UNIVERSAL JOURNAL OF MEDICAL AND NATURAL SCIENCES
ISSN 2992-8826
https://sr-journals.org/index.php/UJMANS

MORPHOLOGICAL CHANGES OF INVASIVE DUCTAL CARCINOMA AFTER RADIATION THERAPY

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Abstract. Breast cancer is a common disease, particularly in postmenopausal women (see Fentiman 1993). Each year, in the United Kingdom, there are approximately 40,000 new cases diagnosed and 14,000 deaths. Male breast cancers constitute up to 1% of all mammary malignancies and may include tissue beyond the areolar boundary.Breast cancers arise within the epithelia of lobules or ducts. As they increase in size and infiltrate the stroma, they often lead to a fibrous tissue reaction. Breast lumps may be classified as benign or malignant masses. Malignant breast lumps may have the clinical signs of infiltrating adjacent structures, leading to a hard and irregular mass with skin- tethering, muscle fixation, skin infiltration or oedema of the overlying skin.**Invasive Ductal Carcinoma (IDC)** accounts for approximately 75% of all breast cancers and is referred to as **invasive Ductal Carcinoma**, Not Otherwise Specified (NOS).It represents a heterogeneous group that includes different histologic types and significant variations in genetic profiles,impacting prognosis. It is the most common breast cancer.The abnormal cells spread to surrounding tissue is invasive ductal carcinoma.**Radiation therapy** is used after surgery or chemotherapy.Radiation therapy is often used pre-operatively (neoadjuvant) or post-operative ly (adjuvant) for breast cancer. It induces cellular, stromal, and vascular changes in both the tumor and surrounding tissue.

Keywords: breast cancer , Invasive ductal carcinoma , radiation therapy.Neoadjuvant chemotherapy, Breast cancer, Histomorphological, Fibrosis, Pyknosis.

Аннотация. Рак молочной железы является распространённым заболеванием, особенно среди женщин в постменопаузальном периоде (Fentiman, 1993). Ежегодно в Соединённом Королевстве диагностируется около 40 000 новых случаев и регистрируется приблизительно 14 000 летальных исходов. Рак молочной железы у мужчин составляет до 1% всех злокачественных новообразований молочной железы и может распространяться за пределы ареолярной зоны. Рак молочной железы развивается в эпителии долек или протоков. По мере увеличения размеров опухоли и инфильтрации стромы часто возникает фиброзная тканевая реакция. Опухолевые образования молочной железы подразделяются на доброкачественные и злокачественные. Злокачественные опухоли характеризуются инфильтрацией окружающих структур, что приводит к формированию плотной, неровной опухоли с втяжением кожи, фиксацией к мышцам, инфильтрацией кожи или отёком покрывающей кожи. Инвазивная протоковая карцинома (Invasive Ductal Carcinoma, IDC) составляет около 75% всех случаев рака молочной железы и классифицируется как инвазивная протоковая карцинома, неуточнённая (NOS). Данная форма представляет собой гетерогенную группу, включающую различные гистологические типы и значительные вариации генетических профилей, что влияет на прогноз заболевания. Инвазивная протоковая карцинома является наиболее распространённой формой рака молочной железы и характеризуется распространением атипичных клеток в окружающие ткани. Лучевая терапия применяется после хирургического лечения или химиотерапии, а также может

использоваться в предоперационном (неоадъювантном) и послеоперационном (адъювантном) периодах. Она индуцирует клеточные, стромальные и сосудистые изменения как в опухолевой ткани, так и в окружающих тканях.

Ключевые слова: Рак молочной железы, инвазивная протоковая карцинома, лучевая терапия, неоадъювантная химиотерапия, гистоморфологические изменения, фиброз, пикноз.

