 2010). Anthracycline-based regimens include AC (doxorubicin, cyclophosphamide) followed by T (docetaxel) or TAC (docetaxel, doxorubicin, and cyclophosphamide) (Connolly & Stearns, 2010). According to the 2005 Early Breast Cancer Trialists’ Collaborative Group, meta-analysis studies revealed a survival advantage and a reduction of recurrence risk with anthracycline-based therapies compared to nonanthracycline-based therapies (Gajria, Seidman, & Dang, 2010).

TAC is given via IV every 21 days, with a total of four cycles given, which takes three months to complete the prescribed regimen (Cancer Research UK, 2012; Health Canada, 2007). Rare, but serious, long-term effects of anthracycline-based regimens include congestive heart failure and secondary malignancies (Gajria et al., 2010). The more common side effects of a TAC regimen include neutropenia, anemia, nausea, diarrhea, vomiting, fatigue, stomatitis, nail changes, fever, hair loss, fluid retention, rash, nerve pain, and swelling at the injection site (Cancer Research UK, 2012; Health Canada, 2007).

Locoregional treatment of TNBC does not differ from other invasive breast carcinomas (Brouckaert, Wildiers, Floris, & Neven, 2012). Breast-conserving surgery followed by radiation therapy is the standard treatment; however, mastectomy may be recommended for extensive or multifocal disease (Maughan, Lutterbie, & Ham, 2010). Radiation therapy following lumpectomy decreases local recurrence and improves cancer-specific survival rates to survival rates equivalent to mastectomy (Maughan et al., 2010). One distinct factor concerning locoregional
treatment in TNBC is the choice for contralateral prophylactic mastectomy in patients with BRCA1 mutations (Brouckaert et al., 2012). The benefits of contralateral prophylactic mastectomy compared to chemoprevention are uncertain because no prospective, randomized trials comparing the two treatment protocols exist (Lostumbo, Carbine, & Wallace, 2010).

Therapies Under Investigation

Several clinical trials have been investigating a variety of newer therapies to treat TNBC. Poly (ADP-ribose) polymerase (PARP) inhibitors, platinum salts, angiogenesis inhibitors, epidermal growth factor receptor (EGFR) inhibitors, vascular endothelial growth factor receptor (VEGFR) inhibitors, Rous sarcoma virus (SRC) inhibitors, vaccines, high-dose chemotherapy, mammalian target of rapamycin (mTOR) inhibitors, notch or secretase inhibitors, heat-shock protein 90 (HSP90) inhibitors, marine natural product DNA-damaging agents, histone deacetylase (HDAC-I), and interleukin-6/Janus kinase 2 (JAK1 and JAK2) inhibitors are among those investigational treatments.

According to Crown, O’Shaughnessy, and Gullo (2012) and Joensuu and Gligorov (2012), PARP inhibitors that are showing promise in clinical trials against TNBC include olaparib, veliparib, MK-4827, and PF-01367338. The phase III trials of the once-classified PARP iniparib demonstrated no difference in overall survival or progression-free survival in patients with TNBC (Crown et al., 2012). However, Liedtke and Kiesel (2012) reported that iniparib may have a role in second- or third-line treatment for metastatic breast cancer.

Cisplatin appears to have superior disease-free and overall survival rates as compared to carboplatin in the platinum salts class of chemotherapeutic drugs (Gelmon et al., 2012). Telli and Ford (2010) noted that five clinical trials testing platinum salts in neoadjuvant regimens reported increased pathologic complete response over the regimens without the platinum salts.

Potential for the EGFR inhibitors cetuximab, erlotinib, lapatinib, and panitumumab in combination with taxanes or platinum salts also has been noted in trials (Crown et al., 2012; Gelmon et al., 2012; Joensuu & Gligorov, 2012; Telli & Ford, 2010). Vascular endothelial growth factor receptor (VEGFR) or angiogenesis inhibitors like bevacizumab have been reported by many to show promise in progression-free survival in metastatic TNBC and increasing pathologic complete response in early TNBC neoadjuvant therapy (Gelmon et al., 2012; Joensuu & Gligorov, 2012; Liedtke & Kiesel, 2012). Crown et al. (2012) mentioned that a newer VEGFR, ramucirumab, is in phase III clinical trials with docetaxel for metastatic HER2-negative breast cancer, and Hudis and Gianni (2011) reported the initial outcome of trials testing sunitinib had an overall response rate of 15%.

