Review

The Connection between Breast Cancer and Microbiome Composition

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Abstract: Many of the microorganisms that compose the microbiome of human are favorable or even helpful to the host's health, and this group play a crucial part in the body's physiological functioning. A number of microorganisms, meanwhile, have been related with cancer and other disorders defined mostly by abnormal inflammation and are thus thought to be harmful to human welfare. Cancer is only one of several diseases that may develop as a result of dysbiosis, a microbiological disequilibrium in which hazardous bacteria species compete effectively harmless bacteria. The skin microbiome, the urogenital microbiome and the gut microbiome, are especially clearly defined, although the microbial diversity differs between body locations. Nevertheless, there is little knowledge about the human microbiome and about the way, it relates to both healthy and diseased breasts. According to a variety of research, breast tissue has a unique microbiome, with certain types being elevated in the tissue alone; along with in the gut and nipple aspirate microorganism of the breast cancer patients. In addition, the breast microbiome and its surroundings can influence the treatment reaction and function as conceivable biomarkers in the detection and evaluation of breast cancer at any stage.

Keywords: Gut, Flora, Immune response, Microbiome, Breast cancer, Bactria, Microorganism

1. Introduction

When it comes to cancer diagnoses across the America, breast cancer continues to dominate. With an anticipated 267,000 confirmed cases and approximately 41,000 fatalities in 2018 [1], breast cancer is responsible for almost 30% of all cancer incidence in women. Even while breast cancer death rates have dropped substantially over the last 20 years thanks to improvements in diagnosis and therapy, the causes of the most cases are not clear. It is intriguing to consider that a person's unique microbiome, that also contains about 31013 bacterial cells, the identical intensity as cells within the body affect the successive therapeutic reaction and the risk of developing breast cancer and in light of the latest focus on the composition of microbiome and its helpful effect on diseases [2]. Many spontaneous incidences of breast cancer develop in women who are not at significant risk, despite the notion that there are certain known genetic risk indicators such as mutations in BRCA1/2 and environmental exposures like hormone replacement, alcohol, obesity and a sedentary lifestyle. That raises the prospect of further, as-yet-unidentified sources of danger. Hyperactive immune reactivity and persistent inflammation are hallmarks of the cancer microenvironment, which consists of immune, stromal and tumor cells in a medium of extracellular and cytokines proteins. Research demonstrates that perhaps the immune system monitors for immature altered cells and is essential for immune editing of tumor along with the prevention of ca [3, 4]. It is certainly not unexpected that some

microorganisms are linked to the formation of certain malignancies due to the significance of immune resistance, inflammation-mediated carcinogenesis pathways and bacterial dysbiosis in persistent inflammation. In the case of colorectal cancer, Fusobacterium, gastric cancer and H. pylori, similar associations have been established [5-7]. The link connecting breast cancer and the microbiota is, meanwhile, very loosely understood.

2. Microbiome composition of skin and the tissue of breast

There was a misconception that milk and breast tissue were sterile, but recent studies have shown that they really host a rich and varied bacterial population [8, 9]. Fluid of Nipple aspirate from individuals having a breast cancer background was shown to have a greater prevalence of the species Alistipes and a less prevalence of a group from Sphingomonadaceae family compared to healthy counterparts [10]. Some microorganisms, such as Bacteroidetes, Comamonadaceae, Staphylococcus, Enterobacteriaceae, Bacillus, Hydrogenophaga, Gluconacetobacter, Atopobium and Fusobacterium have been shown to be elevated in tissue of the breast and swabs of breast skin from women suffering from breast cancer compared to healthy counterparts [9, 11].

3. Immunotherapy

The gut microbiome may have a role in the therapeutic outcome to immunological circuit inhibitors, as shown by mounting data. A research found that Bacteroides types, especially the B type. The taiotaomicron and fragilis, may help boost the effectiveness of anti-CTLA-4 antibodies as a therapeutic immunological circuit inhibitor [12]. Similarly, the fecal microbiome of patients suffering from melanoma who are classified as respondent part to anti-PD-1 therapy seems to be highly diversified, having an elevation of bacteria from Ruminococcaceae family. Not only had that, but individuals who had a more varied fecal microbiome had a considerably greater development-free longevity compared to those who had medium or poor microbial diversification. By improving antigen expression or boosting T cell mobilization with in local neoplasm microenvironment, the gut microbiome of immunotherapeutic patients might activate the immune reaction [13]. Other research has shown that particular bacteria, such as Akkermansia muciniphila and Bifidobacterium [14, 15], are linked to a better reaction to anti-PD-L1 therapy. All of this suggests that a person's microbiota might be exploited to give tailored, personalized therapies for breast cancer, even though no investigations have yet evaluated the influence of microbiome makeup on treatment outcomes in this disease. Furthermore, microbiota environment management could serve as a strategy to circumvent tolerance to specific breast cancer monoclonal antibodies.