Annotatsiya. Ko‘krak bezi saratoni, ayniqsa postmenopauza davridagi ayollarda keng tarqalgan kasallik hisoblanadi (Fentiman, 1993). Buyuk Britaniyada har yili taxminan 40 000 ta yangi holat aniqlanadi va 14 000 ga yaqin o‘lim qayd etiladi. Erkaklarda uchraydigan ko‘krak bezi saratoni barcha ko‘krak bezi yomon sifatli o‘smalarining taxminan 1% ini tashkil etadi va areola chegarasidan tashqariga tarqalishi mumkin. Ko‘krak bezi saratoni lobulalar yoki duktal epiteliydan rivojlanadi. O‘sma hajmining ortishi va stroma to‘qimasiga infiltratsiyasi natijasida ko‘pincha fibroz to‘qima reaksiyasi yuzaga keladi. Ko‘krak bezi o‘smalari yaxshi va yomon sifatli turlarga bo‘linadi. Yomon sifatli o‘smalar atrofdagi tuzilmalarni infiltratsiya qilib, terining tortilishi, mushaklarga birikishi, teri infiltratsiyasi yoki ustki terining shishi bilan kechadigan qattiq va notekis massa hosil qiladi. Invaziv duktal karsinoma (IDC) ko‘krak bezi saratonining taxminan 75% ini tashkil etadi va “invaziv duktal karsinoma, aniqlanmagan (NOS)” sifatida tasniflanadi. Ushbu turli gistologik shakllar va genetik profillardagi sezilarli farqlarga ega bo‘lgan geterogen guruhni tashkil etib, kasallik prognoziga ta’sir ko‘rsatadi. Invaziv duktal karsinoma eng ko‘p uchraydigan ko‘krak bezi saratoni turi bo‘lib, atipik hujayralarning atrofdagi to‘qimalarga tarqalishi bilan tavsiflanadi. Nurlanish terapiyasi jarrohlik yoki kimyoterapiyadan keyin, shuningdek operatsiyadan oldin (neo-ad’yuvant) yoki keyin (ad’yuvant) qo‘llaniladi. U o‘sma va atrofdagi to‘qimalarda hujayraviy, stromal va qon tomir o‘zgarishlarni yuzaga keltiradi.

Kalit so‘zlar: Ko‘krak bezi saratoni, invaziv duktal karsinoma, nurlanish terapiyasi, neo-ad’yuvant kimyoterapiya, gistomorfologik o‘zgarishlar, fibroz, piknoz.

Introduction

Breast cancer is a common disease, particularly in postmenopausal women (see Fentiman 1993). Each year, in the United Kingdom, there are approximately 40,000 new cases diagnosed and 14,000 deaths. Male breast cancers constitute up to 1% of all mammary malignancies and may include tissue beyond the areolar boundary.Breast cancers arise within the epithelia of lobules or ducts. As they increase in size and infiltrate the stroma, they often lead to a fibrous tissue reaction. Breast lumps may be classified as benign or malignant masses. Malignant breast lumps may have the clinical signs of infiltrating adjacent structures, leading to a hard and irregular mass with skin-tethering, muscle fixation, skin infiltration or oedema of the overlying skin.Breast cancer is the most frequently diagnosed cancer among women and is the second leading cause of mortality globally [1]. Breast cancer encompasses the entire spectrum from ductal carcinoma in situ to invasive ductal/ lobular carcinoma to metastatic carcinoma. Fine needle aspiration cytology with core needle biopsy is among the first-line investigations along with mammography/ ultrasound. The prognosis of breast cancer is multifactorial and is dependent on- tumor size, nodal status, distant spread, bilaterality, and surrogate molecular classification. The treatment modalities available for breast cancer include surgery, chemotherapy, radiotherapy, hormonal therapy, and targeted therapy including trastuzumab. Although surgery is usually the first-line modality for operable tumors, however, neoadjuvant chemotherapy may be administered before the breast-conserving mastectomy. In addition, neoadjuvant chemotherapy may be given in advanced disease to shrink large tumors and downstage them so they may become amenable to surgeryThus, the majority of the resection specimens received in the histopathology laboratory are post-chemotherapy specimens. The morphological assessment of these specimens requires the pathologist to be acquainted with the stromal and nuclear changes following neoadjuvant chemotherapy so that he can accurately diagnose and grade the tumor. This study was performed to evaluate the stromal and nuclear changes in breast cancer following neoadjuvant chemotherapy. In addition, the specimens were classified based on the residual tumor as exhibiting pathological complete, partial, or no response. Signs are

