Evolving Paradigms in Triple-Negative Breast Cancer

Breast cancer is a leading cause of cancer death in women with approximately 12 to 20% of these being classified as triple-negative breast cancer (TNBC). These tumors are characterized by a lack of estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptor (HER2), which limits the use of trastuzumab and hormonal based treatments. Research into treatment options for TNBC is of significance because it is often diagnosed in younger women, African American women, its aggressive nature, its poor prognosis, and a lack of targeted therapy specific to TNBC.[1]

Furthermore, when compared to other subtypes triple negative breast cancer only has a median survival of 12 months and is associated with visceral metastases and recurrence within 3 years of diagnosis.[2]

The heterogenous nature and limited biomarkers of TNBC have restricted the development of drugs specific to TNBC, however new research has opened the door for targeted therapies based on distinct morphological features.[2,3]

Pathophysiology of TNBC

Breast cancer is divided into 18 difference subtypes based on histology and morphological characteristics. However, this does not take into account disease specific treatment options and prognosis. Furthermore, accuracy of classification is pathologist dependent. Further studies into DNA microarrays allowed division based on gene expressions including hormone receptors. The breast cancer subtypes luminal A, luminal B, basal-like, normal-like, and HER-2 positive have individualized treatments and prognoses.[4]

Triple negative breast cancer is a heterogenous group of tumors with an absence of HER2, ER, and HR and can be further divided into apocrine, adenoid cystic, metaplastic, and medullary histopathological subtypes. Frequently encountered mutations in TNBC include mutations in TP53 and PIK3CA (Figure 1).[3]