4. Radiotherapy

When it comes to treating breast cancer, radiation therapy (RT) is also crucial. To decrease the risk of a local reappearance and increase the chance of a patient surviving after a mastectomy, RT may be utilized during post-mastectomy and conservation of breast settings. The majority of patients tolerate ionizing RT well, but approximately to 95% develop either chronic dermatitis or acute as a side effect. Cancer therapy may need to be put on hold if symptoms of acute radiation dermatitis (which might include ulceration, blistering, epilation, erythema and pain) develop. Recovery and life quality may be significantly impacted by persistent dermatitis, which develops months or even years

following RT and comprises of gradual and permanent skin abnormalities including pigmentation, atrophy and fibrosis modifications. Although radiation dermatitis may be alleviated with good skin care and applied steroids, numerous individuals ultimately endure substantial skin damage after RT. As of yet, the specific process of dermatitis that induced by RT is unclear; however, an abnormal proinflammatory reaction is highly suspected [16, 17]. Inflammation that induced by RT may be made worse by microbial super antigens, especially the ones from S. aureus. This is done by more activation of T cells and inhibition of epidermal healing [18].

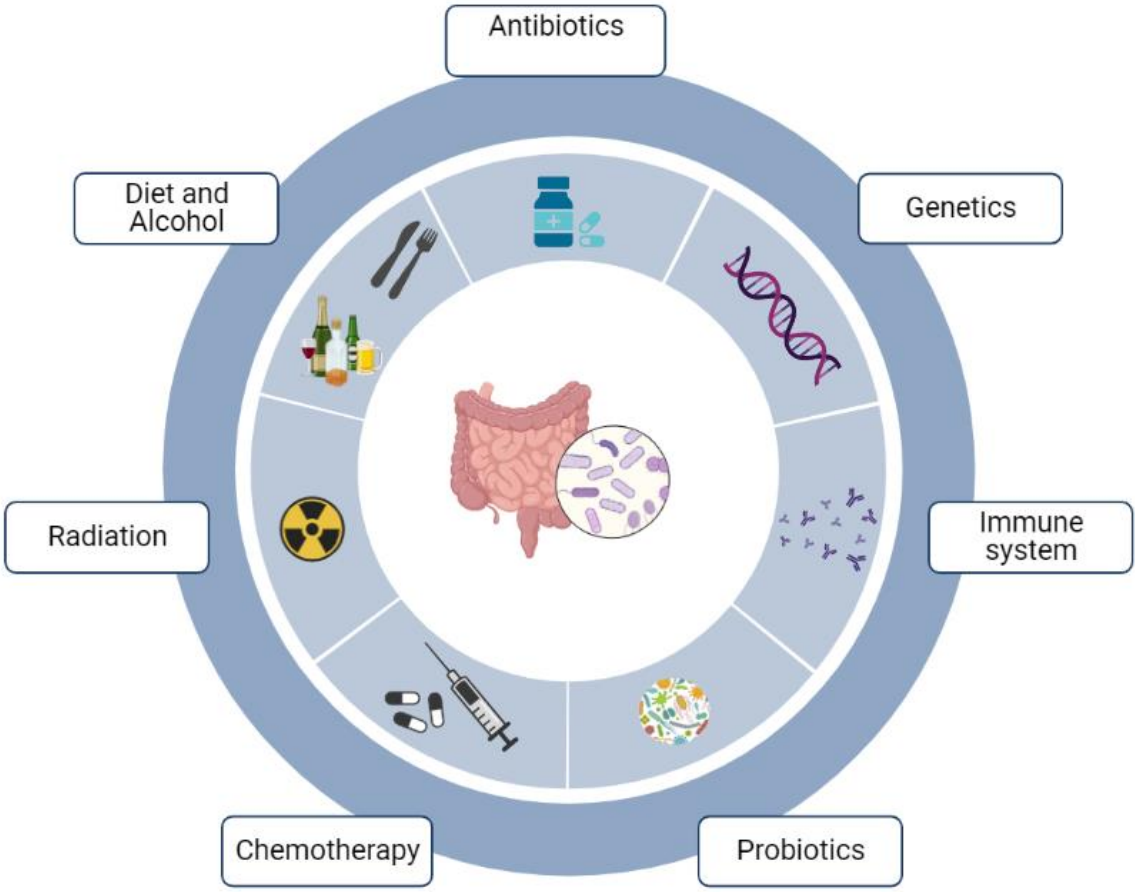
5. Chemotherapy

The distribution of microorganisms in the digestive tract may influence the immunological reactivity, metabolic activity and translocation to chemotherapy, according to mounting findings [19]. Furthermore, the recognized involvement of microbiome of the gut in regulating the effectiveness of various chemotherapeutic drugs, it is plausible that perhaps the breast local microbiome might have a different function in modifying chemotherapeutic performance [20]. An impaired reaction to platinum-based chemotherapy drugs and immunotherapeutic has been linked to antibiotics consumption [21]. Our research adds to the increasing evidence that patients' microbiomes must be healthy in order to benefit fully from cancer treatments. Previous investigations on the gut microbiome's function in affecting a patient’s reaction to a treatment have been reached through various research [22].