lump, change in size , nipple changes, nipple discharge,skin changes (red or inflamed),skin dimpling.Risk factor older age ,dense breast,parent or siblings with breast cancer, inherited gene mutations (BRCA 1& BRCA 2), alcohol use, overweight or obesity.Role of Radiation Therapy in Invasive Ductal Carcinoma .Indications After breast-conserving surgery (lumpectomy),After mastectomy (high-risk cases),Locally advanced breast cancer,Palliative treatment for metastasis (bone, brain).

Morphological Changes. Tumor Cells-Nuclear pyknosis, karyorrhexis,Cytoplasmic eosinophilia,Multinucleated giant cells,Reduced tumor cellularity.Stroma-Dense fibrosis,Collagen deposition,Hyalinization,Scar formation.Vasculature-Endothelial damage,Capillary obliteration,Reduced microvascular density.

Functional changes . At the functional level, radiation therapy significantly impairs the viability and growth potential of IDC cells. DNA double-strand breaks caused by ionizing radiation disrupt the cell cycle, commonly arresting cells in the G2/M phase. This results in reduced tumor cell replication and long-term growth suppression. Radiation also alters tumor metabolism. Reduced blood supply due to vascular damage limits oxygen and nutrient delivery, leading to hypoxia and metabolic stress within residual tumor tissue. These conditions further inhibit tumor progression and may sensitize cells to additional treatments. Another important functional change is the modulation of the tumor immune environment. Radiation can enhance antigen presentation by tumor cells and increase infiltration of immune cells such as lymphocytes and macrophages. This immune activation may contribute to delayed tumor regression beyond the direct effects of radiation.

Literature review

Radiation therapy produces characteristic morphofunctional changes in invasive ductal carcinoma (IDC) and surrounding breast tissue. Histologically, irradiated tumors show reduced mitotic activity, nuclear atypia, cytoplasmic vacuolization, apoptosis, and focal necrosis, reflecting radiation-induced DNA damage and cell death. Stromal remodeling is prominent, with increased fibrosis, collagen deposition, and fibroblast activation replacing regressed tumor areas. Vascular injury, including endothelial damage and luminal narrowing, leads to reduced tumor perfusion and hypoxia. Functionally, radiation suppresses tumor proliferation, alters metabolic activity, and modulates the immune micro environment, contributing to improved local tumor control but complicating post-treatment pathological interpretation.Stromal alterations are a dominant morphological feature following radiation therapy. Progressive fibrosis with increased collagen deposition replaces viable tumor tissue, accompanied by activation of fibroblasts and thickening of the extracellular matrix. Radiation also affects the vascular compartment, producing endothelial cell injury, vessel wall thickening, and reduced capillary density, which contribute to hypoxia and metabolic stress within the tumor bed.Functionally, these changes lead to long-term suppression of tumor proliferation and reduced potential for local recurrence. Radiation additionally modifies the tumor immune microenvironment by enhancing immune cell infiltration and antigen presentation, which may contribute to sustained antitumor effects. However, radiation-induced epithelial atypia and stromal changes can mimic residual or recurrent carcinoma, posing diagnostic challenges in post-treatment histopathological evaluation.

Conclusion and recommendations

Radiation therapy plays a crucial role in the management of invasive ductal carcinoma by targeting rapidly dividing malignant cells. It produces significant morphofunctional changes, including reduction in tumor cellularity, nuclear damage, decreased mitotic activity, stromal fibrosis, and vascular injury. These changes reflect effective destruction of cancer cells and suppression of further tumor growth. Evaluation of post-radiation tissue helps in assessing treatment response and planning further therapy. Extensive fibrosis with minimal residual tumor indicates a favorable response, whereas persistence of viable malignant cells is associated with increased risk of recurrence and poorer prognosis.

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