Everolimus, an mTOR inhibitor, has demonstrated mixed results according to Gelmon et al. (2012). In one study conducted by Andre et al. (2010), combining it with paclitaxel revealed encouraging results; however, another randomized trial did not display significant increase in pathologic complete response (Gelmon et al., 2012). Crown et al. (2012) indicated that among the many clinical trials occurring with mTOR inhibitors, no preliminary data revealed their efficacy in breast cancer treatment.

Some interventions are too new for data reporting, such as notch or secretase inhibitors, marine natural product DNA-damaging agents, and HDAC-I. HSP90 inhibitors have demonstrated anticancer properties in preliminary testing, as well. In addition, JAK1 and JAK2 inhibitors have been identified as possibly having therapeutic benefits in breast cancer and are being trialed in solid malignancies (Crown et al., 2012).

Outcome of Interventions

R.D. underwent a left axillary lymph node biopsy prior to treatment. Methylene blue dye and a radiotracer were injected into the right breast using the peri-areolar approach one hour prior to surgery. During surgery, six nodes were identified by their blue hue and the readings on a gamma probe. These nodes were harvested and sent for histologic review. Only one of these sentinel nodes was positive with metastatic disease, giving R.D. a staging classification of IIB, T2N1M0. Stage IIB is considered early breast cancer (National Cancer Institute, n.d.).

R.D. experienced seroma, a surgical complication, which persisted for two months. It was large and caused significant discomfort as she performed the activities of daily living. This lesion was drained five times of blood-tinged serous fluid in amounts ranging from 20–90 ccs. The first two aspirates were sent for culture and sensitivity, but no pathogens were present. Nevertheless, R.D. was treated with cephalexin for seven days and then amoxicillin and clavulanate for five days. These antibiotic therapies did not serve to resolve the seroma. R.D.’s breast health navigator suggested a compression bra. Within three days, she experienced relief from the pain of the seroma; however, the breast remained enlarged and red until surgery.

Four weeks after the final round of chemotherapy, R.D. had a double mastectomy. She was discharged from the hospital within 24 hours with Jackson Pratt (JP) drains drawing fluid from each surgical site. She was instructed to begin slowly exercising her arms, not to lift anything heavier than five pounds, and to document the amount of fluid each JP collected. R.D. was told that once the drain output was less than 20 ccs in a 24-hour period, they would be removed. She was given hydrocodone and acetaminophen for pain and was told she could take ibuprofen for lesser pain. The left JP drain was removed 17 days after surgery, and although the right site continued to drain 33–35 ccs

Implications for Practice

- Increase awareness of triple-negative breast cancer (TNBC) by incorporating TNBC risk factors into patient education on breast cancer risk factors.
- Empower patients by educating them in breast self-awareness for detecting breast problems and emphasize routine screening tests.
- Decrease emotional distress in patients diagnosed with TNBC by supplying them with resources to assist in understanding disease process, treatment, testing and prognosis; dealing with emotional distress and living with a chronic disease; and connecting with peers who have, or are experiencing, the same diagnosis.
per day, it was removed 24 days after surgery to mitigate the risk of infection. Her mastectomy incisions healed well.

With removal of the breast tissue, pathology can determine if any residual tumor exists after neoadjuvant chemotherapy. In R.D., pathologic complete response of the cancer occurred from chemotherapy, which means that no disease was detected in the affected breast tissue under microscopic examination. According to von Minckwitz and Martin (2012), TNBC patients with pathologic complete response to neoadjuvant chemotherapy have survival rates that are comparable to non-TNBC patients.