6. The relationship between the microbiome of the gastrointestinal tract and dysbiosis

The interaction of the human microbiome with metabolic activities nutrition consumption and immune responses is crucial to human health. The interactions of microorganism and its host in a condition of symbiotic fend against infiltrating invaders and stop the formation of tumor [23]. Dysbiosis might develop if homeostasis is disturbed due to modifications in the microbial species (Figur1). Disturbances in the composition of the microbiome of a given area have been linked to illness development [23, 24]. Research has shown that, despite the microbiome's adaptability, women suffering from breast cancer have a different gut microbiota than their healthy counterparts [25]. There is a substantial association between elevated estrogen levels and the onset of breast cancer, and expanding data suggests that the environment of microbiome plays a role in the metabolism of estrogen. Ampicillin-treated individuals exhibited more excretion of conjugated estrogen in their feces, a finding that supports a dynamic role for gut flora in the metabolism of estrogen [26]. Therefore, altering one's microbiome composition could have certain implications on development of breast cancer, since gut flora could indeed be implicated in the metabolism of estrogen. Furthermore, Overall makeup of the gut microbiota may potentially be affected by sex hormones [27]. Comparing individuals suffering from postmenopausal breast cancer to healthy counterparts, a case-control research found that the fecal microbiome of the former group was less diverse and had a different distribution overall [25]. Methylobacterium radiotolerans was shown to be enriched in breast tumor compared to Sphingomonas yanoikuyae in comparable normal breasts, as was the case in a separate investigation. Bacterial burden was shown to be inversely related to the stage of breast cancer as determined by total DNA measurement. Comparing stage 1 individuals suffering from breast cancer to stage 2 and stage 3 sufferers, stage 1 had the most

copies of bacterial DNA. There was also a correlation between this disparity in bacterial burden and the decreased antibacterial genes expression. In individuals with advanced breast cancer, such results imply dysbiosis could be a factor in the formation of breast cancer tumors, where a decrease or change in bacterial composition can result in abnormal immune system activity that promotes tumorgenesis. Further research is warranted since these results show that bacterium burden might function like marker for both classification and diagnosis [28].



Figur1. The causes of dysbiosis in the gastrointestinal microbiome and the parameters that affect its bacterial composition.

7. Breast abnormalities that are not cancerous

While malignant breast tumors have been the primary center of research into the involvement of microbiome in breast abnormalities, non-malignant breast conditions are much more frequent and have been demonstrated to increase risk of developing cancer as well as severely effect life quality [29]. These non-cancerous breast disorders comprise mastitis/breast abscesses, Ductal Carcinoma In Situ (DCIS), and atypical ductal hyperplasia (ADH). Milk from mastitis patients revealed microbiome compositions, such as decreased

nonpathogenic microbes, greater unscrupulous pathogenic organisms and relatively low diversity of microbes, according to a latest report. This is despite the fact that only certain organisms, many remarkably S. aureus, have been allegedly involved as direct causal in mastitis [30]. Even while there are certain established risk indicators for DCIS and ADH, both of which are defined by irregular, neoplastic cell proliferation and may be linked to or be the precursor to aggressive breast cancer, underlying pathogenesis is mainly unclear. The question of how the microbiomes of gut and breast affect non-cancerous breast disorders like ADH and DCIS arises in light of evidence demonstrating bacterial variations in other tissues may be connected to neoplastic non-cancerous development [31].

8. Clinical trials

Currently, there are many different kinds of scientific studies looking at how the microbiome affects breast cancer. In women suffering from breast cancer, one research is looking at whether or not probiotics might improve the immune system's capacity to spot tumor cells [32]. Within 4 weeks of probiotic medication, the amount of tumor T cells that are cytotoxic is being tracked throughout this experiment. The relationship between the predominance of certain microbiome species and full pathological reaction in women suffering from breast cancer after neo-adjuvant chemotherapy is being investigated in some other research [33]. In a third investigation, researchers are trying to determine whether the composition of microbes in the digestive tract has any bearing on the efficiency with which immune cells resist cancer [34].

9. Conclusions

Due to the wide variety of possible interactions involving the microbiota and mild and aggressive breast disorders, we want to expand our knowledge of human microbiome within the framework of breast cancer therapy and causation. The human microbiome has been shown to modify the immune system in terms of sensitivity to and potential complications of radiation and immunological treatment, and it may also impact medication responsivity to both chemotherapy and hormone treatments.

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