**Nursing Implications**

Women living with breast cancer may experience depression, anxiety, low self-esteem, and poor quality of life (Boutin, 2007). Breast cancer frequently causes emotional trauma in patients, expressed with increased feelings of vulnerability, loss of control, and doubt (Schmid-Büchi, van den Borne, Dassen, & Halfens, 2010). Women affected by breast cancer may not seek help from family and friends because of feelings of guilt in burdening others (Boutin, 2007). Women with TNBC may experience increased emotional distress when faced with their higher odds of early recurrence and poorer survival rates.

Healthcare professionals, particularly nurses, are positioned to identify signs of emotional distress and plan interventions to help alleviate it early (Lim, Devi, & Ang, 2011). Having a list of resources readily available to share with patients is a key item for nurses to maintain for this purpose. Number one on any list of resources should be a breast health navigator. Breast health navigators intimately assist patients in understanding the diagnosis and available treatment options; the roles of a navigator also can include finding transportation, exploring solutions for work or financial issues, education on prescribed medication, and providing support. They assist in compiling all of the patient medical information and presenting it to them in a concrete, organized, understandable manner. This serves to decrease anxiety and reduce an overwhelming medical issue into pieces that can be comfortably managed by the patient. If institutions do not offer the services of a breast health navigator, a case manager or outpatient social worker can assist with many of the needs of patients diagnosed with TNBC. Because of the short, disease-free interval and low overall survival rate of TNBC, these patients need someone who can offer them hope. Knowledge and information is a powerful tool to decrease anxiety related to a cancer diagnosis (Cho et al., 2011). A list of psychologists is the next needed item in the nurse’s resource list. Psychologists can assist patients in dealing with the emotional distress caused by a cancer diagnosis and the uncertainty of living with this chronic condition. Specific issues for patients with TNBC are the risks of earlier recurrence and lower survival rates seen in this group.

Face-to-face and online support group information are other items the nurse should provide to their patients. Winzelberg et al. (2003) found that an expertly led, web-based support group decreased distress in patients with breast cancer. Pamphlets, flyers, and internet addresses of peer support groups should be made available to patients with TNBC.

Many patients and their families will explore and gather as much data as they can. Suppling them with a list of patient education sites that are medically based and known to be accurate will help to decrease any additional distress brought on by erroneous information (see Figure 2). In addition, providing evidence-based education to patients has become recognized as standard of care. Research has shown that most effective educational methods include patient decision aids, counseling, videos, computer-based information or education, and interactive computer and multimedia interventions (Johnson et al., 2011).

The risk factors for TNBC are an additional facet that nurses should incorporate into teaching women about risks for breast cancer. TNBC is more prevalent in younger women, African American and Hispanics, and women with BRCA1 mutation (Chu et al., 2011).

Interval breast cancer is defined as in situ or invasive cancer that is discovered after a negative screening mammogram and before the time of the next suggested mammogram. A larger number of interval breast cancers are TNBC (Rayson et al., 2011). Nurses must teach women about breast self-awareness to detect breast problems and emphasize routine screenings. According to the American College of Radiology (2008) and Smith, Brooks, Cokkinides, Saslow, and Brawley (2013), women aged 40 years and older should have a yearly screening mammogram. Women in their 20s and 30s are advised to have a clinical breast examination with their regular physical examination at least every three years and annually thereafter (Smith et al., 2013).

**Conclusion**

TNBC is a type of breast cancer diagnosed by not having ERs and PRs and lack of over-expression of HER2 receptors. Because of these characteristics, TNBC is unresponsive to endocrine and monoclonal antibody therapies, making it more difficult to treat. This cancer yields tumors with a high proliferative rate, leading to a poorer prognosis and increased recurrence rate. In addition, risk factors for TNBC differ from those of typical breast cancer, leaving a gap in patient education that nurses must address. Therapeutic treatment options consist of
neoadjuvant or adjuvant chemotherapy and primary surgery, with or without radiotherapy. Nurses can assist women in many ways both prior to and after a diagnosis of breast cancer. Understanding risk factors, screening, disease process, and effects of treatments will prepare nurses to help patients with early diagnosis and treatment of this uncommon breast cancer.

References


